Functional Properties of Monkey Caudate Neurons

I. Activities Related to Saccadic Eye Movements

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SUMMARY AND CONCLUSIONS

1. We recorded single cell activities in the caudate nucleus of the monkeys trained to perform a series of visuomotor tasks. In the first part of this paper, we summarize the types and locations of neurons in the monkey caudate nucleus. In the second part, we report the characteristics of neurons related to saccadic eye movements.

2. Neurons were classified into two types in terms of spontaneous discharge pattern. A majority of the neurons (2,287/2,559, 89%) had very low-frequency discharges (mostly < 1 Hz). The rest (n = 272) showed irregular-tonic discharges (3–8 Hz) with broad spikes.

3. Of 2,559 neurons tested, 867 showed spike activity related to some aspects of the tasks; 502 neurons showed discharges in response to environmental changes outside, not in relation to, the tasks. None of the neurons responsive in or outside the tasks belonged to the irregular-tonic type.

4. The task-related activities were classified as: Saccade-related, Visual, Auditory, Cognitive, Fixation-related, and Reward-related. The activities detected outside the tasks were classified into: Visual, Auditory, Movement-related, Reward-related, and Other. Few neurons had both task-related and task-unrelated activities.

5. The locations of recorded neurons were determined using a coordinate system based on the anterior and posterior commissures. Task-related neurons were clustered longitudinally in the central part of the caudate. Neurons responsive outside the tasks were more widely distributed; specifically, auditory neurons were in the medial part, whereas movement-related neurons were in the lateral part. The irregular-tonic neurons were dispersed all over the caudate.

6. The monkey was trained to fixate on a spot of light on the screen and, when the spot moved, to follow it by making a saccade. A visually guided saccade occurred when the spot moved to another location without a time gap (saccade task). A memory-guided saccade occurred when the spot disappeared and reappeared after a time gap at a fixed location (saccade with gap task). By delivering a cue stimulus while the monkey was fixating, a memory-guided saccade was elicited to a randomly chosen location (delayed saccade task).

7. Among 306 neurons with saccade-related activities, 266 were further classified into 4 subtypes: neurons related preferentially to memory-guided saccade (SAC/MEM, n = 102); neurons related preferentially to visually guided saccades (SAC/VIS, n = 64), neurons related to both types of saccade (SAC/V&M, n = 80), and neurons showing tonic, preparatory activity increasing toward a saccade (SAC/PRP, n = 27).

8. The neurons related preferentially to memory-guided saccade also showed discharges before saccades that the monkey made to search for a spot of light. Only a small number of these neurons showed discharges with spontaneous saccades made in the darkness.

9. The neurons related preferentially to visually guided saccade could, in addition, show a visual response to the target.

10. Onsets of saccade-related activities preceded onsets of saccades by 0–300 ms in most cases. The memory-guided, saccade-related activity tended to start earlier than other activity types.

11. The saccade-related neurons had movement fields that were large and usually centered in the contralateral visual field. The centers of movement fields were distributed almost uniformly in the contralateral visual field, regardless of the activity types.

12. The results suggest that the caudate nucleus contains a part of the neural mechanism by which saccadic eye movement is initiated in the specific context of learned behaviors, either based on memory/anticipation or in response to visual information.

INTRODUCTION

The concept that the basal ganglia have motor roles originates largely from clinical observations. Motor disorder is a feature common to the diseases involving the basal ganglia (82). This view has been confirmed repeatedly by experimental studies (17, 56). However, the relation of the caudate nucleus to movement is far from clear. Arrest of ongoing movements is a typical effect of intracaudate electrical stimulation (16, 55). A movement elicited reliably is contralateral turning of the head (25, 54, 61), but this requires much higher currents than for movements evoked from the putamen, the other part of the striatum (1). Caudate neurons respond to behaviorally significant stimuli (9, 60), for example, a visual stimulus that acted as the cue for subsequent behaviors (73). Although caudate neurons may discharge with an overt behavior (60), it is unknown whether the activity is related to specific movements.

A breakthrough might be sought by investigating eye movements. Hikosaka and Wurtz (39–41) and Joseph and Boussaoud (46), in monkey and cat respectively, found saccade-related cell activities in the substantia nigra pars reticulata. These neurons showed tonic, high-frequency discharges during the resting period, but stopped discharging prior to a saccade. A striking feature of the nigra neurons was that their activity was selective for how the saccade was initiated. Discharge was unrelated to saccades that were made spontaneously in the dark. Furthermore, many of them were even selective for whether the saccade was made to a visual target or to the remembered location of a visual target (39, 40). These saccade-related nigra neurons were shown to project their axons to the intermediate layers of the superior colliculus, in which neurons burst before saccades (41). The mirror image-like relationship between the substantia nigra and the superior colliculus led Hikosaka and Wurtz to conclude that the substantia nigra exerts a tonic inhibition on the superior colliculus.
and removes the inhibition transiently to allow the colliculus neurons to fire; the substantia nigra would contribute to the initiation of a saccade by means of a disinhibition of the superior colliculus. This hypothesis was confirmed in a subsequent series of pharmacologic studies (42, 43) in which an agonist or antagonist of γ-aminobutyric acid (GABA) was injected in the superior colliculus or the substantia nigra. Those studies suggested that GABA is a neurotransmitter released by substantia nigra neurons.

The above results led to a question of how and from where the substantia nigra gets the saccadic information. Anatomic studies have shown that the striatum, especially the caudate nucleus, is a major origin for afferent connections to the substantia nigra (see Ref. 31 for review). In the present series of study, therefore, we investigated the functional properties of caudate neurons in monkeys trained to perform different kinds of behavior. We found that a large number of caudate neurons are, indeed, related to saccades made to a visual target or to a remembered target.

We have divided the results of our experiments into three parts, emphasizing different aspects of caudate function. In the present paper we summarize the types of neurons, illustrate their locations, and then describe the characteristics of saccade-related neurons. In the vicinity of the saccade-related neurons, we also found other types of neurons: those with visual or auditory responses, and those with more complex activities. In the second and third papers (36, 37) we will describe the sensory neurons and the cognitive neurons, respectively, and discuss how these activities might be integrated in the basal ganglia. A preliminary report appeared elsewhere (35).

METHODS

We studied single cell activities in the caudate nucleus of two alert behaving monkeys (Macaca fuscata). A total of four hemispheres were surveyed. The monkeys were trained to perform a series of behavioral paradigms.

Surgical procedures

Several devices were installed under general anesthesia (pentobarbital sodium) and aseptic conditions. These included head holder for restraint of the head during the experiments, stainless steel chambers for microelectrode recording (20), and an eye coil for measurement of eye position (47). The center of the chamber was aimed at a point in the caudate nucleus [23 mm anterior, 5 mm lateral, and 13 mm above the origin based on the atlas of Kusama and Mabuchi (52)]. Held by an electrode manipulator, the chamber was lowered to the surface of the exposed and trephined skull and was fixed with dental acrylic resin. The head holder was connected to the skull by implanted bolts and also was fixed with dental acrylic. For two hemispheres, the direction of the chamber was tilted laterally by 25–30°. For the other two hemispheres, the chamber was tilted in two planes: laterally by 25–30° and anteriorly by 20°.

Recording procedures

We recorded single cell activities from the head and body of the caudate nucleus using glass-coated platinum-iridium electrodes (83). The electrode was driven by a micromanipulator (Narishige, MO-95), with an X-Y coordinate, which was attached to the implanted chamber over the caudate nucleus. We surveyed the caudate as widely as possible in the area allowed for each chamber (19 mm id) to determine the locations of neurons related to the tasks. At the later stage of experiments, we implanted a guide tube (stainless steel tube, 1 mm od) for electrode penetration. The insertion of the guide tube was performed under ketamine hydrochloride anesthesia using the same micromanipulator. It was directed to the location in which task related cells were clustered and was fixed using acrylic resin. It could be removed and reinserted at different locations within the cylinder. The tip of the guide tube was 2–3 mm above the dorsal edge of the caudate nucleus. We introduced glass-coated platinum-iridium electrodes through the guide tube.

Eye movements were recorded using the magnetic search-coil technique (26, 70) (Enzanshi-Kogyo, MEL-2U) with the magnetic search coil implanted under the conjunctiva. At the first stage of the present study, we used electrooculogram for eye movement recording.

Behavioral tasks

Two monkeys were trained on a series of behavioral tasks, which are shown schematically in Fig. 1. They were trained first to fixate on a small spot of light on a tangent screen. During experiments, the monkey sat in a primate chair facing the tangent screen 57 cm in front of him. The basic paradigm was a fixation task (84). When the monkey depressed a lever on the chair, a small spot of red light (fixation point, F) came on at the center of the screen (hatched area on scheme line F). After a random period of time, this light spot dimmed, as indicated by depression of the hatched area. The monkey's task was to release his hand from the lever within a short period of time (0.5–0.6 s) to receive a drop of water (filled area at the end of line F). If he released the lever earlier or later, he received neither reward nor punishment. While the monkey fixated, another visual stimulus came on (hatched area) if monkey released his hand from lever within dim period. E, schematic eye position. See METHODS for detail.

FIG. 1. Behavioral paradigms. F, fixation point; a central spot of light that monkey must fixate to start a trial. T, target point; a similar spot of light that appeared as a final target at a selected position on screen. Hatched area: time during which spot of light came on. Depression at end of hatched area: dimming of spot, followed by delivery of reward (filled area) if monkey released his hand from lever within dim period. E, schematic eye position. See METHODS for detail.
area on line T), which could be used to study the characteristics of visual responses. In most cases, the stimulus was a spot of red light similar to the fixation point and was used as the target of a saccade in other tasks (see below), thus called "target point" for comparison. In the fixation task, the visual stimulus had little significance for subsequent behaviors. Successive trials were separated by an intertrial interval of 3-5 s by inactivating the lever.

The saccade task was designed to induce the monkey to make a saccade to a visual target. In most of the trials, the fixation point went off after a random period of time, and another spot of light (target point, T) came on at the same time. The target point dimmed for 0.5-0.6 s after a random period between 0.5 and 1.5 s. This task required the monkey to move his line of sight from the fixation point to the target point by making a saccade. The saccade with overlap task was the same as the saccade task except that the target came on before the fixation point went off. This task was designed to separate in time the visual response of a neuron from its saccade-related activity. In the saccade with gap task, a time interval (usually 0.6 s) was interposed between the offset of the fixation point and the onset of the target point. If the position of the target was fixed throughout a block of trials, the monkey made a saccade to the target position before the target actually appeared; the saccade was not guided by visual information but by the memory of a visual stimulus.

The delayed saccade task was designed to elicit such memory-guided saccades to random targets (40). Usually 0.7-1.0 s after the fixation point appeared, a spot of light (T) came on for a short period (0.1-0.3 s), indicating the location of the target that would appear later (target cue). The monkey was required to continue fixating for another 2-4 s while the fixation point (F) remained on; failure to do so terminated the trial. Unlike the other tasks, the durations of fixation point illumination and the time gap were fixed within a block of trials. After the fixation point went off, the monkey was free to move his eyes; in fact, he made a saccade to the location in which the target cue had been presented. He did so because the actual target point came on at the same location, usually 0.6 s after the disappearance of the fixation point. The target point dimmed after a random period between 0.5 and 1.5 s, and the monkey had to respond during the dimming period (0.5-0.6 s) to obtain the water reward. The location of the target was changed with the trials so that the monkey had to remember the location of the target cue each time to prepare for the saccade. As in the saccade with gap task, the saccade was guided by memory, but the memory was renewed for each trial. Each of the above tasks was done in a block of trials, and the task was changed without an explicit signal; the monkey would realize the change in a series of consecutive trials.

**Experimental procedure**

During the experimental sessions, the monkey sat in a primate chair with his head fixed and faced the tangent screen. The field coils of a magnetic search coil system were lowered over the chair, and these coils narrowed the unobstructed view of the tangent screen to the central 90° on the horizontal and vertical meridians. The fixation point and the target point were back-projected spots of light from light-emitting diodes (Toshiba, TLRA150-C) and had a diameter of 0.2°. The projection system consisted of LED light source, pinhole aperture on aluminum foil, and projector lens. Three LED projectors were used: the first one was for the fixation point, and its light was projected directly onto the screen. The second and third ones were for the target point and another irrelevant stimulus, and their lights were reflected via two galvano-mirrors that controlled the horizontal and vertical positions of the light spots. The positions of the target point were controlled by a computer or manually. The behavioral tasks, as well as storage and display of data, were controlled by an experimental system (MONK11) operated on a PDPl l/73 computer (29). The experimental room was dimly lit.

The session was divided into working and resting periods. The monkey was allowed to eat food pellets during the resting period. The meal break gave us, in addition, a chance to observe the characteristics of neurons related to behaviors outside the tasks. The appetite of the monkey was an important indicator of his physical condition; in case the monkey lost his regular appetite, we terminated the experiment and waited for his recovery. At the end of an experimental session, which lasted 4-7 h, the monkey was returned to his home cage. Body weight was checked each day, and supplemental water and fruit was provided as needed so that the monkeys kept their original weight.

**Data base**

We made 173 electrode penetrations into 4 hemispheres in 2 monkeys inside and around the caudate nucleus. In the first

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**TABLE 1. Classification of activities of caudate neurons**

<table>
<thead>
<tr>
<th>Cell Types</th>
<th>No. of Cells*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Task-related</td>
<td>867</td>
</tr>
<tr>
<td>Saccade-related</td>
<td>306</td>
</tr>
<tr>
<td>Visual</td>
<td>217</td>
</tr>
<tr>
<td>Auditory</td>
<td>21</td>
</tr>
<tr>
<td>Cognitive</td>
<td>315</td>
</tr>
<tr>
<td>Fixation-related</td>
<td>72</td>
</tr>
<tr>
<td>Reward-related</td>
<td>104</td>
</tr>
<tr>
<td>Responsive outside tasks</td>
<td>502</td>
</tr>
<tr>
<td>Visual</td>
<td>189</td>
</tr>
<tr>
<td>Auditory</td>
<td>86</td>
</tr>
<tr>
<td>Skeletal or mouth movement</td>
<td>35</td>
</tr>
<tr>
<td>Reward-related</td>
<td>65</td>
</tr>
<tr>
<td>Others</td>
<td>267</td>
</tr>
<tr>
<td>Unresponsive</td>
<td>1375</td>
</tr>
<tr>
<td>Irregular-tonic</td>
<td>272</td>
</tr>
<tr>
<td>Others</td>
<td>1104</td>
</tr>
<tr>
<td>All tested</td>
<td>2559</td>
</tr>
</tbody>
</table>

*Activity types are classified in 2 levels. *No. of cells that showed the response indicated; a cell could show different responses and thus could be numbered among >2 different types.
monkey, 77 penetrations were made on the left side, 17 of which were made through guide tubes at 4 different locations; 58 penetrations were made on the right side, of which 20 were made through guide tubes at 2 locations. In the second monkey, 30 and 8 penetrations were made on the right and left sides, respectively. Guide tubes were not used. During the last 2-3 penetrations on the right side of the first monkey, eye movements became irregular, and we terminated the experiments; otherwise, no significant changes were observed in the task performance.

Data analysis

Data on spike activity derived from single caudate neurons were stored as sets of rasters aligned on different task-related events. Because neural activity was often selective for the behavioral context in which a saccade was made or a sensory stimulus was presented, the following procedures were employed to compare neuronal activity between different conditions. First, we set two windows on the raster displays: one for the control period (background activity) and the other for the test period (e.g., discharges around saccades). We counted the number of spikes in each window for each trial. The magnitude of neuronal response was determined for each trial by subtracting the number of spikes within the control period from the number of spikes within the test period. Using Mann-Whitney's U test, we then examined whether the magnitudes of neuronal response were statistically different between two conditions.

Estimation of cell locations

One of the main objectives of the present study was to quantify objectively the locations of recorded neurons. For this purpose, we adopted the coordinate system proposed by Percheron (66) that is based on ventricular landmarks, instead of the coordinate system based on cranial landmarks (44). Several procedures were

![Fig. 3. Two types of caudate neurons and their discharge patterns. A: very low-frequency type. B: irregular-tonic type. A and B, upper: superimposed extracellular spike potentials of 2 representative neurons; lower: discharge pattern. Amplitude calibration, 100 µV, upward positive. Records were high-pass filtered at 300 Hz.]

![Fig. 4. Photomicrographs of 2 histological sections showing caudate nucleus, anterior (A) and posterior (B) to anterior commissure. Sections correspond to levels b and f indicated in Fig. 6. Arrowheads indicate positions of electrode penetrations. Calibration, 5 mm.]

![Fig. 5. Reconstruction of caudate nucleus (Cd) and putamen (Put) from histological sections. They are viewed from 3 different directions that are orthogonal to each other. Points along borders that appeared in same section are connected, except for Sagittal view. Radii of circles are proportional to distances in direction orthogonal to plane shown: the larger the circles, the more dorsal (in Horizontal view), lateral (Sagittal), and caudal (Frontal) are points. AC (open star) and PC (filled star): centers of anterior commissure and posterior commissure, respectively. Lines marked by X, Y, and Z indicate axes of coordinate system used to quantify cell locations. Ventral borders in Frontal view include ventral striatum or olfactory tubercle; in Sagittal view only borders of caudate nucleus are shown. Tail of caudate nucleus is only partially shown. See METHODS for detail.]
used to estimate the locations of neurons in the histologically identified caudate nucleus.

1) The first step was to determine three-dimensional coordinates of each neuron. The manipulator we used allowed us to determine the position of each neuron in an X-Y coordinate system (X, mediolateral direction; Y, anteroposterior direction). The length of the electrode protruding from the bottom of the manipulator was made constant before starting the penetration so that the depth reading of the manipulator provided the position in the Z axis. To transform this tentative coordinate system such that the anterior commissure assumed the origin, electrolytic marks were made at several points in the caudate with known three-dimensional coordinates (manipulator-based) that later served as intermediary landmarks for the coordinate transformation described as follows:

2) Mark cell-recording sites in the caudate nucleus. At the later stage of experiments, we made several electrolytic marks at sites of cell recording by passing currents through the recording electrode (10–20 μA, 20–30 s, electrode negative). The guide tube also served as a useful landmark, because it was introduced into the brain using the same manipulator with the same coordinate system. These landmarks were later identified in histological sections, and thus their locations relative to the anterior commissure appearing in other histological sections could be calculated. Based on the results, the coordinates of all recorded cells were recalculated such that they were now measured from the anterior commissure.

Because the chamber was tilted laterally in the frontal plane and in some cases anteriorly in the sagittal plane as well, we rotated the coordinate system such that the axes of the new coordinate system were parallel with those of the Horsley-Clarke system. It was then shifted such that the center of the anterior commissure was the origin.

FIG. 6. Locations of neurons recorded in 1 hemisphere of a monkey. Locations of neurons are projected onto a horizontal (top) and sagittal (bottom) planes. Profiles of caudate nucleus (Cd) and putamen (Put) are also indicated, which were derived from data shown in Fig. 4. Anterior is to the left. All: all neurons recorded; arrows denoted by a–f indicate representative histological sections shown in Fig. 7 and 21. Task-related: neurons that showed some activities while monkey was performing sensory-motor paradigms. Other Responsive: neurons that showed sensory or motor responses outside behavioral paradigms. Irregular-tonic: neurons that showed characteristic irregular, tonic discharge pattern. AC (open star): anterior commissure. PC (filled star): posterior commissure.

FIG. 7. Locations of task-related neurons (circles) and other recorded neurons (dots) plotted on representative histological sections. a–f: levels indicated in Fig. 6 (All); they are nearly frontal but tilted anteriorly. Bars: neurons with high-frequency discharges. Cd: caudate nucleus; Put: putamen; GPe: globus pallidus, external segment; GPi: globus pallidus, internal segment; AC: anterior commissure. Cross on each section indicates location of center of anterior commissure projected on this plane. Shaded area indicates lateral ventricle.
TABLE 2. Classification of saccade-related activities of caudate neurons

<table>
<thead>
<tr>
<th>Cell Types</th>
<th>No. of Cells</th>
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</thead>
<tbody>
<tr>
<td>Task-related</td>
<td>867</td>
</tr>
<tr>
<td>Saccade-related</td>
<td>306*</td>
</tr>
<tr>
<td>Visually contingent saccade</td>
<td>64</td>
</tr>
<tr>
<td>Memory-contingent saccade</td>
<td>102</td>
</tr>
<tr>
<td>Related to both</td>
<td>80</td>
</tr>
<tr>
<td>Preparation of saccade</td>
<td>27</td>
</tr>
</tbody>
</table>

The activity types are classified in 3 levels. SAC/VIS, visually contingent saccade; SAC/MEM, memory-contingent saccade; SAC/V&M, saccade related to both (visually and memory-contingent). SAC/PRP, preparation of saccade. Task-related, the number of all neurons that showed spike activity related to some aspects of the tasks (see Table 1). *Includes 40 neurons that were not further classified as one of the subtypes indicated below, so the sum of the subtypes is less than the total number of saccade-related cells.

Histological procedures were established as follows: after fixation the brain was cut into two hemispheres, dehydrated, and then embedded in celloidin. The dehydration caused a shrinkage of 15–20%. The shrinkage was determined for each brain by comparing the distances between landmarks on histological sections and those read from the manipulator at the time of experiments. Sections (thickness: 50-μm thickness) were stained with the Klüver-Barrera method. The distances between the electrolytic and guide tube-induced landmarks (n = 8) did not match precisely the distances expected from the coordinates read from the micromanipulator at the time of the experiments, even after compensating for shrinkage. We estimated the actual locations of the landmarks such that the square sum of the deviations from the coordinates read from the manipulator was minimized. The largest error remaining after this procedure was 0.3 mm, which should also be applied to the estimates of cell locations.

3) To determine the estimated cell locations with respect to the locations of the basal ganglia nuclei, we traced and digitized the borders of the caudate nucleus, the putamen, and other useful landmarks. This digitized data gave the profiles of the anatomic structures as seen from different perspectives (see Fig. 5). The XYZ coordinates of each neuron and those of the caudate boundaries, both based on the anterior commissure, allowed us to view the coordinates of neurons with a given activity type from different perspectives, especially in relation to the profile of the caudate nucleus (see Figs. 6 and 21).

To align serial histological sections, we inserted a tungsten needle into each hemisphere of the fixed brain parallel to the anteroposterior axis of the stereotaxic coordinate system (44). This holes appeared in each histological section with the same X (medialateral) and Z (dorsoventral) coordinates, allowing measurement of the X and Z coordinates of electrolytic and guide tube-induced landmarks. The distance along the Y (rostrocaudal) axis was calculated as the product of the thickness of the histological sections and the number of intervening sections. Note that the reduction in the size of the brain was taken into account to determine the coordinates.

RESULTS

Classification of caudate neurons

CLASSIFICATION OF TASK-RELATED NEURONS. Out of 2,559 neurons tested, 867 showed changes in spike discharges in relation to some aspects of the behavioral paradigms (Table 1). The neurons related to the behavioral tasks were further classified as: Saccade-related, Visual, Auditory, Cognitive, Fixation-related, and Reward-related. Each of these groups was composed of several subtypes, and their characteristics will be detailed in this and the following papers (36–37). It should be noted that single neurons could and frequently did have 1 different type of activities; hence, the sum of the numbers in subtypes exceeds the actual number of neurons. Therefore, what we classified was actually types of neural activities rather than types of neurons. How different types of activities were combined in single neurons will be described in the third paper (37).

We classified the task-related neurons and termed them as such in the hope of conveying our conclusions, based on a variety of experiments described in this and the following papers (36–37), as to what their functions might be. Some of these classifications are still speculative.

CLASSIFICATION OF NEURONS RESPONSIVE OUTSIDE THE TASKS. A total of 502 neurons were found to be active in relation to some sensory or motor events occurring outside the tasks (denoted as responsive outside tasks). Visual neurons include those that responded to complex shadows moving across the screen or to the appearance of the investigator’s face. Neurons related to eye movements might be included in this type, but none of them showed discharges specifically with saccades that were made outside the tasks. Auditory neurons include those that responded to the sound of punching the computer keyboard, a feeble stepping sound, or the sound of the laboratory door opening or shutting. A common feature in the visual and auditory

FIG. 8. Sample records of saccade-related caudate cell activity. Left: saccade task; saccades to a contralateral visual target (20° from center, 5° down). Center and right: delayed saccade task. Center: saccades to same but remembered target. Right: saccades to an ipsilateral remembered target (19° from center, 1° up). In this and subsequent figures F, fixation point; T, target point; H and V, horizontal and vertical eye positions; U, spike activities of a caudate neuron. Time scale: 100 ms for each division.
Contra Ipsi H* (20")

FIG. 10. Movement field of a caudate neuron. Number of spikes occurring with each saccade is expressed as the relative size of a circle and is plotted on vector coordinates of saccade. Actual record of a sample saccade (indicated by star) is shown on lower right; horizontal and vertical eye positions, and spike discharges. The saccades were made to remembered targets that were randomly chosen (delayed saccade task). Neuron's activity was selective for such memory-guided saccades.

responses was that the neurons were more responsive to stimuli that were likely to signify a following change in environment and, therefore, could be very slight in itself.

We noted an interesting class of neurons called irregular-tonic neurons (IT). They were distinct from other neurons in terms of their irregular, tonic discharge pattern and of their long-duration action potentials (see Fig. 3). They were all unresponsive both in and outside the tasks.

General characteristics and locations of caudate neurons

DISCHARGE PATTERN OF CAUDATE NEURONS. Discharge rates of caudate neurons were typically very low when the monkey just sat quietly performing no task, as shown in Fig. 2. Sixty-one percent of the neurons had spontaneous discharge rates < 1 spike/s. Task-related neurons were most likely to show such low-frequency discharges. There was a group of neurons whose discharge rates were ~3–8 spikes/s. They were distinct from other neurons in terms of discharge pattern. Figure 3 compares these two groups of neurons. Whereas the very low-frequency neurons showed spike discharges only sporadically, sometimes as a burst (Fig. 3A, bottom), the higher-frequency neurons showed discharges tonically but with irregular intervals (Fig. 3B, bottom) thus called irregular-tonic neurons. Being recorded extracellularly, the very low-frequency neurons showed initially positive spikes. The irregular-tonic neurons hardly changed their discharge pattern during or outside the task situations. They were found scattered all over the caudate nucleus (see Fig. 6).
RECONSTRUCTION OF THE CAUDATE NUCLEUS AND ITS NEURONS. Figure 4 shows typical features in rostral and caudal parts of the caudate nucleus. The sections are nearly frontal but tilted anteriorly by 20° so as to be parallel with electrode penetrations. The section in Fig. 4A is slightly anterior to the anterior commissure (see Fig. 5). The section in Fig. 4B is close to the caudal end of the surveyed part of the caudate nucleus.

The caudate nucleus reconstructed as described in METHODS (Fig. 5) confirmed the previously reported features (67). Its rostral portion fused with the putamen and the ventral striatum. Its rostrocaudal axis was slightly tilted such that, more caudally, it became deviated laterally and dorsally. It is impractical to separate the caudate nucleus into head and body. The last point further strengthened the necessity to have an objective coordinate system to indicate the locations of neurons studied physiologically.

LOCATIONS OF TASK-RELATED NEURONS. Figure 6, top left, shows the locations of all neurons recorded from a single caudate nucleus; separately shown are neurons that showed a change in activity in the behavioral paradigms (Fig. 6, top right), those that changed their activity outside the tasks (Fig. 6, bottom left), and the irregular-tonic type neurons (Fig. 6, bottom right). A large area in the caudate nucleus was surveyed, its rostral and caudal ends being excluded. Figure 6, top left, may give the impression that the central region was overly sampled. This was partly because our electrode penetrations were biased toward this region in which task-related neurons were clustered (Fig. 6, top right). It should also be noted, however, that the central region shares a dominant volume of the nucleus so that penetrations into the region were more probable.

A typical electrode penetration went as follows. After passing through the white matter overlying the caudate nucleus in which unitary activity was seldom recorded, the entrance of the electrode into the caudate was signified by the appearance of low-frequency firing units.

Task-related neurons were found in a relatively restricted area in the caudate forming a longitudinal zone (Fig. 6, top right). The task-related zone was most sharply demarcated at its dorsal border because the dorsalmost part of the caudate nucleus was nearly devoid of this class of neurons. The ventral border of the task-related zone was less clear, because many electrode penetrations had to be terminated before passing through the task-related zone (Fig. 6, top left).

Neurons responsive outside the tasks were more widely scattered, quite numerous in the dorsal and medial parts as well (Fig. 6, bottom left). We encountered the irregular-tonic, unresponsive neurons (IT) (see Fig. 3) in almost every electrode penetration (Fig. 6, bottom right). They were dispersed in the caudate nucleus without obvious localization or clustering. Their proportion to all cells recorded was similar in different hemispheres and in different monkeys (9.3–13.3%). We might have overestimated this proportion because this type of neuron was readily detected by its spontaneous discharges.

Figure 7 shows the locations of task-related neurons projected onto representative histological sections whose levels are indicated in Fig. 6. The task-related neurons were clustered in the central zone, especially at more caudal levels.

How tightly they were packed was appreciated at the time of experiments: once a task-related neuron was encountered while the electrode was advanced, subsequent 5–10 neurons were almost invariably related to the tasks, albeit in different ways. The clustering became looser in more rostral levels.

In the region that bridges the caudate nucleus and the putamen, we found neurons similarly related to the tasks; they are, therefore, included in this report. Some neurons were judged to be outside the caudate nucleus and were, therefore, excluded from the sample: they were in either the cingulate cortex, the dorsal part of the putamen and the globus pallidus, the septum, the anterior nuclei and the reticular nucleus of the thalamus, or the white matter ventral to the caudate in which neurons were scattered. Many of them showed moderate to high background discharges (indicated by bars), quite unlike caudate neurons.

Characteristics of saccade-related neurons

CLASSIFICATION OF SACCADE-RELATED ACTIVITIES. We classified saccade-related neurons into four types: 1) activ-

![Saccade-related neuron activity](https://via.placeholder.com/150)

FIG. 11. Caudate cell activity related to searching saccades. In this delayed saccade task, time interval between fixation point (F) and target point (T) was lengthened so that monkey kept searching for target by making saccades back and forth. Neuron showed spike discharges with each of such searching saccades if they were directed to contralateral side. Initial part of task scheme is compressed just to indicate sequence of events. Same neuron as shown in Fig. 8.
Activity related preferentially to saccade to remembered target or memory-guided saccade (denoted as SAC/MEM). 2) Activity related preferentially to saccade to visual target or visually guided saccade (denoted as SAC/VIS). 3) Activity related equally to memory-guided saccade and to visually guided saccade (denoted as SAC/V&M), and 4) Activity gradually building up toward the onset of a saccade as if preparing for the saccade (SAC/PRP). The numbers of neurons in these groups are summarized in Table 2.

**Activity Related to Memory-Guided Saccade.** A total of 102 neurons (33% of all saccade-related neurons) showed the activity related preferentially to memory-guided saccades; this was the most common type.

Figure 8 shows an example of activity related to memory-guided saccades. In the saccade task (Fig. 8, left), this neuron showed almost no spike discharges in relation to saccades to a visual target that was located in the contralateral visual field (20° contralateral, 5° down); no greater activity was seen by changing the target position. When the monkey made a saccade to the remembered position of the same target (Fig. 8, center, delayed saccade task), the same neuron showed discharges that were time-locked to the saccade and started ~200 ms before its onset. However, saccades to a remembered target in the ipsilateral visual field (Fig. 8, right) were not accompanied by spike discharges. In summary, the cell’s activity was related preferentially to memory-guided saccades that were directed to the contralateral side. Memory-guided saccades were hypometric and slower than visually guided saccades, as previously shown (43). However, there were two reasons why this fact could not account for the marked selectivity of the cell’s activity. First, smaller visually guided saccades were

![Image](https://via.placeholder.com/150)

**Figure 12.** Unusual relation to spontaneous saccades. A and B: task-related saccades, to a visual target and to a remembered target, respectively. C and D: spontaneous saccades in dim and totally dark conditions, respectively. In each condition, contralateral (nearly horizontal) saccades were detected and spike activity of a caudate neuron was aligned on their onsets. Spike frequency calibration: 50 spikes·s⁻¹·trial⁻¹ (this applies to subsequent figures).
not associated with any spike discharges. Second, the cell's activity was weaker when a memory-guided saccade was slower.

Memory-guided saccade activity of another neuron is illustrated in Fig. 9 using raster and histogram display. In the saccade task (Fig. 9, top), when the monkey made saccades to a visual target (T) that came on as the fixation point (F) went off, the neuron showed little activity, except for the first trial in which the monkey made a saccade in an anticipatory manner before the target appeared. In the saccade with overlap task (Fig. 9, center), the monkey made saccades to the same visual target that had stayed on; no spike activity occurred. In the delayed saccade task (Fig. 9, bottom), however, the neuron started discharging toward the end of the fixation period and further increased its discharge rate ~200 ms before the saccade onset. The magnitude of saccade-related activity (test window of 700 ms duration starting 300 ms before saccade onset) was significantly greater in the delayed saccade task than in the other two tasks ($P < 0.001$; Mann-Whitney's U test).

Saccade-related activities were selective for contralateral saccades. Caudate neurons showed spike discharges with saccades that brought the direction of the gaze into a restricted region of the visual field [movement field, Wurtz and Goldberg (86)]. The numbers of spikes occurring with saccades are illustrated in Fig. 10 as circles with diameters proportional to the spike numbers on the plane showing the vectors of the saccades. The caudate neuron of Fig. 10, which was selective for memory-guided saccades, showed activity only when the saccades ended in an area >5° away in the contralateral and slightly downward direction.

If the gap period before target appearance was lengthened, the monkey sometimes made a series of saccades switching back and forth as if expecting and waiting for the target to appear. When this occurred (Fig. 11), the neuron showed clear discharges before each of such searching saccades directed to the contralateral side. Thus the activity of the neuron was temporally correlated with the saccade perse and not with any change in sensory environments. In the second and third trials in Fig. 11, some discharges preceded ipsilateral saccades, but they were incorrectly directed. Among 64 saccade-related neurons examined with the long-gap task, 39 showed activity preceding searching saccades; all of these belonged to the type classified as preferentially related to memory-guided saccades.

After testing a cell's activity using the behavioral paradigms, the investigator gave the monkey food pellets or presented various objects that attracted attention and elicited eye movements. This type of caudate neuron usually showed no activity during such procedures. We found, however, four neurons that showed discharges with such spontaneous saccades. For the case illustrated in Fig. 12, the discharge was related to large, contralateral saccades, and the records were taken while the experimental room was dimly lit (Fig. 12C) or in total darkness (Fig. 12D). The spike activity usually followed the onset of the saccade in dim light, but sometimes preceded it in darkness. However, the activity was less clear than seen with task-related saccades (Fig. 12, A and B), especially those made to remembered targets (Fig. 12B). The spike activity associated with either one of the task-related saccades was significantly greater than the spike activity with spontaneous saccades ($P < 0.01$; 400-ms test window starting 200 ms before saccade onset).

**FIG. 13.** A caudate neuron preferentially related to visually guided saccade. Left: ordinary saccade task. Center: saccade with overlap task. Right: delayed saccade task. Neuron also showed a visual response to target. A vertical bar on raster line indicates offset of fixation point. Trials are realigned in an increasing order of saccade latency. Cell activity is aligned on onsets of saccades, but its initial part is aligned on task-related events as indicated by interruption on time scale. The target was 7° contralateral and 4° up.
dependent on the presence of a visual target; the neuron showed no activity with saccades to the position of the same but remembered target (Fig. 13, right). The magnitude of saccadic responses was significantly greater in the saccade task (Fig. 13, left) or in the saccade with overlap task (Fig. 13, center) than in the delayed saccade task (Fig. 13, right) \((P < 0.001)\). As shown in Fig. 13, neurons with activity related to visually guided saccades frequently showed, in addition, a response to the visual stimulus that was used as the target of the saccade \((18/64; \text{see also Table 5 in the third paper, Ref. 37})\). The visual and saccade-related activities of a given caudate neuron had similar visual fields, be it sensory or motor.

None of this type of neuron showed consistent activity in relation to spontaneous saccade in darkness, even if the monkey was intently searching for a visual target. This contrasts with neurons with discharge related to memory-guided saccades (see Fig. 12).

![SAC/MEM and SAC/VIS Activity](image)

**FIG. 14.** Activity of 4 caudate neurons aligned on memory-guided saccade (SAC/MEM) and visually guided saccade (SAC/VIS). Top 2 neurons were judged to be preferentially related to SAC/MEM; 3rd was equally related to SAC/MEM and SAC/VIS; bottom was preferentially related to SAC/VIS.

![Latency to Saccade Onset](image)

**FIG. 15.** Onset of caudate cell activity relative to saccade onset. Activities preceding saccade onset are plotted to the left (minus); those following, to the right (plus). SAC/VIS, visually guided saccade activity, revealed in saccade task or in saccade with overlap task: \(-49 \pm 75 \text{ (SD) ms, } -30 \text{ ms (median)}\). SAC/MEM, memory-guided saccade activity, revealed in saccade with gap task or in delayed saccade task: \(-106 \pm 127 \text{ ms, } -105 \text{ ms (median)}\). SAC/V&M, those related to both, their latencies being represented by earlier of 2 components, \(-65 \pm 94 \text{ ms, } -57 \text{ ms (median)}\).

**TIME COURSE OF SACCADe-RELATED ACTIVITY.** It became clear that caudate neurons were related differentially to memory-guided saccades and visually guided saccades, as summarized in Fig. 14. Discharge of the top two neurons was related preferentially to memory-guided saccades; for the third it was related almost equally to the two types of saccade, and Fig. 14, bottom, shows a neuron related preferentially to visually guided saccades.

Figure 15 shows the distribution of the onsets of saccade-related activities excluding the saccade-preparatory component. The activity onset was defined as an upward
SACCade-related activity in caudate

deflection in cumulative spike time histogram (not shown)
that was aligned on the onsets of saccades. Memory-guided
saccade activities (SAC/MEM) tended to start earlier,
whereas most of the visually guided saccade activities
(SAC/VIS) started slightly before the saccade onset and
peaked after it. Combined saccade activities (SAC/V&M)
had onset times that appear to be intermediate between the
above two. The mean onset of SAC/MEM was significantly
earlier than the onsets of SAC/VIS and SAC/V&M ($P <
0.05$; Mann-Whitney $U$ test).

Summary of movement fields of saccade-related
neurons. Figure 16, bottom, summarizes approximate
borders (hand-drawn at time of experiment) of movement
fields for different types of saccade-related neuron. Most of
them were located in the contralateral field, but some ex-
tending into the ipsilateral field. In Fig. 16, top, we plotted
the movement field centers of all saccade-related neurons
recorded. They were scattered almost evenly in the contra-
lateral visual field; a small number of neurons had ipsilat-
eral movement field centers. Eccentricities of movement field centers
(mean ± SD, deg): 19 ± 8 for SAC/MEM, 21 ± 10 for SAC/VIS, and 25 ± 10 for SAC/V&M. Different neurons could have same movement field centers (e.g., circle with dot). Bottom: examples of movement field borders.

FIG. 16. Summary of movement fields. Top: SAC/MEM (circles), dis-
tribution of movement field centers (optimal saccade vectors) of neurons
preferentially related to memory-contingent saccade; SAC/VIS (crosses),
those related to visually guided saccade; and SAC/V&M (dots), those
equally related to both saccades. Eccentricities of movement field centers
(mean ± SD, deg): 19 ± 8 for SAC/MEM, 21 ± 10 for SAC/VIS, and 25 ±
10 for SAC/V&M. Different neurons could have same movement field
centers (e.g., circle with dot). Bottom: examples of movement field
borders.

FIG. 17. Caudate cell activity related to saccade preparation (2 exam-
iples) revealed in delayed saccade task. Vertical bar on raster line indicates
onset of saccade. E: schematic eye position. Trials are realigned in an
creasing order of saccade latency. Duration of fixation point was fixed
within block trials.

Otherwise, no significant difference was noted between
different types of saccade-related activity.
ACTIVITY RELATED TO PREPARATION OF SACCADES.

Twenty-seven neurons showed sustained activity that began after target cue presentation and ended with a saccade to the remembered target. Two examples are shown in Fig. 17: a neuron showing a prelude of tonic discharges followed by a burst of spikes just before a saccade (top), and another neuron showing a monotonically increasing activity until a saccade (bottom). The end of the neural activity shown in Fig. 17, top, was time-locked to the onset of saccade, suggesting that the activity was related to the saccade rather than any other external event. The activity shown in Fig. 17, bottom, was less well time-locked to the saccade onset, but the saccade latency tended to be longer if the spike discharges started later in the fixation period.

The activity related to saccade preparation was usually selective for the direction and amplitude of an impending saccade (Fig. 18). In contrast to an increasing activity before a contralateral saccade (Fig. 18, right), the neuron showed no discharges before an ipsilateral saccade (Fig. 18, left); its activity might even be suppressed. If the monkey made an incorrect saccade to the opposite direction, the neuron’s activity followed the forthcoming saccade, not the...
TABLE 3. Locations of saccade-related caudate neurons relative to the anterior commissure

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>X (Lateral), µm</th>
<th>Y (Anterior), µm</th>
<th>Z (Dorsal), µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAC/VIS</td>
<td>17</td>
<td>5366 ± 1274</td>
<td>-1313 ± 2678</td>
<td>8679 ± 1914</td>
</tr>
<tr>
<td>SAC/MEM</td>
<td>44</td>
<td>5440 ± 1074</td>
<td>1 ± 2266</td>
<td>8087 ± 1267</td>
</tr>
<tr>
<td>SAC/V&amp;M</td>
<td>39</td>
<td>5196 ± 848</td>
<td>-363 ± 2086</td>
<td>9200 ± 1342</td>
</tr>
<tr>
<td>SAC/PRP</td>
<td>16</td>
<td>5871 ± 1424</td>
<td>862 ± 2608</td>
<td>8334 ± 1398</td>
</tr>
<tr>
<td>All SAC</td>
<td>138</td>
<td>5322 ± 1097</td>
<td>-104 ± 2390</td>
<td>8799 ± 1403</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD. Positive numbers indicate lateral, anterior, and dorsal directions; negative ones the opposite directions. Data were taken from 1 hemisphere of a monkey (see Results). n, no. of neurons. See Table 2 for abbreviations of activity types.

There remained the possibility that the activity might reflect anticipation of fixation point offset. However, this seems unlikely; the neuron shown in Fig. 19, which discharged before memory-guided saccades (Fig. 19, left) showed only occasional discharges in the saccade task in which the target position was not given beforehand (Fig. 19, right).

LOCATIONS OF SACCade-RELATED NEURONS. Figure 20 illustrates the locations of saccade-related neurons viewed from two different directions. They were clustered in a central, longitudinal core region of the caudate nucleus. The distribution was similar to that of all task-related cells (Fig. 6). The distributions of different types of saccade-related neurons are shown in Fig. 21. The tendency to cluster was especially pronounced in more caudal levels; it may be appreciated by the number of cells contained in each plane.

The different types of saccade-related neurons largely overlapped. Figure 21 may suggest, however, that the neurons related to memory-guided saccade (SAC/MEM) and those related to saccade preparation (SAC/PRP) tended to be more anterior than visually guided saccade-

FIG. 20. Locations of all caudate neurons showing saccade-related activities. Data were obtained in 1 hemisphere of a monkey and projected onto a horizontal (top) and sagittal (bottom) planes. Profile of caudate nucleus is also indicated, which is derived from data shown in Fig. 5. Anterior is to left. AC (open star), anterior commissure; PC (filled star), posterior commissure. Area between two hatched lines indicate region of caudate nucleus that was surveyed for unit recording (see Fig. 6).

FIG. 21. Locations of neurons showing different types of saccade-related activities, plotted on representative histological sections. a-f correspond to levels indicated in Figs. 6 (All) and 7. The leftmost column (All Saccade) shows locations of all neurons showing saccade-related activities; number following n indicates number of cells contained in each plane. On the right four columns are shown locations of neurons showing different types of saccade-related activities; number of cells in each plane is also indicated in parentheses. All caudate contains neurons that were not identified as either one of subtypes, and therefore its number is greater than sum of subtypes.
related neurons (SAC/VIS) and that the neurons related to saccade preparation were distributed more laterally. As shown in Table 3, the SAC/MEM and SAC/PRP neurons were found, on the average, anterior to the anterior commissure, whereas the SAC/VIS and SAC/V&M neurons were posterior to it. However, the differences in mean Y-position were not statistically significant except for the comparison between SAC/PRP and SAC/VIS ($P < 0.05$; Student's $t$ test).

**DISCUSSION**

**General pattern of caudate cell activity**

Background discharge rates of caudate neurons were generally very low, as has been shown in previous studies (57, 59). This also is common to neurons in the putamen (1, 49), which is another area constituting the neostriatum. We noticed two types of cells in the caudate: one showing very low spontaneous discharge rates and the other showing irregular tonic discharges usually with broad spikes. The majority of caudate neurons were of the first type. A similar differentiation of neural activities has been noted in the putamen (1, 49). Anatomic studies have shown that medium-sized cells with spiny dendrites constitute the majority of caudate neurons (19, 48, 50) and send axons to the globus pallidus or the substantia nigra (4). A smaller number of neurons are considered to be interneurons, notably those cholinergic (5, 68) or somatostatinergic (12, 28). The very low-frequency neurons might correspond to such output cells, whereas the irregular- tonic neurons might correspond to one of the interneurons.

**Longitudinal organization of caudate neurons**

Two salient features were apparent in the spatial distribution of caudate neurons: 1) task-related neurons were clustered in a longitudinal zone extending from the head of the caudate to its body, and 2) different types of task-related neurons were, by and large, intermingled. The first feature would be predicted by the anatomic data by Selemon and Goldman-Rakic (78), which showed that cortical areas project to longitudinal territories in the striatum with restricted mediolateral domains. Our task-related neurons were located centrally and in the zone expected to be in the substantia nigra and the caudate, saccade-related activities are selective for how the saccade is initiated. The memory-contingent saccade activity was more common than the visually contingent saccade activity. In both structures, the memory-contingent saccade activity tended to start earlier with respect to the saccade onset than did the visually contingent saccade activity. Onset latencies of saccade-related activities have similar distributions in both structures [compare with Fig. 11 in Hikosaka and Wurtz (40)]. Similarities were also found in the movement fields of caudate and nigra neurons: most of them were large but centered in the contralateral hemifield with response magnitudes tapering off toward their borders that may extend into the ipsilateral field. A small number of caudate neurons, however, had ipsilateral fields, which was rare in the substantia nigra. Nevertheless, the sum of the movement fields of neurons in both the substantia nigra and the caudate covers the contralateral field. There is no particular preference of direction or eccentricity. These similarities suggest that the caudate could contribute to the saccade-related activities in the substantia nigra. If so, the caudate-nigral connection would be inhibitory, because caudate neurons increase whereas nigra neurons decrease their activity with saccades.

This idea of functional coupling is supported by anatomic and electrophysiological studies. Well-known dopaminergic projections are directed from the substantia nigra to the stratum (for review, see Ref. 10), but they originated entirely from the pars compacta that shows no obvious saccade-related activities. Massive fiber connections are present from the caudate to the pars reticulata of the substantia nigra (21, 32, 63); the opposite connection must be feeble, if any (33). That the caudate-nigral connection is inhibitory is supported by electrophysiological studies (22, 87). The inhibition is thought to be mediated by GABA (18, 23, 24, 34, 62, 69). Chavalier et al. (13) showed that chemical activation of rat caudate neurons resulted in striking suppression of substantia nigra cell discharges. In addition, we have preliminary data showing that electrical stimulation of the task-related area in the caudate nucleus produced a clear inhibition in substantia nigra cell activity.

**Behavioral contingency of saccade-related activity in the caudate**

Spontaneous saccades made without a particular target were rarely accompanied by caudate cell activity. These neurons would fire before saccades only when the monkey was engaged in the learned visuooculomotor paradigms. The saccade was part of a sequence of behaviors leading to a reward, and therefore, was purposeful in anticipating its final goal, not only its immediate target. This suggests a role for the caudate nucleus in a learned sequence of behavior. Individual caudate neurons, however, were related to the contexts of the learned tasks in a selective manner. The most prevalent group of neurons were related preferentially to the saccade to a remembered or predicted location of a visual target, thus termed memory-contingent saccade activity; they remained least active if a saccade was made to a real visual target. A second group of neurons showed the inverse relation: they were active only with a saccade to a visual target, not to a remembered one. This observation implies that the brain contains separate mechanisms underlying two types of learned behavior: one including a
visually guided saccade and the other including a memory-
guided saccade, and the caudate nucleus is involved in both
of the mechanisms.

**Origin of saccade-related activities in caudate**

The caudate nucleus is known to receive afferents from
the association cortices (78) including the frontal eye fields
(51, 81). The saccade-related activities in the caudate may
originate in some of the cortical areas. The cortical area
most extensively studied in relation to saccades is the fron-
tal eye fields. Robinson and Fuchs (71) showed that mi-
crostimulation in the frontal eye fields produced a contra-
versive saccade whose amplitude and direction were solely
dependent on the location of the stimulation site. Bruce
and Goldberg (7) described the discharge of neurons in the
frontal eye fields before intentional saccades. These
neurons were maximally active before such a saccade that
would be elicited by microstimulation at the recording site
(8). Their activities are in many ways similar to those of
caudate neurons. Neurons in both structures are related
only occasionally and weakly to spontaneous saccades.
Some of them are related preferentially to visually guided
saccades as opposed to memory-guided (learned) saccades
and, in addition, show visual response to the saccade target.
They have fairly large, contralateral movement fields. A
notable difference is present between the frontal eye fields
and the caudate, however: few neurons have been found in
the frontal eye fields that are related preferentially to mem-
ory-guided saccades.

Another candidate for the source of caudate saccade-re-
lated activity is the supplementary eye field described by
Schlag and Schlag-Rey (75), which is located just rostral to
the supplementary motor area. Microstimulation in this
area evokes contraversive saccades that may or may not be
goal-directed, unlike the ones evoked from the frontal eye
fields. Many of the neurons recorded in this area showed
spike discharges before self-initiated saccades, the onset of
the discharge leading the saccades by >300 ms. The experi-
mental situation of Schlag and Schlag-Rey was similar to
one of our experiments using the delayed saccade task with
a long time gap (Fig. 11); it looked as though the target
disappeared and after the long time gap reappeared at the
previously indicated location, and the monkey sometimes
made saccades apparently searching for the target to ap-
pear. Caudate neurons, as well as supplementary eye field
neurons, show vigorous discharges before such searching
saccades.

The contribution of parietal cortex is less obvious. Elec-
trical stimulation in this area elicits saccades, although they
are suppressed easily by visual fixation (79). Some neurons
in area 7 are active before visually guided saccades (58).
Robinson et al. (72), however, indicated that their activities
were visual responses that were enhanced by the saccade to
the target or by merely directing attention to the target.
Andersen et al. (2) showed that a number of area 7 neurons
did exhibit activity time-locked to a saccade, but its onset
mostly followed the saccade onset. Therefore, a simple
relay of information from the parietal cortex to the caudate
would not yield the saccade-related activities that we have
shown.

As illustrated in Fig. 21, saccade-related neurons were clus-
tered in the caudate forming a longitudinal, central
core region of the nucleus. This region appeared to corre-
spond to the area that is heavily innervated by the frontal
eye field (51, 81) and more diffusely by the supplementary
eye field (78). Therefore, the two eye fields are likely to be
the source of saccade-related activities in the caudate nu-
cleus.

The thalamus may be another source of the saccade-re-
lated activity. Schlag and Schlag-Rey have demonstrated
that the intralaminar part of the thalamus in the cat (74,
76) and the monkey (77) contains many neurons that dis-
charge or pause before saccades to visual targets or before
spontaneous, searching saccades. This part of the thalamus
is a well-known source of afferents to the caudate (for re-
view, see Ref. 64). However, the detailed topography of the
afferents is less clear compared with that of cortical affer-
ents and awaits further studies.

**Activity related to preparation of saccade**

This type of activity started after the target cue (in many
cases only after the contralateral one) gradually built up
during the delay period and ceased abruptly with the sac-
cades. In some neurons, the activity further increased just
before the saccade, whereas in the others it simply ended
with or some time before the saccade. The activity was
unrelated to visual fixation or suppression of saccades. This
type of activity anticipated the occurrence of a saccade to a
remembered target.

The prefrontal cortex, especially the area around the
principal sulcus, is thought to be involved in behaviors that
require short-term memory, especially spatial ones. The
delayed response task or delayed alternation task is widely
used to test such memory-dependent behaviors, and the
monkey's performance in these tasks is disrupted by lesions
of the principal sulcus area (for review, see Ref. 27) as well
as lesions of the caudate nuclei (3, 30). The delayed saccade
task may be regarded as the eye movement version of the
delayed response task. Indeed, Joseph and Barone (45) re-
cently found in the area dorsal to the principal sulcus the
neurons that became tonically active before a delayed,
memory-guided saccade.

**Saccadic eye movement disorders in basal ganglia
dysfunction**

A number of studies have shown that saccadic eye move-
ment is disordered in basal ganglia diseases (for review, see
Ref. 43). Huntington's disease is characterized by a marked
cell loss in the caudate nucleus, and Lasker et al. (53) have
shown that the patients had greater difficulty in making
saccades on command to the remembered location of a
visual target or to a continuously visible target than to the
sudden appearance of a visual target. In early stages of
Parkinson's disease, the deficit in saccades appeared rela-
tively slight if they are tested using simple steps of visual
targets similar to the saccade task we used. The deficits
become more pronounced in other types of saccade. The
patients had more difficulty in making saccades between
two continuously lit targets (15). While tracking target
steps with simple and known sequences, the patients, unlike normal controls, did not make saccades before the target steps in a predictive way (6). In patients with hemi-parkinsonism the velocities of saccades to remembered targets were abnormally slow to the affected side (11). Parkinsonian patients did make anticipatory saccades before a target actually appeared, but they were abnormally slow and hypometric, whereas visually guided saccades were affected only slightly (38). The above findings suggest that deficits in saccades in patients of basal ganglia diseases were more evident if the saccades were made intentionally without being triggered by sensory inputs.

Such conditional nature of eye movement deficits seems relevant to the caudate cell activities, most of which are selective for behavioral contexts. Of particular interest are the neurons that are active only with memory-guided saccades. The basal ganglia might be an important channel through which short-term memory-related information gains access to the superior colliculus, the neural mechanism for saccade initiation.

Oculomotor function of the basal ganglia

The present study, together with the previous ones (39-43), strongly suggests that disinhibition is the way in which the basal ganglia contribute to the initiation of a saccade. A similar scheme has been proposed using different approaches to basal ganglia function (13, 65). The basal ganglia saccade system would be composed of two serial inhibitions: 1) caudate-nigral inhibition that is only phasically active, and 2) nigro-cortical inhibition that is tonically active. If caudate neurons fire, the nigro-cortical inhibition would be removed transiently. The resultant disinhibition, presumably together with other excitatory inputs (notably those from the frontal eye fields), would produce a burst of spikes in superior colliculus neurons. This signal would be transmitted to the midbrain or pontomedullary reticular formation and would be used to generate a saccade to the contralateral side (80).

The superior colliculus is the site at which various signals converge to facilitate the generation of saccade (85). The input from the basal ganglia (substantia nigra) is unique in that it is inhibitory. It would prevent the colliculus neurons from firing uncontrollably under the influence of multiple excitatory inputs; indeed, the loss of the tonic inhibition leads to irresistible saccades (42, 43). A phasic removal of the tonic inhibition (disinhibition) would allow other excitatory inputs to trigger a burst activity in superior colliculus neurons leading to a saccade. It would act as a gate for movement initiation.

The present study on the caudate and the previous study on the substantia nigra (40) both suggested that the signals conveyed by basal ganglia neurons were relatively more dependent on stored information or memory rather than direct sensory information. If this is the case, what happens in the superior colliculus would be the gating of sensory-oriented information by memory-oriented information, and the two types of information would act in a cooperative manner.

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