

Behavioral correlates of activity in basal ganglia neurons

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Changes of neuronal discharge in the striatum, globus pallidus and substantia nigra pars reticulata (SNr) precede movement in certain behavioral situations but not in others. A given SNr neuron may pause in advance of a saccade to a remembered target but not in relation to the same saccade directed to a target that is present. A click or a visual stimulus may evoke a response in SNr, globus pallidus, or striatum when the stimulus is behaviorally significant but not when the same stimulus is delivered without such significance. On the basis of these and other observations it is suggested that the 'internal' initiation of movement in the absence of sensory guidance may be a unique contribution of a system that includes the basal ganglia. In light of the close anatomical connections between frontal cortex and basal ganglia, such a system may include the frontal cortex.

Similar perceptual disorders in humans may result from prefrontal lesions¹ and basal ganglia pathology². Furthermore, prefrontal and caudate nucleus lesions are alike in causing delayed-response deficits in monkeys³. These similarities led Teuber⁴ to propose an interdependence of the frontal lobes and basal ganglia, and, in the years that have followed Teuber's proposal, a number of different research approaches have provided support for his thesis. Thus, anatomical studies have shown that the outputs from the basal ganglia are directed to areas of the frontal lobe lying outside the primary motor cortex (see Wise and Strick, this issue). Since basal ganglia also receive prominent inputs from virtually all cortical areas, as well as from the frontal cortex, they provide a route whereby the cerebral cortex as a whole may communicate with the frontal lobe.

Evidence for functional interdependence between the frontal lobe and basal ganglia has also been provided by studies showing certain similarities in the behavioral correlates of neuronal discharges in basal ganglia and several areas of the frontal cortex. Two articles in this issue (Bruce and Goldberg on the frontal eye field, and Wise and Strick on non-primary motor cortex) will consider movement-related neuronal activity in the frontal lobe and its dependence on motor set, or the context in which movement occurs, rather than merely on the movement *per se*. Like the frontal lobe neurons, with which they are anatomically linked, basal ganglia neurons are also dependent on the context in which move-

ment occurs.

The present article will review results showing how sensory responses and movement-linked discharges of basal ganglia neurons are related to the context in which inputs and outputs occur, and we will argue that the basal ganglia are preferentially involved in

generation of movements initiated on the basis mnemonic traces that may depend on the frontal lobes.

DeLong *et al.*⁵ have proposed a heuristic scheme of basal ganglia organization with a 'complex' loop including frontal association cortex and caudate nucleus, and a 'motor' loop that includes sensorimotor cortex and putamen (Fig. 1). For the purposes of our discussion, two points in this schematic organization should be emphasized. First, in addition to inputs from the frontal association cortex via caudate, there are inputs to the basal ganglia from primary sensorimotor cortex via putamen. Second, the diagram emphasizes that the basal ganglia have two major outputs: the globus pallidus internal segment (GPi) and the substantia nigra pars reticulata (SNr). The targets of both outputs are thalamic areas although the SNr has in addition a prominent projection to the superior colliculus. We will begin by considering the behavioral relations of cells in the SNr and caudate nucleus.

Substantia nigra, caudate and contingent neural responses

A role for basal ganglia in control of

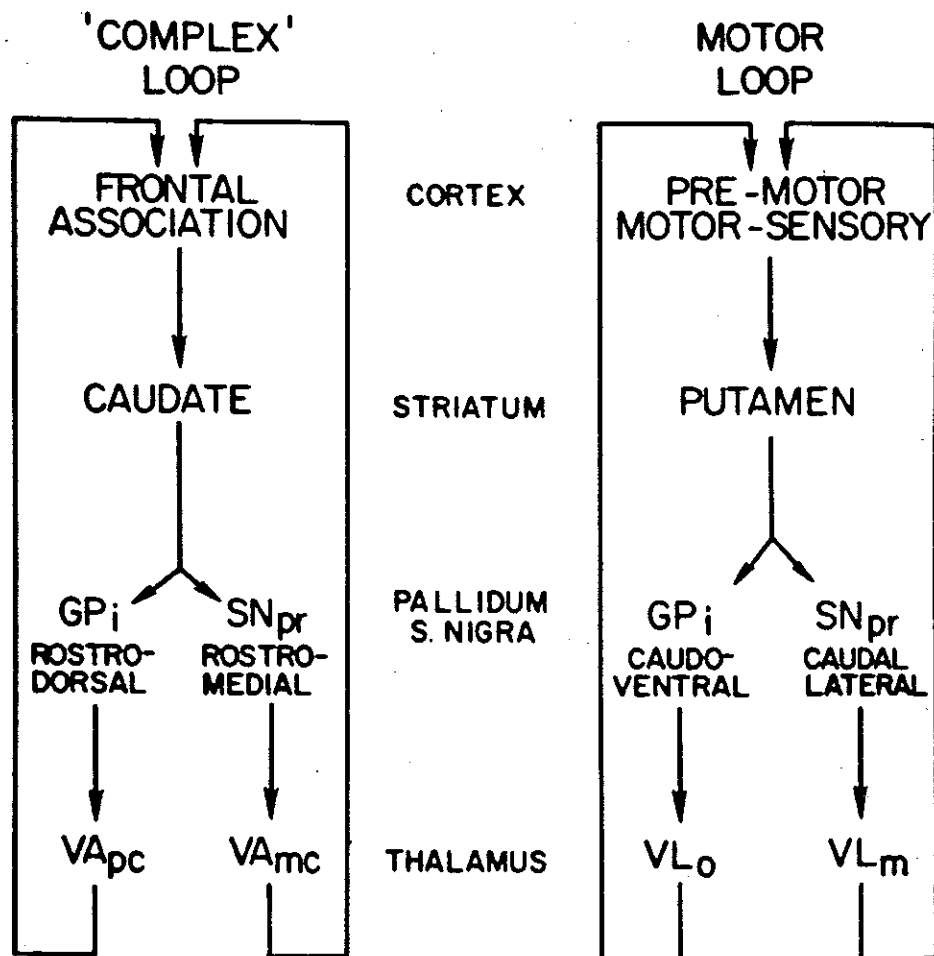


Fig. 1. Schematic depiction of pathways from the 'association' areas (complex loop) and the sensorimotor areas (motor loop) through the basal ganglia and thalamus. (From DeLong *et al.*⁵)

eye movements was suggested some time ago by demonstration of projections from the SNr to the intermediate layers of the superior colliculus⁶. Cells in these layers discharge before the initiation of saccadic eye movements and have prominent connections to brainstem oculomotor circuitry⁷. Hikosaka and Wurtz⁸ found that SNr cells showed activity related to visual stimuli

and to saccadic eye movements. The responses of some of these cells were dependent on spatial memory⁹. This finding was obtained in a paradigm requiring a monkey to remember the location of a spot of light that was presented briefly in the visual field while the monkey was looking at a different location; a later saccade was rewarded if it was made to the location

of the no-longer-present spot of light. Some SNr cells with only minimal saccade-related changes for saccades to the spot of light while it was still present (Fig. 2A), showed much more marked changes in firing rate for saccades directed at the point where such a remembered visual stimulus had been (Fig. 2B). These responses took the form of pauses in a tonic high rate

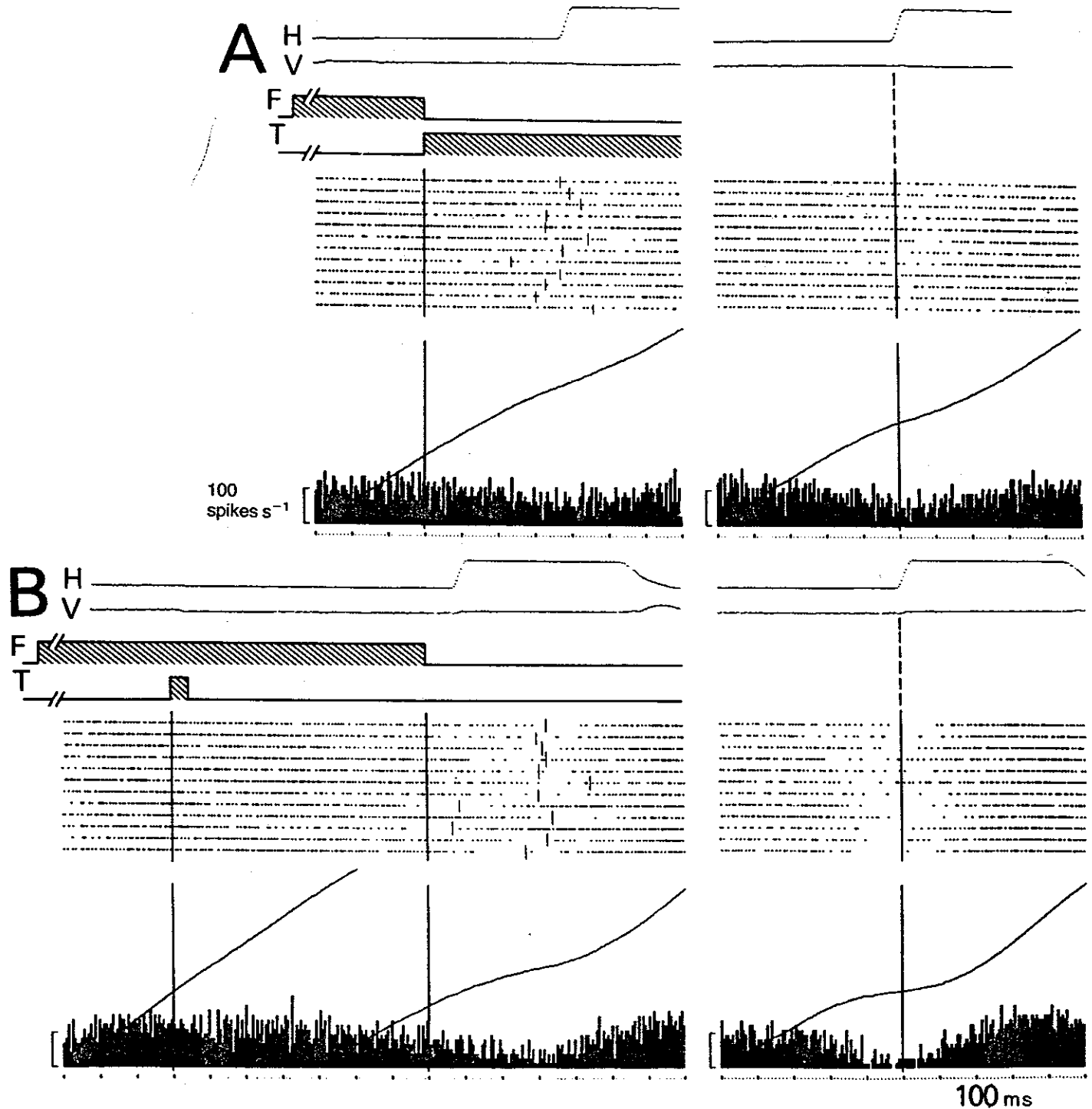


Fig. 2. Response of an SNr neuron related to a saccade resulting from a previously flashed spot of light (memory-contingent saccade response). In (A), the fixation point (F) went off as the target (T) came on. Saccades to the target were associated with only a slight decrease in discharge rate. In (B), saccades with the same direction and amplitude but to the point where the target was flashed previously were associated with a clear decrease in discharge rate. In both (A) and (B), the same trials are aligned on stimulus changes on the left and saccade onset on the right. H and V: sample horizontal and vertical eye-position traces. The raster shows consecutive trials and the single dots indicate single action potentials. Vertical small bars on the raster in (B) (left) indicate onsets of the delayed saccades. The trials are summed to produce time histograms and cumulative time histograms.

Calibration to the side of the time histogram indicates 100 spikes sec⁻¹. Bin width on the time histogram is 6 ms. The interval between large dots on the

of discharge and were termed memory-contingent saccade responses. Another class of SNr cells exhibited memory-contingent visual responses, consisting of pauses of activity that were time-locked to a visual stimulus that served as a target for a later saccade (Fig. 3B); these cells failed to pause in response to an identical visual stimulus delivered when the monkey was not set to remember its location as the target for a future saccade (Fig. 3A). A third type of SNr response was a sustained pause beginning after a briefly presented target for a future saccade which continued until the saccade to the remembered target. The SNr cells with these memory-contingent responses are actually in the lateral part of SNr rather than the medial as implied by Fig. 1.

Basal ganglia functions may be categorized as sensory, motor, or mnemonic, and each of these three functional aspects finds expression in the activity of individual SNr neurons with these three types of responses. In single SNr cells these functions are gated in different ways so that the sensory or motor activities of the cells are specialized for the different contexts in which behavior occurs. Thus, the memory-contingent visual responses involving decreases in SNr discharge following the onset of a visual stimulus, were evident only when the visual stimulus was delivered at a time when the monkey was set to remember the stimulus location as a target for a saccade to be made to the location of the stimulus after it was no longer present. These memory-contingent res-

ponses imply the presence of a neural correlate of spatial memory. Among the possible sources of basal ganglia inputs that might underlie memory-contingent responses, the best candidate is the prefrontal cortex. Elements in prefrontal cortex related to spatial memory might communicate with the SNr via the caudate nucleus.

In addition to its projections to the superior colliculus, the part of SNr concerned with oculomotor control projects to thalamic nuclei that in turn project to the frontal eye fields, a region that returns strong projections to both the superior colliculus and the caudate nucleus¹⁰. The frontal eye fields are thus intimately connected with the basal ganglia, and the activity of its neurons, like the activity of SNr neurons, is related to non-sensory and

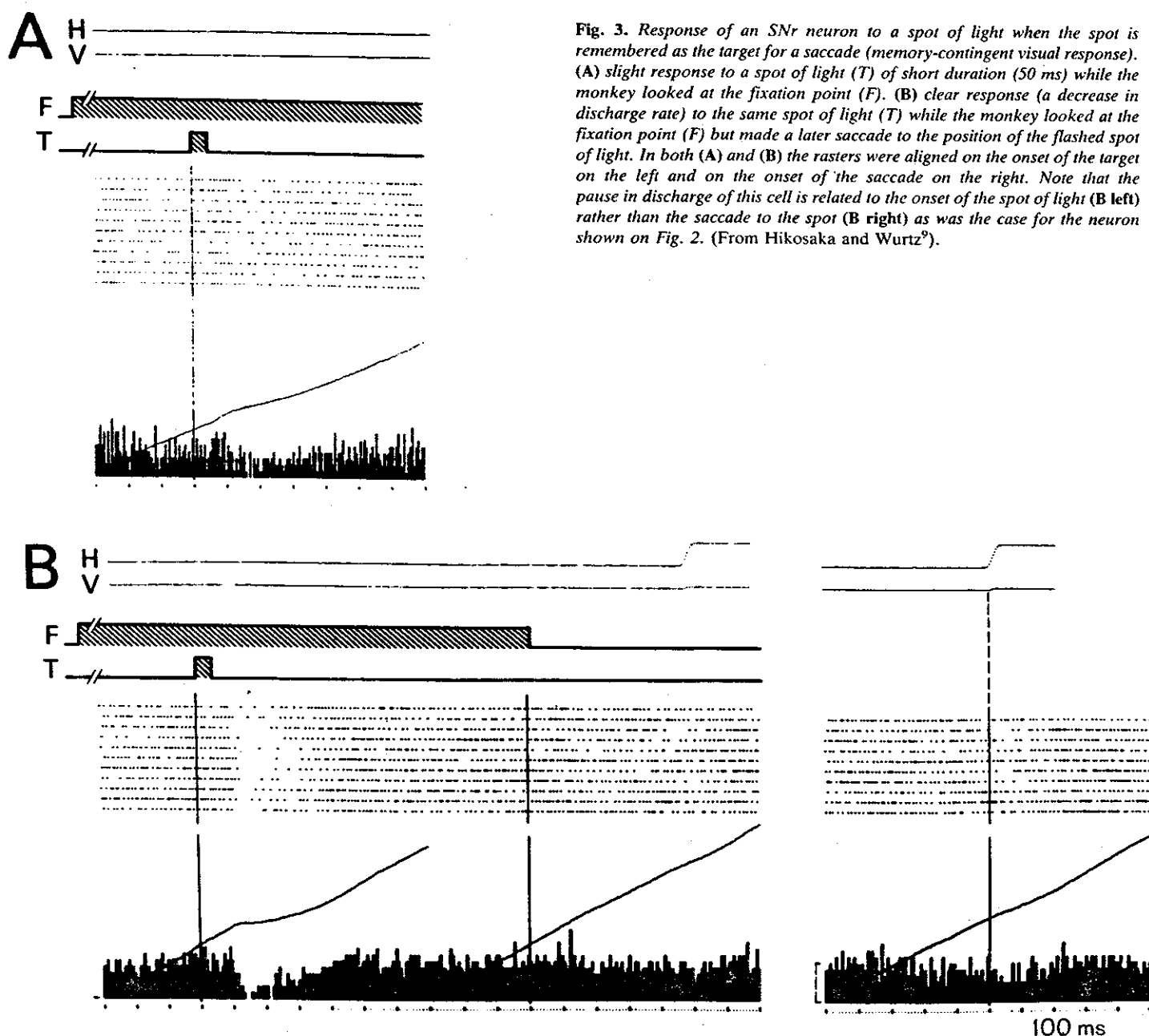


Fig. 3. Response of an SNr neuron to a spot of light when the spot is remembered as the target for a saccade (memory-contingent visual response). (A) slight response to a spot of light (T) of short duration (50 ms) while the monkey looked at the fixation point (F). (B) clear response (a decrease in discharge rate) to the same spot of light (T) while the monkey looked at the fixation point (F) but made a later saccade to the position of the flashed spot of light. In both (A) and (B) the rasters were aligned on the onset of the target on the left and on the onset of the saccade on the right. Note that the pause in discharge of this cell is related to the onset of the spot of light (B left) rather than the saccade to the spot (B right) as was the case for the neuron shown on Fig. 2. (From Hikosaka and Wurtz⁹).

attentional factors rather than to eye movements *per se* (see Bruce and Goldberg, this issue). For SNr projections to both the thalamus and the superior colliculus, the synaptic action is almost certainly inhibitory. Thus the pause of discharge that constitutes the common response of the SNr is likely to result in a release of these target structures from tonic inhibitory drive.

Set-dependent responses reminiscent of those in the SNr have also been seen in the caudate nucleus, a structure that projects to the SNr (Fig. 1). Rolls *et al.*¹¹ found that neurons in the caudate may respond to visual stimuli that are behaviorally significant but fail to respond when the same stimuli cease to be behaviorally significant. These responses were referred to as 'conditional', since they were not linked unconditionally to the sensory inputs or motor outputs themselves, but appeared only when stimuli led to behavioral responses. The conditional visual responses of caudate neurons may thus be thought of as providing a link between prefrontal areas subserving mnemonic processes and the SNr cells with memory-contingent responses.

Putamen and globus pallidus

The internal segment of the globus pallidus (GPi) is analogous to the SNr in being an output stage of basal ganglia, and whereas the SNr contains cells related to eye movements and to orofacial movements, the GPi contains cells related to movements of extremities and other body parts. DeLong¹² and Georgopoulos *et al.*¹³ have described systematic relations between GPi activity and direction of limb movements. It was found that, for most GPi neurons, changes of activity began after the changes of muscle activity that resulted in movement, and in this respect the relations of GPi to movement were different from the memory-contingent relations in the SNr - where pauses of discharge occurred well in advance of the EMG changes underlying saccades. One wonders if these timing differences between the GPi and SNr may have depended, in part at least, on differences in some behavioral aspect of task performance. This possibility is suggested by the finding of DeLong^{14,15}: putamen neurons with intense activity in advance of slow arm movements

had both weaker and later discharges with rapid arm movements (Fig. 4). In this experiment on slow and fast movements the color of a lamp specified the type of movement (fast or slow), and during the period when monkeys were learning this task the major difficulty for the monkeys was in learning to make the slow movement. This raises the possibility that mnemonic difficulty was different for the two movements. Of course, slow and fast movements also differ in their elementary kinesiological aspects, and DeLong suggested that postural fixation involving contraction of perispinal muscles might have been more marked in slow than in fast movements. While such differences of postural support cannot be neglected, neither can one neglect the role of mnemonic difficulty in differences of putamen discharge with fast and slow movements.

The putamen neuron illustrated in Fig. 4 is typical of most striatal neurons in that it has virtually no spontaneous impulses. A second class of putamen neurons has been recognized on the basis of the presence of tonic, virtually continuous discharge. Crutcher and DeLong¹⁶ have reported that tonically active putamen neurons appear unrelated to movement, and subsequent work by Kimura *et al.*¹⁷ has confirmed that tonically active putamen neurons are unrelated to body movements *per se*, but has shown that under certain behavioral contingencies such neurons may exhibit highly reliable responses to external events. It was found that an auditory stimulus (the click of a solenoid valve) elicited short-latency responses in tonically active putamen neurons when the stimulus was a cue for juice delivery and its consumption, but that such a stimulus failed to elicit responses when juice delivery had repeatedly failed to follow the sound, with the result that the sound no longer triggered movements associated with consuming the juice. Responses of tonically active putamen neurons were observed in three behavioral conditions: (i) Self-paced movement, in which a series of elbow movements resulted in a solenoid click and a juice reward; (ii) Free-reward, in which click and juice occurred at regular intervals (every 6 s) while the arm position was fixed; and (iii) No-reward, which was similar to the free-reward condition except that the tube conveying the juice was occluded so that the solenoid click was no longer followed by juice. In the no-

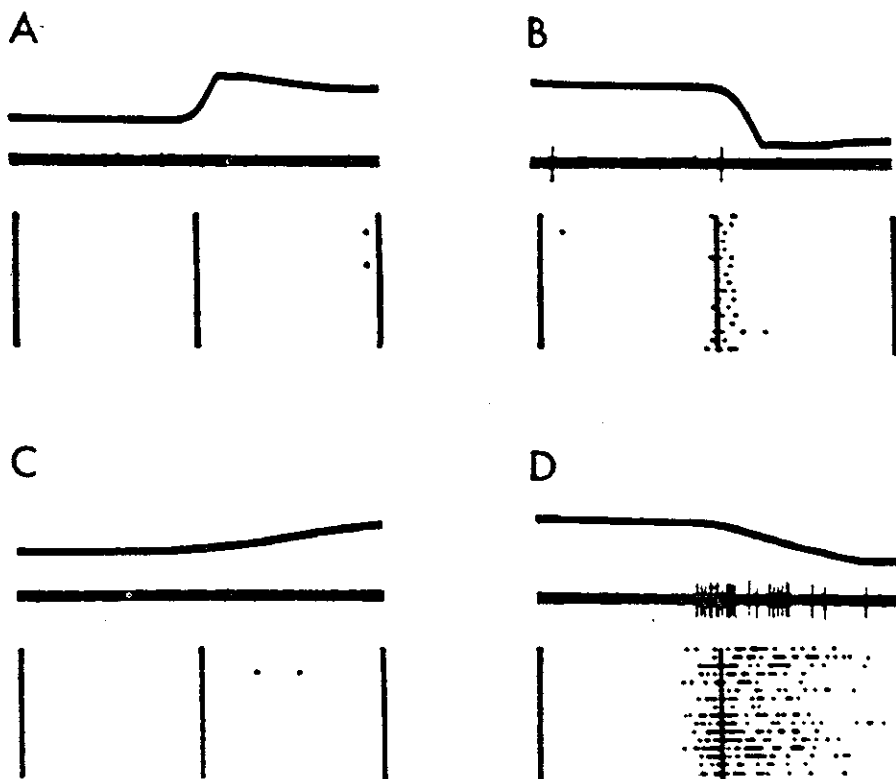


Fig. 4. Activity of a unit from the putamen during pushing and pulling fast (A and B) and slow (C and D) movements. For each case the upper trace represents the position of the arm during a single trial; the middle trace the unit discharge for the same trial; and the lower rows of dots the activity of the unit during 12 successive trials. Each trial is aligned on the time of leaving the zone (center bar). The interval from the center bar to the margin of the figure is 1 s.

This unit discharged strongly during the pulling slow (D) movements but only weakly during the pulling fast (B) movements. (From DeLong¹⁵)

reward condition licking was extinguished after the first few unrewarded solenoid clicks.

Fig. 5 shows responses of a tonically active putamen neuron in the three behavioral conditions. A sequence of 40 consecutive rewards during self-paced movement was followed by 40 consecutive free rewards. There was no apparent difference between solenoid-evoked activity in self-paced movement v. free-reward, showing that

the presence or absence of arm movements prior to the solenoid click made virtually no difference in the neuronal response. Then, without altering the tempo of 6-second intervals between solenoid clicks, the sequence of 40 no-reward clicks was started. The monkeys reacted to the first few unrewarded clicks following the long sequence of 80 rewarded clicks with the motor responses (head torque and sublingual EMG) that would have

been appropriate for consuming the juice, however, these motor responses were quickly extinguished as the series of 40 consecutive unrewarded solenoid clicks proceeded. This rapid extinction was due to the fact that the monkeys had had many months of experience (with many repetitions per day of these three sequences) and had learned that an unrewarded click signalled many more to come. Tonically active putamen neurons that had been re-

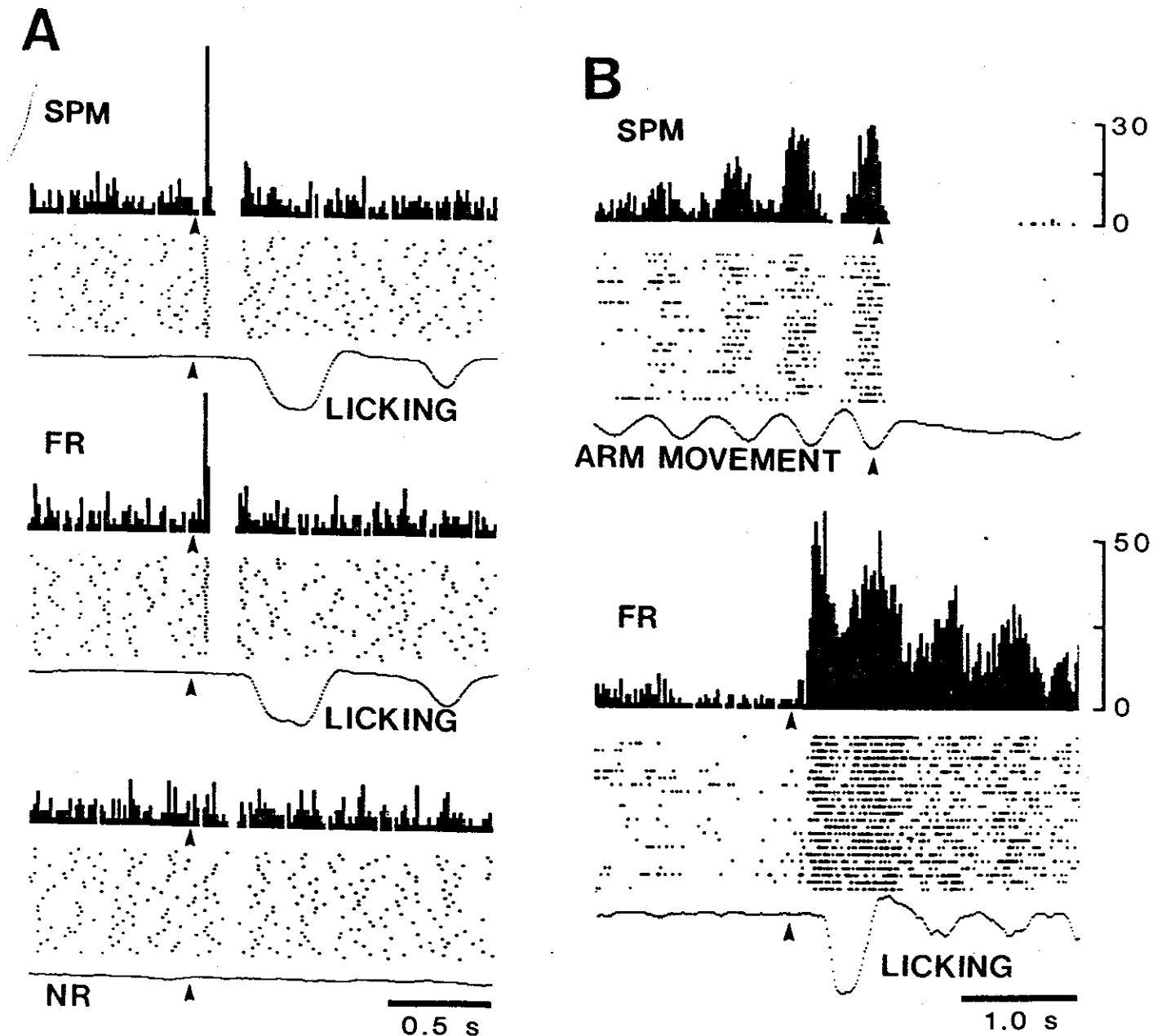


Fig. 5. Set-dependent responses in tonic putamen neurons. (A) The same putamen cell is shown in three sets of displays in three different conditions: (1) SPM (self-paced movement) in which a series of arm movements was followed by a solenoid click (at arrow) with juice delivery; (2) FR (free reward) in which solenoid clicks (at arrow) with juice reward occurred without prior arm movements and (3) NR (no reward) in which solenoid clicks (at arrow) failed to deliver reward. The single trace below each raster shows the average of licking responses following click during SPM and FR, while the trace without deflection in NR indicates the lack of licking responses under this condition.

It can be seen that an impulse (represented by a dot) was evoked by the solenoid click (at arrow) when clicks triggered licks during SPM and FR but not during NR, when motor responses were extinguished. (B) Phasic discharges of putamen neurons with arm movements (above) and licking (below). (From Kimura, M., Rajkowski, J. and Evarts, E. V., unpublished observations¹⁷.)

sponsive to the click lost their responses within a few repetitions of the unrewarded solenoid click, showing that the characteristic responses of these cells to the solenoid click depended on the set of the animal to consume the reward. Though dependent upon the set of the monkey to lick and consume juice upon occurrence of the click, the responses in the tonically active neurons were not related to licking movements themselves. As shown in Fig. 5A, these neurons responded to the solenoid click with single impulses well in advance of the first in the sequence of licking movements, and then showed no apparent relation to the subsequent successive licks. By contrast, Fig. 5B shows typical movement-related neurons that had bursts of discharge with each of the series of self-paced arm movements or licking movements. Fig. 6A illustrates the responses evoked in eight

tonic cells in a single penetration in putamen, and shows the clear synchrony of these responses.

Neuronal activity was also recorded in the globus pallidus in situations with the same three click-reward contingencies, and set-dependent responses were observed in a number of globus pallidus neurons. The globus pallidus cell illustrated in Fig. 6B exhibited a pause of activity in response to rewarded clicks, but this pause disappeared soon after the no-reward sequence started. This pause in discharge, time-locked to a click to which the monkey is set to react, is strikingly similar to the SNr pauses time-locked to visual stimuli whose location the monkey was set to remember as the target for a future saccade.

Conclusions

This paper has considered behaviorally-related physiology of striatum,

globus pallidus and pars reticulata of the substantia nigra. In all of these regions changes of activity precede movement in certain behavioral situations but not in others. As we have seen, a given SNr neuron may pause in advance of a saccade to a remembered target but not in relation to the same saccade directed to a target that is present. A click or a visual stimulus may evoke a response in the SNr, GPi, or the striatum when the stimulus is behaviorally significant, but not when the same stimulus is delivered without such significance. Of course, some cells in these areas respond to sensory stimuli and become active prior to movements, regardless of context. In this sense some basal ganglia neurons are similar to neurons in the motor cortex or superior colliculus, where there are responses to sensory stimulation and discharges before movement regardless of the context or

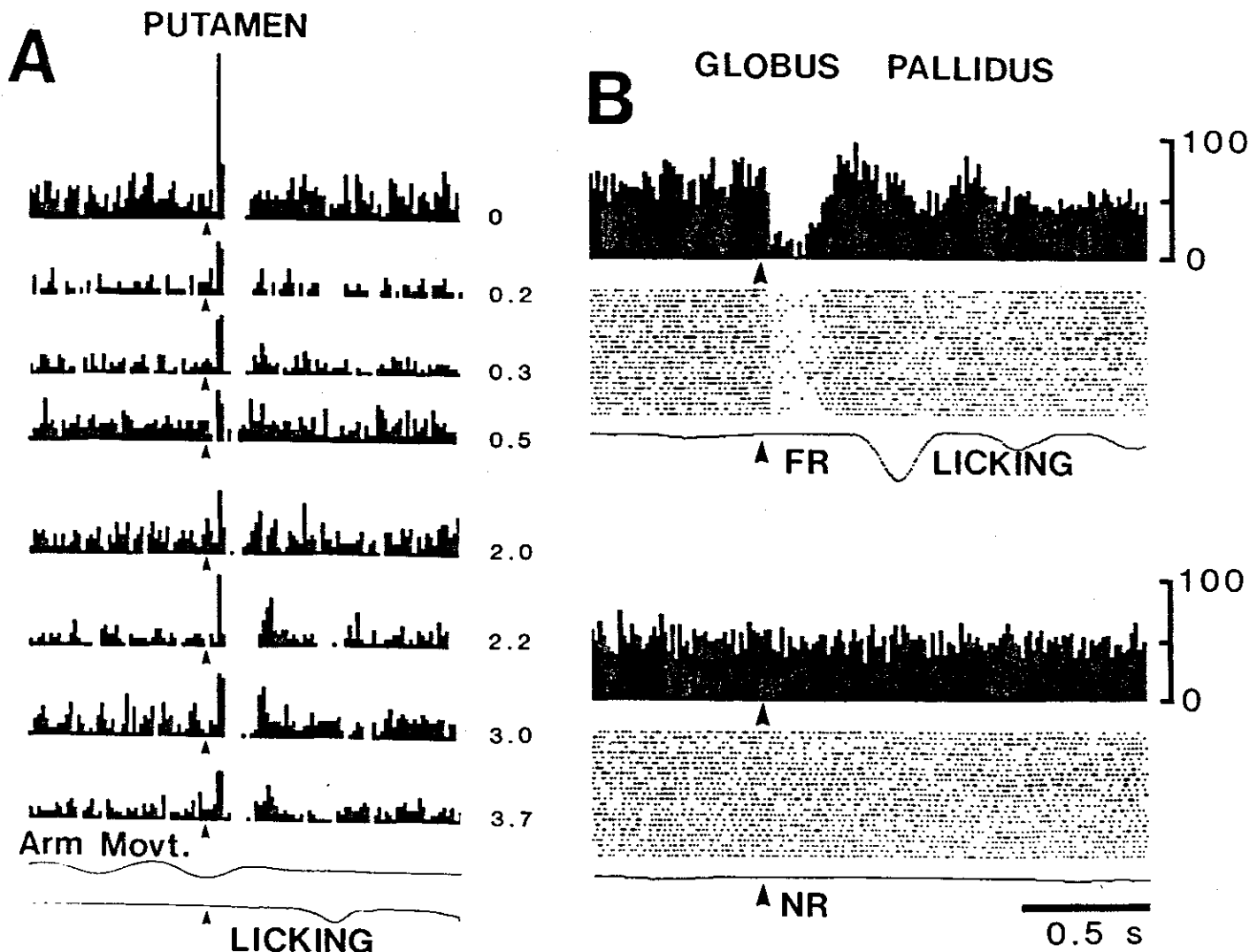


Fig. 6. Response synchrony in putamen and set-dependent pause in globus pallidus (A) Responses in eight successive tonic putamen neurons (recorded in a single microelectrode penetration) when click (at arrow) was followed by licking to consume juice. Numbers at right of histograms correspond to separations (in millimeters) between locations of successive neurons in the penetration. (B) Click-evolved pause of globus pallidus discharge occurred in response to click (at arrow) prior to licking in the free reward (FR) period, but was absent during the no reward (NR) period when no movements were triggered by the clicks (at arrow). (From Kimura, M., Rajkowski, J. and Evarts, E. V., unpublished observations¹⁷.)

contingencies associated with these inputs or outputs. The feature that is distinctive in the basal ganglia is the striking importance of behavioral contingency for the occurrence of responses in many neurons. The nature of this behavioral contingency suggests that basal ganglia output may be especially critical for movements made in the absence of direct sensory guidance.

A possible role of the basal ganglia in the non-sensory control of saccadic eye movements is suggested by the symptomatology in Parkinson's disease and Huntington's disease. Parkinsonian patients exhibit prolonged times for making saccades back and forth between targets that are left on continuously¹⁸. Patients with Huntington's disease have difficulty in making saccades, in a given direction, in response to verbal instructions¹⁹. In both of these basal ganglia disorders the deficits of saccade production occur when the saccades must be initiated by something other than the onset of a visual target, and such 'internally initiated' eye movements have some similarity to saccades aimed at remembered targets. The hypothesis that basal ganglia are involved in generation of movements in the absence of sensory guidance is also supported by certain behavioral deficits following experimental disruption of basal ganglia functions in monkeys. Thus, it has been shown that there is greater impairment of saccades to remembered targets, as

compared to still present visual targets, following an injection of muscimol into the superior colliculus (Ref. 20 and Hikosaka, O. and Wurtz, R. H. unpublished observations) which would reversibly block the consequences of pauses in the GABAergic output of the SNr. For limb movements, this hypothesis is consistent with the observation that inactivation of the globus pallidus (by cooling) disrupted self-paced elbow movements but the addition of a visual display for the guidance of movement improved performance²¹. Thus, the initiation of movement in the absence of sensory guidance might be a unique contribution of a system that includes the basal ganglia. In light of the close anatomical connections between the frontal cortex and basal ganglia, such a system may include the frontal cortex as well.

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Book Reviews

Brewster and Wheatstone on Vision

edited by Nicholas J. Wade, published for The Experimental Psychology Society by Academic Press, 1983. £25.00/\$39.00 (xii + 358 pages) ISBN 0 127 29550 X

Although 'Wheatstone's bridge' is now known to nearly everyone, most people would have difficulty in providing a single fact about his life, or that of Brewster. The author has reprinted the main publications of both men on subjects immediately related to vision, stereoscopy and photography, together with an introduction, their obituaries in the Proceedings of the Royal Society, and a summing up. There is an excellent full biography of Wheatstone written by B. Bowers in 1975, but nine tenths of this is rightly devoted to

Wheatstone's major work on the velocity of conduction of electricity, on the electric telegraph and electric motors, and the beginning of a treatment of the electrical properties of submarine cables. Brewster was recently the subject of a symposium at the Royal Society of Edinburgh, but this ignored his interests in vision. The present book makes it clear that the organisers of the symposium were right, for although Brewster made important contributions to physics, in vision he was either late in the field, as he was with the stereoscope, or he was wrong and dogmatically wrong.

Nevertheless, Wade does his best to treat them both even-handedly, and emphasizes the similarities in their careers. He remarks that it was said of both 'Nihil tangit quod non ornat' (There is little he touches which he does not adorn). Oddly

enough, this appears in the second edition of Brewster's *The Kaleidoscope* published in 1858 in his lifetime, and was therefore presumably put there by him. The same phrase was used of Wheatstone by no less an authority than Michael Faraday.

Wheatstone left school at 14 to work in the family firm making musical instruments. Brewster went to Edinburgh University to train for the Church but left without a degree, gave up preaching and lived by his pen. He had no established post for most of his life and his experiments seem to have been carried out at home. Wheatstone devised a number of musical instruments including the concertina, and from this developed an interest in the physics of sound. He invented the Kaleidophone, a device in which a silver bead was mounted on a vertical square cut rod. This could be made to vibrate in two directions at right angles to each other, and light reflected from the silver bead could trace out a variety of patterns including those we now call Lissajous'