Primate Globus Pallidus and Subthalamic Nucleus: Functional Organization

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SUMMARY AND CONCLUSIONS

1. Neuronal relations to active movements of individual body parts and neuronal responses to somatosensory stimulation were studied in the external (GPe) and internal (GPi) segments of the globus pallidus (GP) and the subthalamic nucleus (STN) of awake monkeys.

2. In GPe (n = 249), GPi (n = 151), and STN (n = 153), 47, 29, and 28% of the cells, respectively, discharged in relation to active arm movements, 10, 11, and 15% to leg movements, and 22, 22, and 18% to orofacial movements. Of the neurons whose activity was related to arm movements, 26, 16, and 21% in GPe, GPi, and STN, respectively, discharged in relation to movements of distal parts of the limb.

3. Of cells whose discharge was related to active limb movements, 37, 22, and 20% in GPe, GPi, and STN, respectively, also responded to passive joint rotation, which was usually specific in terms of joint and direction of movement. Only a small percentage of cells responded to muscle or joint palpation, tendon taps, or cutaneous stimulation. Short-latency, direction-specific neuronal responses to load perturbations confirmed the existence of proprioceptive driving.

4. In both GPe and GPi, leg movement-related neurons were centrally located in the rostrocaudal and dorsoventral dimensions. In contrast, arm movement-related cells were found throughout the entire rostrocaudal extent of both segments, although in greater numbers caudally. In the central portions they were situated largely inferior and lateral to leg movement-related neurons. Neurons related to orofacial movements were largely confined to the caudal halves of both segments, where they were located largely ventral to arm movement-related cells.

5. The STN cells whose activity was related to leg movements were observed largely in the central portions of the nucleus in the rostrocaudal and mediolateral dimensions. Cells whose activity was related to arm movements were found throughout the rostrocaudal extent of the nucleus, but were most numerous at the rostral and caudal poles. Neurons related to movements of the facial musculature and to licking and chewing movements were distributed over the entire rostrocaudal extent of the nucleus, where they generally occupied the ventrolateral regions.

6. In all three nuclei, neurons with similar functional properties were sometimes clustered together. Within the arm and leg areas, however, there was no clear evidence for a simple organization of clusters related to different parts of the limb.

7. These studies provide further evidence for a role of the basal ganglia in the control of limb movements. The demonstration of specific noncutaneous sensory inputs together with the previous demonstration of a relation of neuronal activity to movement parameters suggest a specific role of the basal ganglia in motor function and a prominent role in proprioceptive mechanisms. The demonstration of a general somatotopic organization of movement-related neurons in GPe, GPi, and STN provides a better understanding of the anatomical/physiological basis of the symptoms of basal ganglia dysfunction in humans.

[illegible] Physiological Society

Clinicopathologic studies in humans and experimental studies in animals indicate an important role of the globus pallidus (GP) and the subthalamic nucleus (STN) in motor function (16, 21, 23, 41). The GP is a composite structure formed by an internal (GPi) and an external (GPe) segment. Each segment has distinctive anatomical connections: GPi gives rise to major efferent projections from the basal ganglia to the thalamus and the midbrain (37), whereas GPe projects largely to the STN (37). The STN, in turn, projects to both pallidal segments as well as the substantia nigra (SN) (36). Anatomically, the STN is positioned to modulate the entire output of the basal ganglia, which arises from both the SN and GPi. Discrete lesions of the STN in both humans and monkeys result in involuntary movements of the contralateral limbs, termed hemiballismus (6, 41). Subsequent lesions of GP abolish the involuntary movements of hemiballismus (6), apparently by interrupting the abnormal output from GPi.

Early studies of single-cell activity in the GP in the behaving monkey revealed that changes in neural activity were associated with movements of individual body parts during performance of a motor task (11). For cells whose activity was related to limb movements, changes in neural activity were most often correlated with movements of the contralateral rather than the ipsilateral limb. In those studies, neurons related to movement were localized primarily in the lateral portions of each pallidal segment throughout nearly their entire anteroposterior extent. Although neurons related to leg movements were generally localized dorsal to neurons related to arm movements, uncertainty remained over the degree of separation of the arm and leg representations and the representation of other body parts. In addition, recent studies (1, 24) have failed to find a somatotopic organization in GP.

The present studies were designed to reexamine the functional organization of the GP and STN, by studying the relation of neuronal discharge to active movements and the responses of neurons in these nuclei to natural somatosensory stimulation and controlled proprioceptive perturbations. These studies were undertaken to provide a more quantitative study of the relations between neuronal activity in the GP and STN and parameters of arm movements in a step-tracking task, the results of which have been reported previously (21). In order to be certain that task-related cells studied in the behavioral paradigm were in fact related to the arm movements monitored in the task and not to associated movements of other body parts, the activity of each task-related cell was also studied and characterized outside the behavioral paradigm. Specifically, the discharge of each cell was observed during spontaneous and induced active movements and during natural somatosensory stimulation of individual body parts. In addition, the neuronal responses to controlled prioprioceptive perturbations were studied. Preliminary results of this study have been presented previously (3, 14–16).

METHODS

General

Three rhesus monkeys, weighing 4–6 kg, were used in these experiments. The animals were first trained to perform a visuomotor arm-tracking task (21) and to permit examination of their body parts by an experimenter. After completion of training, under general anesthesia, a recording chamber was stereotaxically positioned over a round opening of the skull and held in place with acrylic. For recordings in the GP, the axis of the chamber was aimed stereotaxically at the center of this structure (A12, L8, H6). The chamber was placed at a 50° angle from the vertical, in order to avoid passage of the electrodes through the arm area of the motor cortex and the internal capsule. For recordings in the STN the recording chamber was positioned vertically at A7. A Narishige microdrive was used to lower glass-coated, platinum-iridium microelectrodes of 0.5–1.5 MΩ impedance (at 1,000 Hz) through the dura and into the brain. Penetrations were separated by 1 mm, so the STN and GP were explored systematically. During experimental sessions the head of the animal was mechanically immobilized. Single units isolated from background noise and meeting the criteria for extracellular recordings from cell bodies were accepted for study. Once a neuronal action potential was isolated, a detailed examination of the animal was carried out by at least two experimenters to determine (*1*) whether cell activity was related to active movements of a particular body part and (*2*) whether the cell responded to passive manipulations of skin, muscles, joints, and deep

tissues with the animal relaxed. Cells whose activity was related to arm movements were studied further while the monkey performed in the task (see below).

A record was kept of the depth at which each cell was isolated along each penetration, from the first recorded cells in the upper layers of the cerebral cortex to the last recorded cells below the GP or STN. During penetrations aimed at the GP, the microelectrode first traversed the putamen, in which characteristic low levels of spontaneous neural activity were observed (10, 12, 13). Entry of the electrode into GPe was reliably indicated by the abrupt increase in background activity and the appearance of neurons with a high-discharge rate typical of this nucleus (11). The recorded depth of the first pallidal activity provided a reliable reference point for the subsequent plotting of neurons along the penetration. Furthermore, in those penetrations in which GPi was encountered, the first appearance of continuously active, high-frequency discharge cells, characteristic of this nucleus (11), provided a second reference point at the beginning of the inner segment. In addition to these neuronal/anatomical landmarks, in many penetrations cells exhibiting the previously described characteristic discharge pattern of "border cells" (11) were recorded within both the external and internal medullary lamina of the GP. Thus the characteristic resting discharge patterns of GPe and GPi neurons and of border cells within the laminae provided consistent and useful reference points for each penetration.

During penetrations directed at the STN, characteristic neural activity was encountered in the overlying thalamus and zona incerta. Electrode advancement into the STN was less clearly distinguishable in some penetrations because of the similarities of neural discharge in the STN and zona incerta (unpublished observations). As the electrode was advanced beyond the lower border of the STN, recordings from the internal capsule in lateral penetrations or characteristic high-frequency neural activity in the pars reticulata of the substantia nigra (19) in medial penetrations provided consistent and useful neural landmarks for determining the depth and location of recording sites. Electrolytic marking lesions were placed at the end of the final penetrations in order to confirm histologically the location of recording sites.

Histology and reconstruction of penetrations

At the end of each experiment the animal was deeply anesthetized with pentobarbital and then perfused successively with isotonic saline and buffered formalin. The brain was embedded in celloidin and sectioned in the coronal plane every 25 μm, [illegible] data from penetrations identified histologically are included in this study.

Methods of examination

Simple methods of examination were employed for determining responses to natural stimulation and active movements. Neuronal activity was monitored by audio and displayed on an oscilloscope. Correlations between neuronal discharge and active movements of the animal's limbs, face, trunk, and eyes, and the neuronal responses to passive manipulations were confirmed by two observers. Neuronal relations to movements of the tongue, jaw, and face were studied in relation to juice delivery in the behavioral paradigm and the presentation of food objects and liquid from a syringe. Neural relations to limb movements were studied as the animal manipulated objects of interest and attempted to reach for and retrieve small pieces of fruit. The animals were conditioned to permit passive examination as individual joints were palpated and the limbs rotated throughout the joint's physiological range. Neuronal responses to muscle and tendon taps, light touch of the skin, and hair stimulation over the entire body were also determined. In addition to determining neural responsiveness to deep and superficial stimulation of body parts, the responsiveness of each neuron to gross visual stimuli and to eye movements was determined. In one animal, eye movements were monitored by means of implanted electro-oculography (EOG) electrodes.

On the basis of demonstrated response to active movements and/or passive manipulations of specific body parts during the examination, cells were categorized as related to arm, leg, orofacial, trunk, or eye movements. Cells that showed definite alterations of discharge during the examination, but without a clearly discernible relation to active movements or stimulation of specific body parts were categorized as "nonspecific." Cells that showed no discernible alteration of discharge during examination were labeled nonresponsive.

Torque task

The animals were trained to grasp a lightweight, low-friction handle that they moved from side to side or in a push-pull direction. A torque motor was attached to the handle for the application of loads (see below). The display consisted of two rows of light-emiting diodes (LEDs) arranged in two horizontal rows, one below the other. Each row contained 128 LEDs and was 32 cm. The illuminated LED of the upper low indicated the target position; the illuminated LED of the lower row corresponded to the current position of the handle. The illumination was enhanced when the two LEDs were aligned within a posi- [illegible] the handle to align the lower LED with the upper LED. A trial began by turning on the target LED. The animal had to move the manipulandum to align the handle position LED with that of the target LED and hold in that position for at least 2 s (control period). A load was then applied to the handle unpredictably while the animal was holding it aligned to the initial LED. This forced the arm out of the positional window. The animal had to bring the handle back to the initial position to receive a liquid reward. Torques of opposite directions were applied at a strength of 0.225 Nm and with a time constant on the order of 5 ms. The experiment was carried out under computer (PDP 11/10) control. Neuronal discharge data were collected as interspike intervals in absolute time. The position of the handle was differentiated on-line by an analog circuit to provide velocity and acceleration. The position, velocity, and acceleration records were sampled at 100 Hz with analog-to-digital converters. All data were stored in the computer in digital form. Neuronal response onset times were determined by inspection of raster and histogram display of neural data.

The activity of 400 GP neurons and 153 STN neurons was recorded in 73 histologically identified penetrations in five hemispheres of three monkeys. Of these penetrations, 45 were in GP and 28 in STN. In GP, 249 neurons were in GPe and 151 in GPi.

Spontaneous activity

As described previously (11, 21), neurons in GPe exhibited either a high-frequency discharge (HFD) interrupted by pauses (88% of cells) or a lower frequency of discharge with occasional, brief, high-frequency bursts (12%). Cells in GPi had a characteristic, sustained, but irregularly fluctuating, high-discharge rate. The mean discharge rates for HFD cells in GPe and GPi during the control period of the behavioral task (see Ref. 21) were 71 and 79 imp/s, respectively. The patterns of ongoing discharge of pallidal neurons were quite stable over long periods of

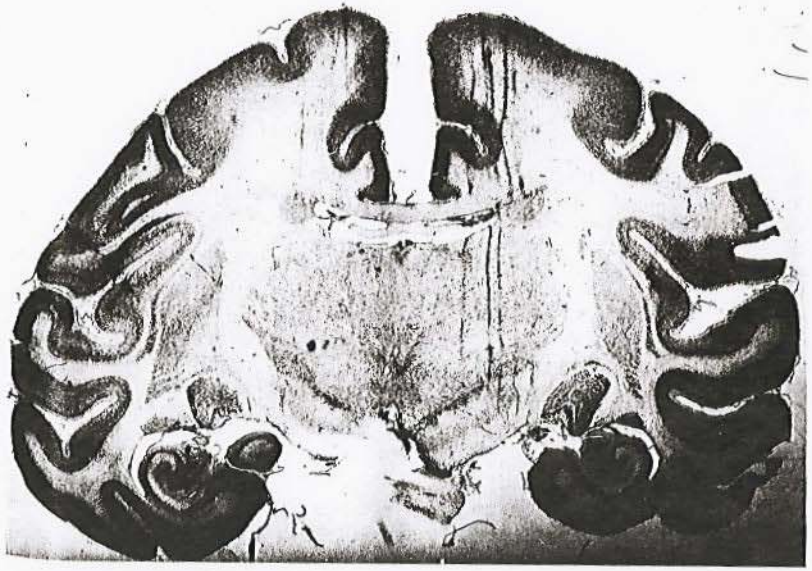

FIG. 1. Coronal section showing sites of penetrations through regions studied. On *left*, GP and on *right*, STN. Marking lesions were produced by passing current (10 μA × 10 s) through microelectrodes.

TABLE 1. *Classification of cells in each structure based on responses to active movements and/or passive manipulations*

	GPe		GPi		STN	
	n	%	*n*	%	*n*	%
Arm	117	47	44	29	43	28
Leg	24	10	16	11	23	15
OF	55	22	34	22	27	18
Axial	5	2	1	1	0	0
Visual	4	2	1	1	4	3
NS	31	12	28	18	26	17
NR	13	5	27	18	30	19
	249	100	151	100	153	100

OF, orofacial; NS, nonspecific activation; NR, nonresponsive.

observation, as long as the animal remained relaxed. The properties of border cells within the laminae of GP and neurons of the nucleus basalis located below GP will be the subject of a separate report.

The mean firing rate of STN neurons during the control period of the behavioral task was 24 imp/s (see Ref. 21). STN cells frequently discharged in doublets or triplets, giving a characteristic "bursting" quality to the discharge.

Relations to active movement

The discharge of the majority of cells in both pallidal segments and STN was clearly modulated during active movements of individual body parts. It can be seen from Table 1 that, of neurons studied in GPe, GPi, and STN, the activity of 47, 29, and 28% of cells, respectively, was related to arm; 10, 11, and 15% to leg; and 22, 22, and 18% to orofacial movements. The activity of a number of cells in all structures studied

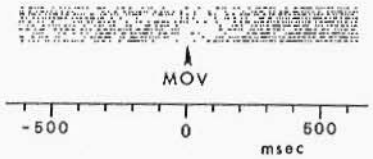

FIG. 2. Example of neural activity in GPi related to arm movements. Ten trials aligned to movement onset (MOV).

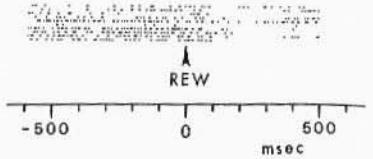

FIG. 3. Example of neural activity in GPe related to licking following juice delivery. Ten trials aligned to juice delivery (REW).

related to axial movements or manipulations of the trunk. The discharge of a few cells in STN was modulated in relation to saccadic eye movements. Nonspecific activation during the examination was observed in 12% of the cells in GPe, 18% in GPi, and 17% in STN. Finally, other cells (5% in GPe, 18% in GPi, and 19% in STN) showed little or no alteration of discharge rate or pattern during the examination or in the behavioral task.

Although the activity of most cells categorized in Table 1 as "arm cells" was modified solely during arm movements, the activity of some of these cells in GPe (32/117) and GPi (12/44), was also modulated during chewing and licking movements. These cells were active during reaching arm movements rather than during more distal manipulative movements of the limb. This suggested a relation to more proximal, shoulder girdle or cervical musculature. In fact, in the course of electromyographic studies several muscles (e.g., trapezius, supra- and infraspinatus) were

TABLE 2. *Arm and leg cells in each structure responding to passive manipulations of the arm and leg*

	GPe		GPi		STN	
	n	%	*n*	%	*n*	%
Joint rotation	52	37	13	22	13	20
Joint palpation	1	1	0	0	0	0
Muscle palpation	5	4	0	0	0	0
Tendon taps	2	1	3	5	0	0
Light touch	0	0	0	0	0	0
Hair stimulation	0	0	1	2	0	0
Nonresponsive	81	57	43	71	53	80
	141	100	60	100	66	100

TABLE 3. *Arm cells responding to rotation of different joints of the upper extremity*

	GPe		GPi		STN	
	n	%	*n*	%	*n*	%
Shoulder	10	34	4	36	3	33
Elbow	10	34	5	46	3	33
Wrist	8	28	2	18	2	23
Fingers	1	4	0	0	1	11
	29	100	11	100	9	100

found to be active during both reaching and chewing (unpublished observations).

Of cells identified on the basis of the sensorimotor examination as related to arm movements, the majority showed rather clear and consistent changes in discharge during the phasic movements in the visuomotor step-tracking task, as reported previously (21) and illustrated in Fig. 2. In addition, however, it was not uncommon to find that cells clearly related only to leg movements by examination outside the task also exhibited a consistent task-related modulation of discharge in the arm-movement task. Although overt leg movements were not consistently seen during task performance, some animals presumably cocontracted muscles or made small leg movements in association with the phasic arm movements. No attempt was made to record from cells related to leg movements during performance of the tracking task or to statistically compare these changes with those of cells clearly related to arm movements within and outside the behavioral paradigm. The goal of the present study was to identify and eliminate from our sample of task-related neurons all such spuriously correlated activity changes.

For many cells whose activity was related to active arm movements it was often difficult to be certain, in the absence of clear responses to passive manipulations (see below) whether the neuronal activity was related to movements about a single joint, to compound movements involving two or more joints, or to whole arm synergies (such as reaching). In some cases, however, cell discharge was

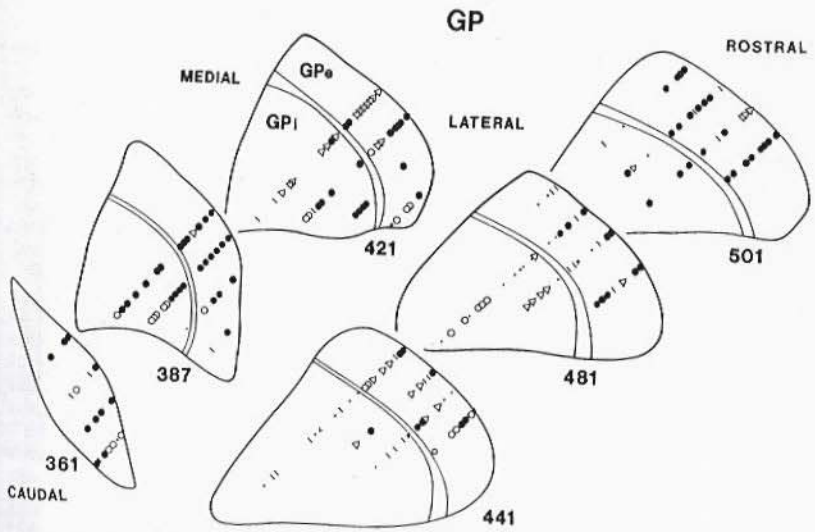

FIG. 4. Location of different cell types in GPe and GPi in 1 hemisphere. Leg, △; arm, ●; orofacial, ○; axial, ×; visual (or eye movements), V; nonspecific, —; and nonresponsive, small dot.

clearly correlated with active movements of either distal or proximal parts of the upper extremity. Of the arm-related neurons, 28% in GPe, 16% in GPi, and 21% in STN, respectively, were related to active movements of the distal arm, i.e., wrist and fingers.

Of the cells related to orofacial movements, the activity of the majority in all three structures was related to licking and/or chewing movements, although a small number was clearly related to movements of the face, lips, or forehead. An example of the activity of a neuron following the delivery of a reward in the behavioral task is shown in Fig. 3. Moreover, a few cells in each structure consistently discharged with a latency of half a second or more from the delivery of the reward, and their activity was temporally correlated with swallowing movements.

Responses to passive manipulations

The number of neurons in GPe, GPi, and STN responsive to manipulation of deep structures (rotation of joints, palpation and squeezing of muscles, tapping of tendons) and cutaneous stimulation (light touch and hair bending) are shown in Table 2. The most effective stimulus was joint rotation. Only a small percentage of cells responded to tendon taps or palpation of muscle or joint structures. No responses to stimulation of glabrous skin were observed and only one cell responded to hair stimulation (over the entire contralateral upper extremity, trunk, and neck). The percentage of cells responsive to somatosensory stimulation was greater in GPe and GPi than in STN.

Table 3 shows the number of cells responding to passive rotation of the joints of the upper extremity. In almost every case neural responses to passive joint rotation were detected only for movements about a single joint. The far greater proportion of cells responding to passive manipulations of proximal rather than distal portions of the limb, especially the digits, is remarkable. Only two cells in GPe and one in STN showed a response to movement of two joints, and in each case the response to movement of one joint was far greater than of the other. Similarly, for cells responding to muscle or tendon taps, responses were seen only in response to tapping of a single muscle or tendon.

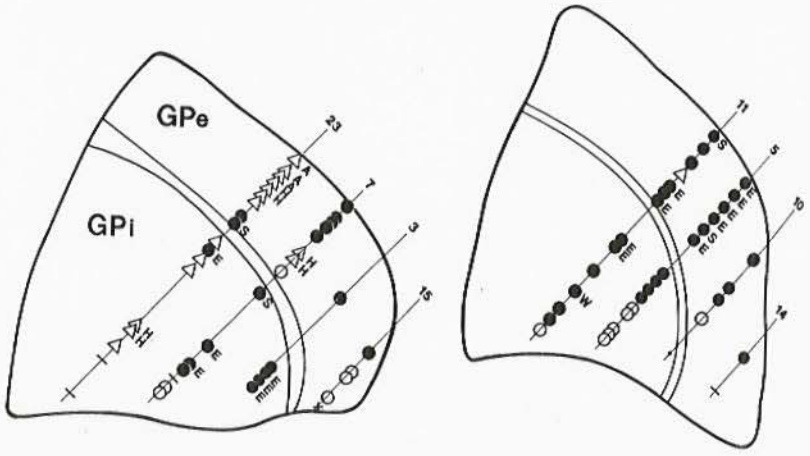

FIG. 5. Examples of clustering of cells with similar functional properties within GP. Symbols are same as in Fig. 2. Additional symbols are as follows: W, wrist; E, elbow; S, shoulder; H, hip; K, knee; and A, ankle. Two levels are 1 mm apart. Symbols without adjacent letters indicate neurons related to active but not passive movements of body part.

Functional grouping

GLOBUS PALLIDUS. In both GPe and GPi a general somatotopic organization of movement-related cells was observed, which was similar for both segments as shown in Fig. 4. In both GPe and GPi, leg movement-related neurons were primarily centrally located in the rostrocaudal and dorsoventral dimensions. By contrast, arm movement-related cells were found throughout a large rostrocaudal extent of both segments, although in greater numbers caudally. In the central portions they were situated largely inferior and lateral to leg movement-related neurons. Neurons related to orofacial movements were largely confined to the caudal halves of both segments where they were located largely ventral to arm movement-related cells. It can be seen in Fig. 4 that exceptions to this general summary of the localization of movement-related cells occurred, but that they were infrequent. Within both GPe and GPi a clustering of several neurons with similar relations to active movement and responses to stimulation were found in a single penetration. Examples of such clustering in GP are shown in Fig. 5, which shows several penetrations from one animal at two adjacent anteroposterior levels. For example, in penetration 5, five of the cells in GPe were related to passive elbow flexion, and in penetration 11, there were two cells in GPi related to passive elbow extension. Two clusters of cells in GPi related to passive elbow movements were also encountered in penetrations 3 and 7, and cells related to the ankle and hip were found in close proximity in penetrations 23 and 7.

Within the arm or leg areas there was no clear evidence for a simple representation of the limb. Instead, cells related to similar active and/or passive movement of different joints were encountered separately along the rostrocaudal extent of the nucleus. There was no apparent order in the arrangement of cells or clusters of cells related to different joints or regions of the arm or leg. Thus separate cells related to distal and proximal movements or joints of the arm were found intermingled throughout a large rostrocaudal extent of the arm areas of the both GPe and GPi.

STN. In the STN, cells related to movements of individual body parts were found throughout the rostrocaudal extent of the nucleus, especially in the lateral portions. As in GP, a general somatotopic organization of movement related cells was found, as shown in Fig. 6. Cells related to leg movements were found largely in the central portions of the nucleus in the rostrocaudal and mediolateral dimension. Cells related to arm movements were found throughout the rostrocaudal extent of the nucleus, but were most numerous at the rostral and caudal poles. Neurons related to movements of the facial musculature and to licking and chewing movements were distributed also over the entire rostrocaudal extent of the nucleus, where they

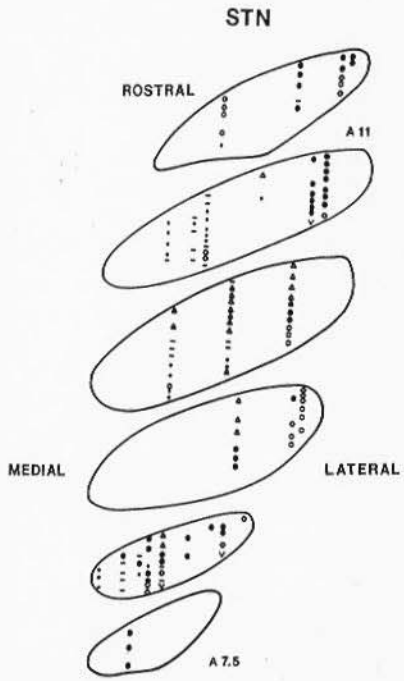

FIG. 6. Location of cell types in STN. Data from 2 hemispheres of same animal are plotted on outline drawings from 1 hemisphere. Conventions and symbols are same as in Fig. 2.

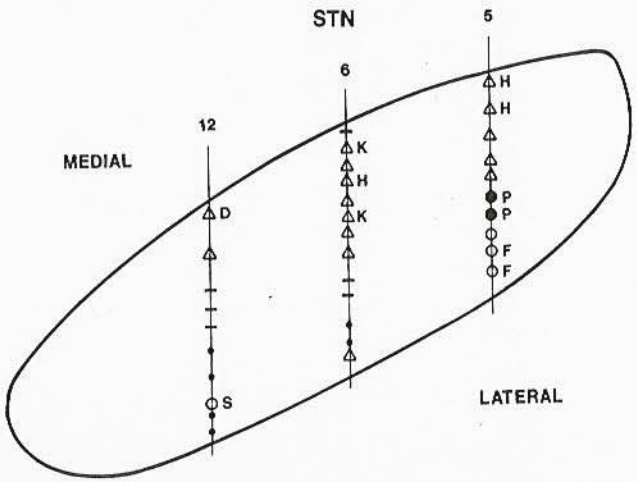

FIG. 7. Examples of clustering of cells with similar functional properties within STN. Conventions are same as those in Fig. 3. In addition D, distal; P, proximal; F, face; and S, swallowing.

generally occupied the ventrolateral regions. In the central portion of the nucleus in the rostrocaudal dimension, a mediolateral segregation of the representation of the leg, arm, and face was present, with the leg dorsomedial, the face ventrolateral, and the arm between. A small number of cells in the rostromedial portions was consistently activated after some delay following the delivery of juice, suggesting a relation to swallowing.

An occasional clustering of neurons with similar properties along the penetration was observed in the STN in a manner similar to, but not as clear as, that in GP. This is seen in Fig. 7, which shows data from three adjacent electrode penetrations. As in GP, cells related to each portion of the arm and leg were located at several sites in the nucleus.

Responses to load application

Changes in neuronal discharge rate following sudden application of loads were observed in all three structures studied at latencies as short as 40 ms. Examples from GPi and STN are shown in Fig. 8. Figure 9 shows the distribution of latencies of the first change in cell discharge after load application in GPe and GPi. Neuronal responses were usually directional, i.e., responses occurred for a single direction of displacement or were reciprocal.

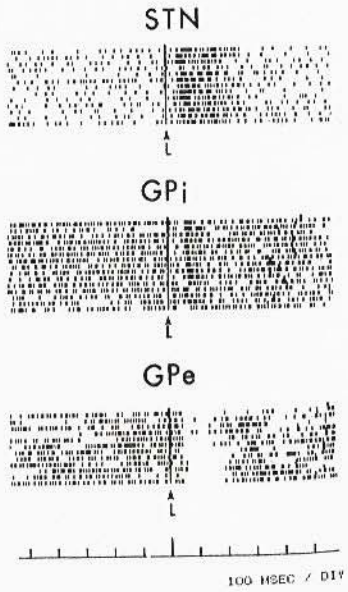

FIG. 8. Rasters of activity of 3 cells in STN, GPi, and GPe, whose discharge changed at short latency in response load application (L).

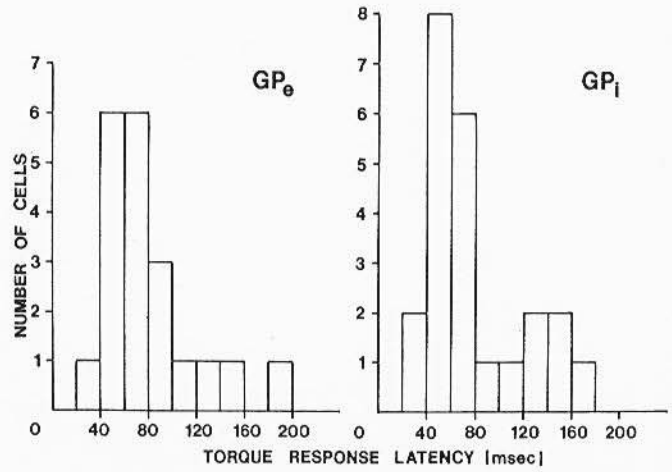

FIG. 9. Distribution of onset times of changes in neuronal discharge in following load application.

DISCUSSION

Relations to active movement and responses to sensory stimuli

The finding that a large proportion of neurons in both segments of GP and the STN are related to active movements of the extremities provides further evidence for a role of the basal ganglia in the control of limb movements. This is consistent with the profound disturbances of limb movements in Parkinson's disease, the primary involvement of the limbs in hemiballismus and chorea, as well as the finding of disruptive effects on both distal and proximal arm movements in the trained monkey by reversible cooling (23) of the basal ganglia. These findings are also in accord with the heavy projection to the basal ganglia from the limb areas of the motor and somatosensory cortices (22, 26, 30, 31).

The present study has also shown that the activity of "task-related" neurons is not necessarily related to movements of the body part being monitored in a behavioral paradigm. This is not surprising because, even when movements are restricted to a single joint, associated movements, postural adjustments, or fixations of remote or proximal body parts may occur. Therefore it is important to determine that a task-related cell is in fact related to movements of the body part under study, before any correlation with behavior or quantitative analyses of cell discharge in relation to movement parameters are attempted. This study of neuronal response properties was in part undertaken to ensure that the task-related neurons studied and analyzed in detail, reported on earlier (21), were in fact related to the arm movements monitored during performance of the tasks. The problem of spurious correlations is one that potentially confounds all combined behavioral/single cell studies, even those carried out in known somatotopically organized cortical areas such as the motor cortex. This holds true especially for regions such as the globus pallidus, which have no direct connections with the somatotopically organized motor and somatosensory areas of the cortex and whose functional organization is only now becoming understood.

A large proportion of limb-movement related neurons in GPe, GPi, and STN responded to somatosensory stimulation. Joint rotation was the most effective stimulus,

whereas responses to superficial cutaneous or hair stimulation were rare. These results are similar to those obtained in the primate putamen (10), which projects to GP.

It is necessary to comment on the methods of testing for responses to peripheral manipulations, because the question frequently is raised as to whether the neuronal responses to joint rotation and other "passive" manipulations are truly sensory and not simply related to an active movement of the animal in response to the passive manipulation. Although this objection cannot be refuted absolutely by the data presented here, this possibility seems unlikely because *1*) the animals were conditioned to relax during the examination, *2*) the neuronal responses were consistently observed with repeated examination, and *3*) the responses were generally obtained only by specific movements about a single joint or in response to palpation of a discrete area. In addition, the latencies of neuronal responses (40–60 ms) to application of loads to the limb (see *Response to load application*) are most consistent with sensory driving.

Response to load application

Neuronal responses to sudden displacement of the arm at latencies of 40–60 ms were observed in all three structures studied. This indicates that information concerning peripheral events is rapidly conveyed to the basal ganglia. This information is probably transmitted through the cortex, because responses at slightly shorter latencies (25–40 ms) have been observed in the putamen (9) and at even shorter latencies (15–20 ms) in the motor cortex (19). These results, together with the fact that changes in discharge rate of many cells began after the first electromyographic changes and continued throughout the movement in the behavioral paradigm (21), suggest that the basal ganglia may play a role in the control of ongoing movements.

It should be emphasized that, although the responses to joint rotation were usually distinct when present, in the majority of cells exhibiting significant changes in discharge during active arm movements, it was not possible to demonstrate any response to joint rotation or to other passive manipulations. This was particularly true for STN. Note that in this regard, although the STN receives a significant input from the motor and premotor cortices, it does not appear to receive input from the somatosensory cortex (22, 37).

There have been few studies of the responses of pallidal neurons to natural stimulation in the awake primate. In a recent study in the monkey, Iansek and Porter (24) were unable to activate GP neurons by passive manipulations of essentially the same type employed in this study. Their findings conflict in other ways with the results of the present as well as earlier studies. For example, they found that movement-related neurons in the GP were generally located in the most caudal and dorsal regions of the pallidum without any somatotopic arrangement and did not exhibit any discharge in the absence of movement. These workers attributed the differences in spontaneous discharge to the greater degree of relaxation in their animals than in animals studied by others. However, neither in the present study nor in an earlier study (11) were neurons found in either segment of the GP that were silent with the animal at rest. The high discharge rates of GP neurons have also been observed by other investigators (2, 20, 34). In summary, both anatomical (input from the somatosensory cortex) and physiological (present study and Ref. 9) evidence indicate the presence of somatosensory input to the basal ganglia. Earlier results, largely performed in anesthetized and paralyzed animals (see Refs. 29 and 17 for a more detailed discussion) suggested "polysensory" inputs to the striatum and led to a view of the basal ganglia as playing a major role in orienting behavior. However, in the behaving primate we have found in the present study and in the putamen (10) that inputs from the somatic periphery are restricted and modality-specific, with little evidence of convergence from other sensory modalities. This, together with the observed correlation between cell discharge and movement parameters (10, 21), supports a more specific role of basal ganglia in motor function.

Functional organization

The findings of the present study confirm and extend the results of earlier studies (11), which indicated a possible somatotopic organization of limb movement-related neurons within both segments of the GP and provide additional evidence for a similar organization within the STN. Because the GP does not receive direct projections from the cerebral cortex it is not possible to relate the organization apparent in GP to that in the somatotopically organized motor or somatosensory cortices.

Note, however, that the motor representations in GPe and GPi were found essentially in those portions that receive input from he putamen (7, 40). Because a somatotopic organization of the putamen has been shown by both anatomical (30, 31) and physiological studies (9), it is reasonable to assume that the observed somatotopic organization of movement-related neurons in GPe and GPi results in a large part from the topographic projections from the putamen to these structures (7, 40).

The somatotopic organization in the STN revealed by present studies is generally consistent with that indicated by anatomical studies (22, 38), which showed topographically organized projections from the motor cortex to the lateral portions of the STN with the representation of the face ventrolateral, the leg dorsomedial, and the arm between. The STN also receives a topographically organized projection from GPe that appears to conform to the scheme described here, i.e., the ventral (face) portion of GPe projects to the most lateral portion of the STN, the more dorsal (leg area) to the middle portion, and the central (arm area) to the area between the leg and face areas (5, 28). Reciprocal, topographically organized projections from the STN to both pallidal segments have also been reported (36), which are likewise consistent with the scheme observed in the present studies. From the above considerations, it appears that the somatotopic organization in these closely related nuclei is due to the topographically organized interconnections between them. The arm area of the putamen, for example, projects to the arm areas of GPe and GPi. The arm area of GPe projects to the arm area of STN that in turn projects back to arm areas in both GPe and GPi. On the input side, the arm areas in the putamen and the STN receive projections from the arm areas of the motor and premotor cortex.

Another important feature of the motor representation in the basal ganglia revealed by these studies is the long rostrocaudal extent of the limb areas in GPe, GPi, and STN. This finding is consistent with the known pattern of projections from the motor cortex to the putamen (25, 30) and the subsequent projections from the putamen to the GP (7, 40). Additional physiological evidence for the extensive rostrocaudal representation of the limbs has been observed in the primate putamen in recent single-cell studies (9). The more restricted rostrocaudal extent of the leg representation in GPe, GPi, and STN observed in these studies is unexplained. This may in part reflect an inherent bias in this study for identifying cells related to orofacial and arm movements because the animals were trained to perform an arm-movement task and received a juice reward during the task. In addition, the leg was more difficult to examine because of the animal's seated posture.

The present studies failed to reveal any simple somatotopic representation of the different portions (proximal and distal) of the limbs within the arm and leg areas of GP and STN. For example, instead of a single wrist, elbow, or shoulder subarea within the larger arm area, neurons related to each part of the limb were found at several different sites. A similar lack of internal organization within the arm and leg area of the primate putamen has been observed as well (9). The present study is inadequate to assess the fine grain internal organization of the limb areas in GP and STN. More closely spaced penetrations might help to reveal the shape, size, and discreteness of the clusters of cells related to different parts of the arm. It is likewise possible that such studies might reveal a more continuous representation.

A further unknown is whether separate clusters might ultimately influence different areas in motor and premotor cortex. This is a distinct possibility because both the pallidothalamic (28, 32) and thalamocortical (27) projections are topographically organized. A recent study indicates that a portion of pallidal output is directed to the supplemental motor area via the thalamic nucleus ventralis lateralis pars oralis, VLo, (39). It is likely that the caudal regions of GPi project to VLo, whereas the more rostral regions project to the thalamic nucleus ventralis anterior (VA).

organization in the basal ganglia demonstrated by these studies is consistent with a large clinicopathologic literature pointing to such an organization in the basal ganglia (16). The question of somatotopy has been examined in experimental animals, primarily in the primate model of hemiballismus resulting from coagulative lesions of the STN. Analysis of such cases suggested that the arm representation was caudal and the leg rostral (4). The present study indicates that such a simple organization is not the case, because the arm representation extends throughout the rostrocaudal extent of the nucleus. In view of the present findings, it is now clear why lesions of the STN almost invariably result in involuntary movements of either the leg alone or the arm and leg together, but never of the arm alone. Although the leg representation is located in the dorsal portion of the nucleus, the arm representation appears to extend over the entire extent of the nucleus almost surrounding the leg area inferiorly as of the dorsal portion of the STN might selectively destroy the leg area, but lesions involving the arm area would almost invariably involve the leg area as well, unless they were placed at the extreme poles of the nucleus. It is of interest that in a single monkey a lesion in the caudal pole of the nucleus resulted in transient dyskinesia involving only the arm (35).

The existence of a general somatotopic organization of movement-related neurons in the putamen, GP, and STN provides an anatomical/physiological substrate for the appearance of involuntary movements confined to a single body part (leg, arm, or face) or portion thereof in disorders such as chorea, athetosia, dystonia, ballism, and tardive dyskinesia.

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