Strio-pallidal projection in the monkey

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The corpus striatum in the mammalian brain appears to receive only two major groups of afferents: from the intralaminar nuclei of the thalamus and from most areas of the cerebral cortex. A common feature of both groups of afferents is their well-developed topographical organization. Rostral and caudal parts of the thalamus and cortex are related to the corresponding parts of the striatum (Powell and Cowan, 1956; Webster, 1961, 1965; Carman, Cowan, and Powell, 1963); in the medio-lateral dimension the organization is more complex, and does not conform, as might have been supposed, to the simple division of the striatum into a medial caudate nucleus and a laterally placed putamen. Instead, the available evidence suggests that the efferents from the greater part of the cerebral cortex and most of the intralaminar nuclei terminate on both sides of the internal capsule. Thus, for example, in the rabbit the cortex on the dorso-lateral surface of the hemisphere sends fibres both to the caudate and putamen (Carman *et al.*, 1963), and in the monkey, following a lesion in the centromedian nucleus degenerating fibres can be traced into both the caudate and putamen (Mehler, 1966).

In view of this evidence it was of some interest to determine whether the functional organization imposed upon the architectonically homogeneous striatum by its afferents is reflected also in its efferent connexions. Our attention was drawn to this question several years ago when studying the thalamo-striate connexions (Powell and Cowan, 1956) because in most of the material used in that study discrete areas of intense gliosis were observed in different parts of the globus pallidus and substantia nigra with experiments involving varying portions of the caudate nucleus and putamen. The publication in 1960 and 1962 of papers by Voneida and by Szabo on the distribution of striatal efferents showed a close correspondence between the pattern of the projection of the striatum as determined by the Nauta method and our own findings on the distribution of gliosis in our earlier material and in several additional brains prepared since that time (Powell and Cowan, 1966). It was considered worthwhile, therefore, to put our observations on record not only because they provide independent con-

firmation of the organization of strio-pallidal and strio-nigral connexions, but also because they demonstrate the value of the study of the distribution of gliosis as an analytical method in fibre systems in which the direction of conduction is known.

The organized nature of the afferent and efferent connexions of the striatum has assumed greater significance with the demonstration by Nauta and Mehler (1966) that the small-celled external segment of the globus pallidus sends fibres only to the subthalamic nucleus, whereas the large-celled inner segment is related to the thalamus and midbrain. Their additional finding that part of the projection from the internal segment is to the centromedian nucleus is of particular interest: first, because it may provide a 'circular pathway' from the striatum to the globus pallidus and thalamus, and back to the striatum; second, because of the substantial projection to the intralaminar nuclei of the thalamus (including the centromedian nucleus) from the cerebral cortex (Auer, 1956; Niimi, Kishi, Miki, and Fujita, 1963; Astruc, 1964; Petras, 1964; Mehler, 1966; Powell and Cowan, 1966).

In the present paper, on the basis of our own and other workers' findings on the strio-pallidal projection, an attempt will be made to synthesize some of the recent anatomical work on the inter-relationships between the cerebral cortex, thalamus, and the striopallidum.

MATERIAL AND METHODS

The brains of 28 monkeys (*Macaca mulatta*) were available for this study (cf. Powell and Cowan, 1956, 1966). In 26 of these brains lesions of varying size had been placed in either the caudate nucleus or in the putamen. The lesions in the putamen were all placed stereotactically with the aid of Olszewski's Atlas (1952). Several of those in the caudate nucleus were made in the same way, but a number were placed under direct vision, through a transcallosal approach to the lateral ventricle. In a few of the brains bilateral lesions had been placed, but they were always in distinctly different parts of the striatum on the two sides. The remaining two brains had large neocortical lesions, without involvement of the striatum, and were used as controls to show that incidental involvement of cortical projection fibres does not contribute significantly

to the gliosis seen in the globus pallidus after striatal lesions.

The animals were allowed to survive for periods ranging from one to four months after operation, following which the brains were removed, fixed either in 70% alcohol and 2% acetic acid or in 10% formalin and embedded in paraffin wax. From the serial sections cut throughout the extent of the cerebral hemisphere a regular one-in-five or one-in-ten series was routinely mounted and stained with thionin.

RESULTS

As the lesions in the striatum and the distribution of the resulting gliosis in the globus pallidus in several of the brains are similar both in their site and extent, only a small number of representative experiments will be described in detail. The first two experiments demonstrate that localized lesions, either in the putamen or in the caudate nucleus, result in heavy gliosis in distinctly different parts of the globus pallidus. In the brain of monkey OM 21 a narrow lesion was placed in the ventro-lateral part of the putamen; the damage extends from just behind the rostral end of the putamen back to the level of junction of its rostral and middle halves (Fig. 1). In the globus pallidus there is a focus of intense gliosis in the ventral and lateral parts of the external segment beginning just behind the caudal limit of the lesion and extending back to about the middle of the antero-posterior extent of that segment. The gliosis reaches as far laterally as the junction between the putamen and globus pallidus, and medially for a short distance into the internal segment; just as its medio-lateral and supero-inferior limits are sharply defined so it stops quite abruptly over the space of a few sections at both its rostral and caudal ends. It may be noted that within the area of gliosis there does not appear to be any appreciable change
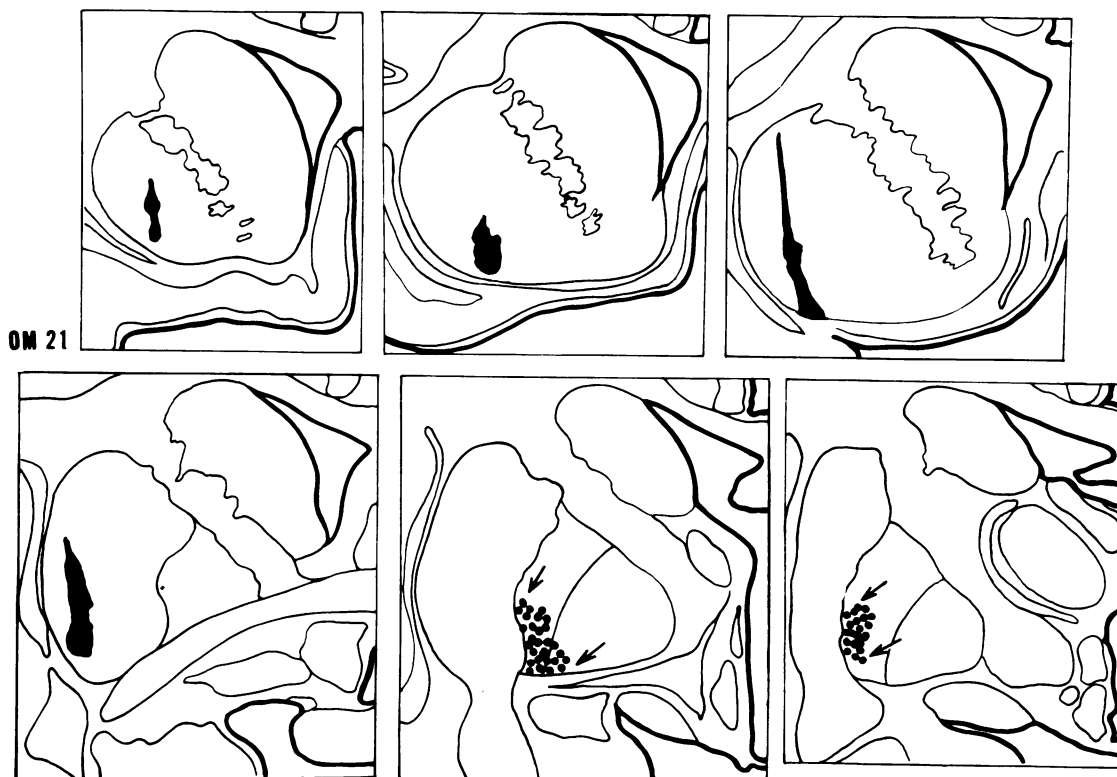

FIG. 1. *Diagram to show the site and extent of the lesion in the putamen in experiment OM 21 and the distribution of the resulting gliosis in the globus pallidus. In this and the subsequent illustrations in which only one lesion is shown, the area of the striatal damage is indicated in solid black and the pallidal gliosis marked by bold arrows and filled-in circles.*
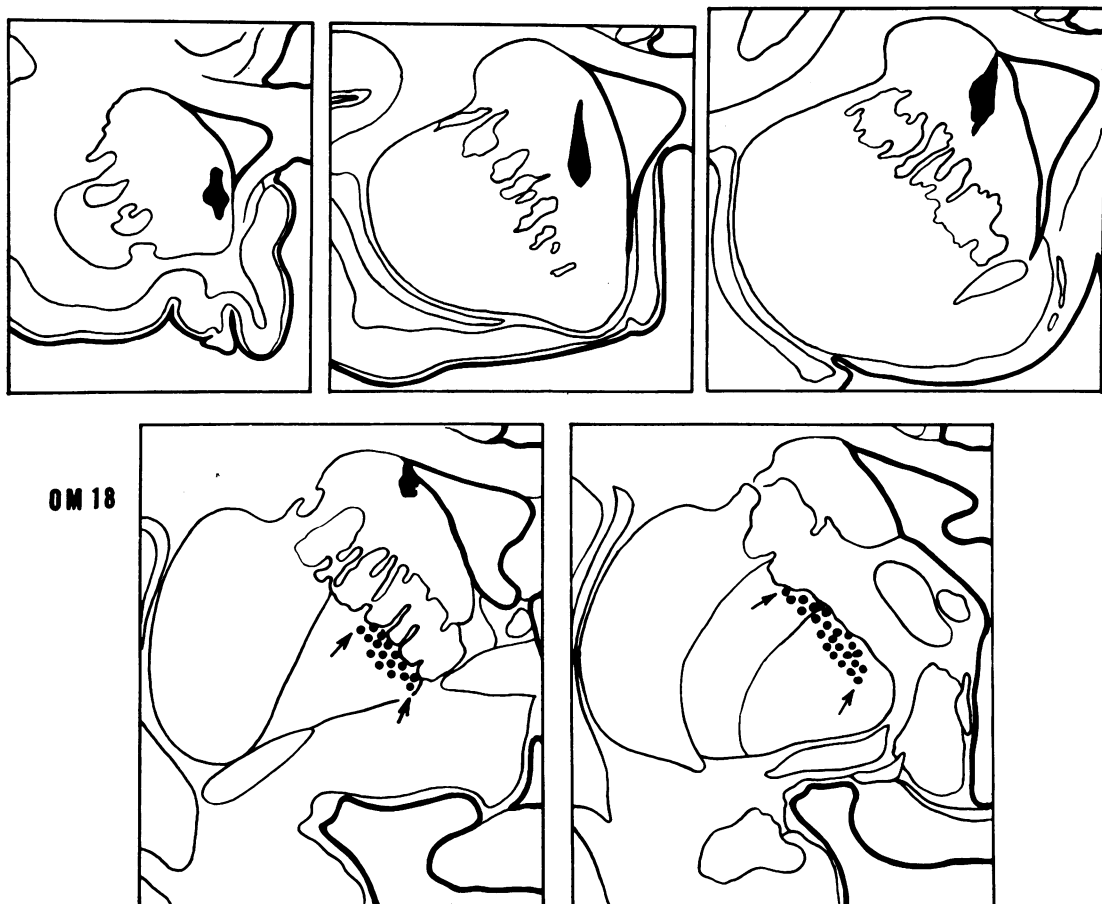
FIG. 2.   *The lesion in the head of the caudate nucleus together with the pallidal gliosis in experiment OM 18.*

in the number, size, or staining of the pallidal neurones, although, of course, they are more compactly arranged than normal.

The findings in this brain may be compared with those in experiment OM 18 in which the lesion is situated in the head of the caudate nucleus. Again, the damage begins just behind the rostral end of the caudate as a small, oval area of destruction close to the ventricular margin; further posteriorly the lesion occupies a more lateral position at the junction of the middle and medial thirds of the nucleus, but at no point does it encroach upon the internal capsule (Fig. 2). In the rostral half of the globus pallidus there is a dense band of gliosis along the dorso-medial border of both the external and internal segments immediately adjoining the internal capsule. Anteriorly the gliosis occupies only the dorso-medial corner of the external segment, but when traced

posteriorly it comes to involve the dorso-lateral part of the internal segment. The similarity in the antero-posterior extent of the gliosis in the pallidum in these two brains is almost certainly correlated with the fact that the lesions in the two cases are more or less co-extensive in this dimension. In the medio-lateral dimension, on the other hand, there is a distinct topographical difference in the distribution of the gliosis within the pallidum as a whole.

The next group of six experiments has been selected to illustrate in more detail the principles of the organization of the projection of the putamen upon the globus pallidus. The site and extent of the lesions in the first two of these experiments are shown in Figure 3. In experiment OM 9 the lesion occupies a considerable part of the dorso-lateral region of the putamen from just in front of the middle of its antero-posterior extent back almost to

FIG. 3. *The site and extent of the lesions in experiments OM 9 (solid black) and OM 7 (cross-hatching) and the ensuing gliosis in the pallidum (filled-in and open circles, respectively).*

its caudal end, while that in OM 7 is in the most ventral part of the putamen extending over approximately the caudal one-fourth of its antero-posterior extent; in OM 7 the most ventral part of the lesion also extends through the white matter inferior to the putamen to involve the tail of the caudate nucleus. In both brains areas of dense gliosis are found in the globus pallidus. That due to the more dorsal lesion in OM 9 occupies a wedge-shaped area, the base of which coincides with the junction between the putamen and pallidum, while the apex reaches for a short distance into the internal segment of the globus pallidus (Fig. 4). The gliosis is found over approximately the middle three-fifths of the antero-posterior extent of the globus pallidus which corresponds reasonably well with the relative antero-posterior extent of the lesion in the putamen. The gliosis in OM 7, on the other hand, is confined to a triangular area in the most ventral part of the globus pallidus over its caudal one-fourth. Together, these two experiments establish one feature of the pattern of the projection of the putamen upon the globus pallidus in showing that the ventral part of the

putamen projects to the corresponding part of the globus pallidus while dorsal parts of the putamen are related to more dorsal regions within the pallidum. But it should be noted that the most dorsal quarter of the globus pallidus is free of gliosis in OM 9 despite the fact that the lesion in this case extends right up to the dorsal margin of the putamen. The significance of this observation will be discussed more fully later, but it may be recalled that the gliosis resulting from the lesion in the caudate in experiment OM 18 occupies this area, but at a slightly more rostral level. That there is a comparable medio-lateral organization in the projection of the putamen is illustrated by the findings in the next two experiments.

In experiment OM 8, there is a narrow electrolytic lesion along the lateral edge of the putamen involving approximately the middle third of its antero-posterior extent (Fig. 5). The resulting gliosis in the globus pallidus is restricted to a small area in the external segment only from about the level of the posterior limit of the lesion back to about the middle of its antero-posterior extent leaving the most
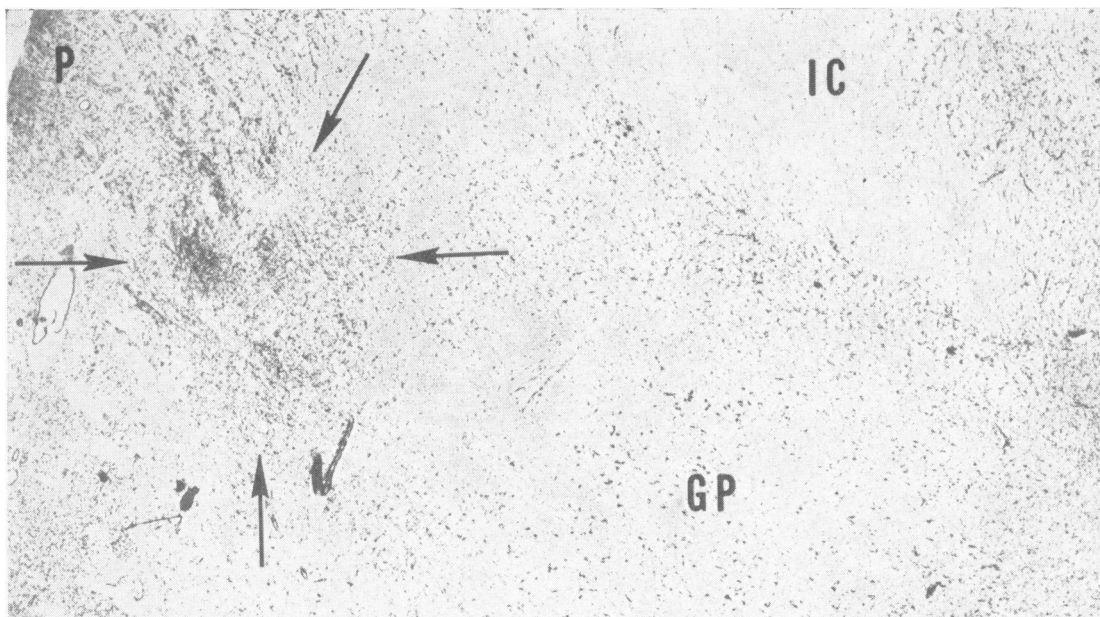
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FIG. 4.   *A low-power photomicrograph to show the intensity of the gliosis in the lateral part of the globus pallidus in experiment OM 9. The margins of the affected area are indicated by the arrows. P—putamen; GP—globus pallidus; IC—internal capsule. × 28.*
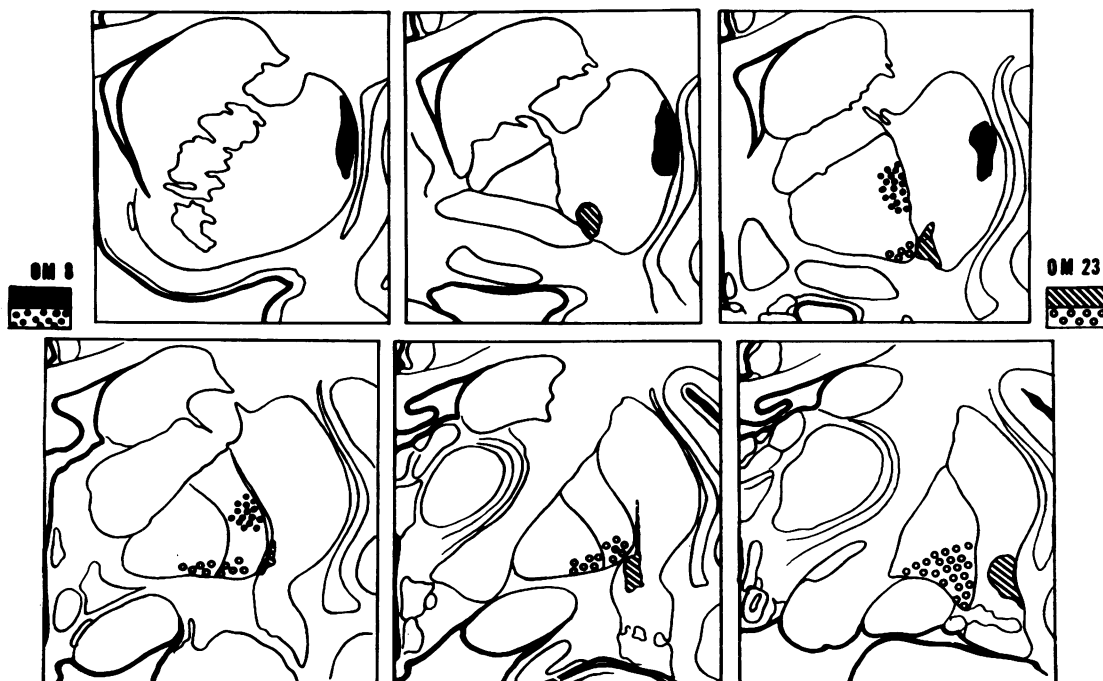

FIG. 5.   *Tracings of representative sections through the basal ganglia in experiment OM 8 to show the extent of the lesion and the distribution of the resulting gliosis in this brain (solid black and filled-in circles, respectively), together with superimposed tracings of the lesion and gliosis in experiment OM 23 (hatching and open circles).*

anterior part of the external segment and the whole of the internal segment free of gliosis. In the other experiment, OM 23, the ventro-medial edge of the putamen has been damaged in its caudal half, and in this brain the gliosis involves both segments of the globus pallidus but only in their most ventral parts. Again, as Fig. 5 shows, the antero-posterior extent of the gliosis corresponds quite closely to that of the lesion.

In Fig. 6 a composite diagram is shown of the extent of the lesions at one level, together with the resulting gliosis, in two additional experiments, OM 5 R and OM 22, together with OM 23. This clearly indicates that with lesions which are situated progressively more medially in the putamen, the gliosis in the globus pallidus comes to occupy progressively more of its medio-lateral extent, and in particular, comes to involve the internal as well as the external pallidal segment. Whether the gliosis in the external segment after a medially placed lesion, such as OM 23, is due solely to the interruption of fibres from more peripheral parts of the putamen or whether the medial part of the putamen projects to both segments cannot be resolved. The above experiments, and all others with lesions in the putamen, are consistent in showing quite clearly that the putamino-pallidal projection is distinctly organized in all dimensions and that it is confined to the ventro-lateral two-thirds to three-quarters of the globus pallidus. The experiments which follow demonstrate a similar degree of organization within the projection of the caudate nucleus to the dorso-medial part of the pallidum.

The first of these experiments, OM 34, is described for two reasons. First, it is the largest lesion of the caudate nucleus which we have been able to place without additional involvement of the internal capsule, and secondly, because a comparison of the findings in this case with others in which there are smaller, centrally placed lesions in the caudate head strongly suggests that with small central lesions a considerable number of fibres from the peripheral part of the caudate are inevitably interrupted. The large lesion in the head of the caudate nucleus in experiment OM 34 was placed by way of a trans-callosal approach. The damage extends from the anterior end of the striatum back almost to the level of the junction of the head and body of the nucleus and is greatest at about the middle of the antero-posterior extent of the lesion where all but the lateral
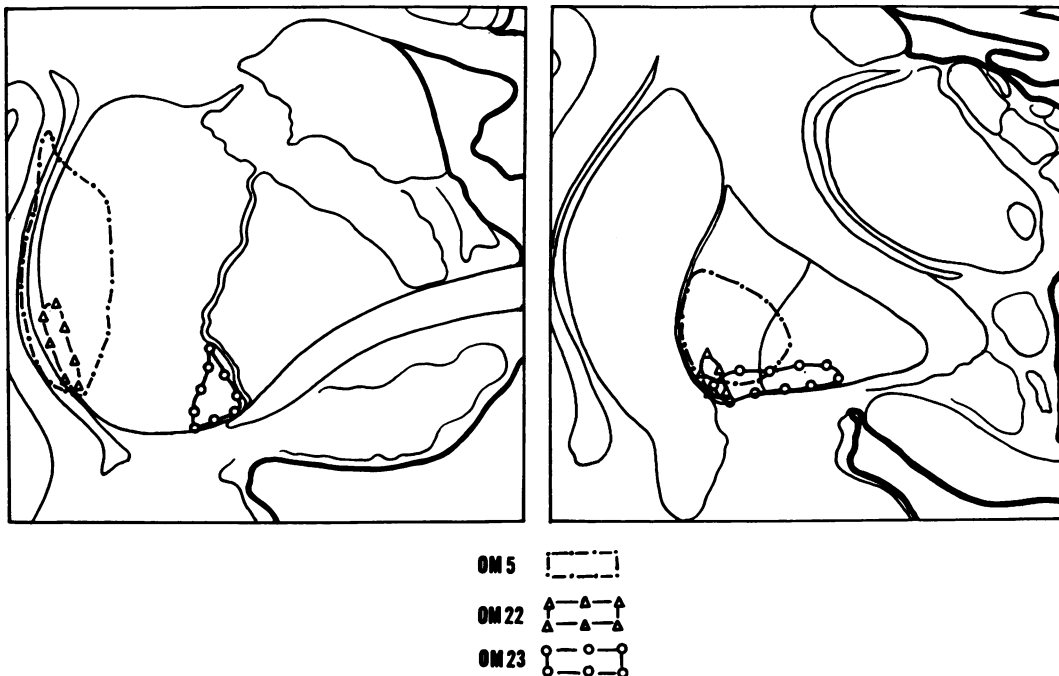

OM 5

OM 22

OM 23

FIG. 6. *A composite diagram to show the extent of the lesions at the level of crossing of the anterior commissure and the distribution of the gliosis in the rostral third of the pallidum, in experiment OM 5(R), OM 22, and OM 23. For convenience, all the tracings appear as though on the left side.*
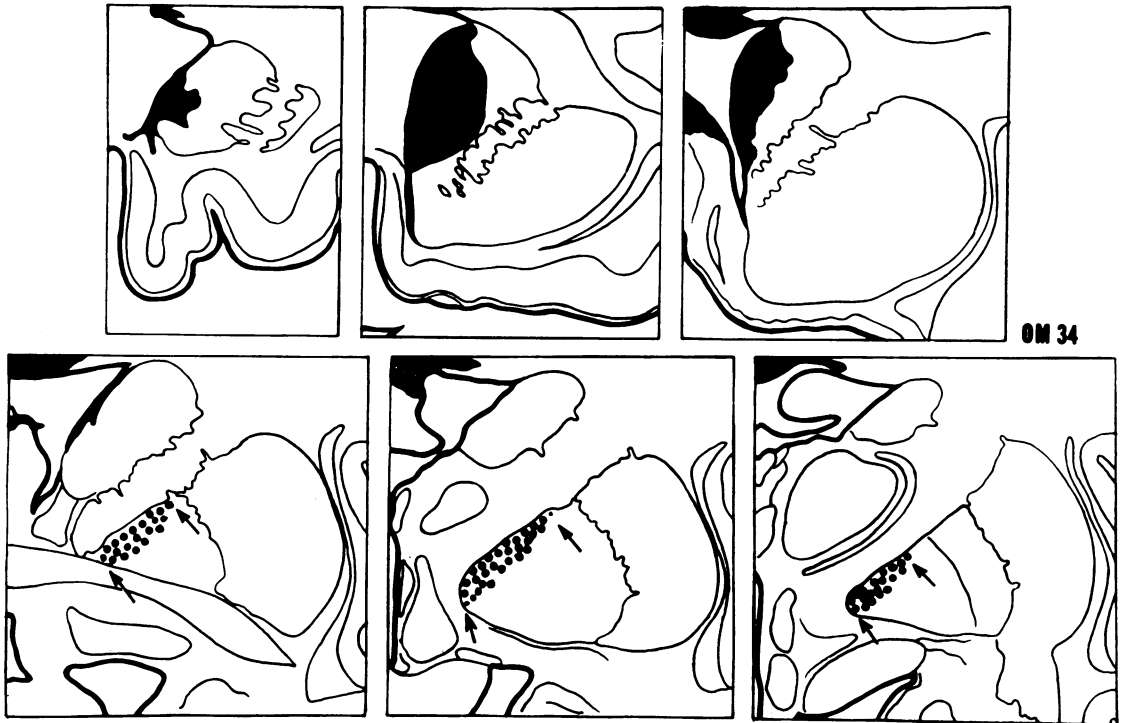
OM 34

FIG. 7.   *The extent of the lesion in the head and the caudate nucleus in experiment OM 34 and the distribution of the gliosis in the dorsomedial part of the globus pallidus.*
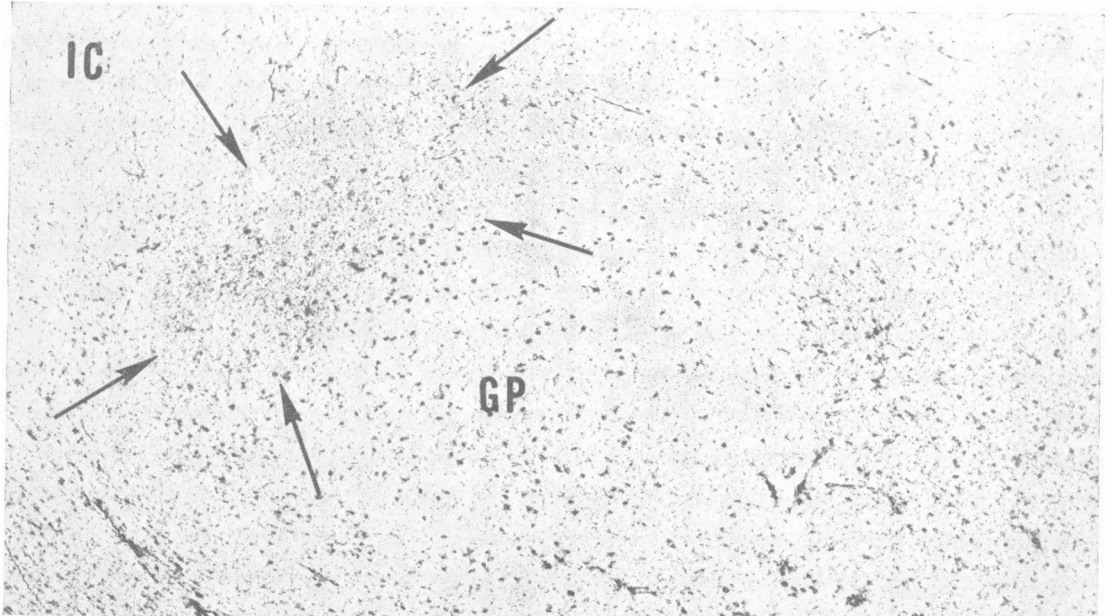

FIG. 8.   *A photomicrograph of the rostral part of the external segment of the globus pallidus in experiment OM 34 to show the intensity of the gliosis (marked by bold arrows) in its dorso-medial one-third adjacent to the internal capsule. IC—internal capsule; GP—globus pallidus. × 28.*

part of the caudate nucleus has been destroyed (Fig. 7). Ventrally, the lateral edge of the lesion abuts upon the internal capsule, but as far as can be determined the fibres of the capsule have not been involved, nor is there any damage on this side to other structures except for the dorsal part of the septum, a small area of the cingulate gyrus, and the rostral half of the corpus callosum. The gliosis in the globus pallidus in this case is found in its dorso-medial part over the anterior two-thirds of its extent (Fig. 8). Anteriorly the area of gliosis occupies approximately the dorso-medial third of the cross-sectional area of the external segment of the globus pallidus, but posteriorly it becomes progressively restricted, so that near its caudal end it is confined to the margin of the internal segment.

In the next two experiments, OM 5(L) and OM 12, small electrolytic lesions were placed along the medial edge of the caudate nucleus (Fig. 9). In

OM 5 the damaged area is limited to the anterior one-third of the head of the caudate, while that in OM 12 extends over the posterior half of the head of the caudate and the anterior one-third of the body. In neither brain has there been any involvement of white matter except over the very limited area of the electrode track. The difference in the antero-posterior positions of the lesions is reflected in the distribution of the gliosis in the globus pallidus in the two brains. Following the more anterior lesion of OM 5 there is a small area of gliosis in the dorso-medial corner of the external segment of the pallidum extending from its anterior end to a level just in front of the appearance of the internal segment. In experiment OM 12, the gliosis is limited to the internal segment, beginning a little behind its anterior end and extending back to about the level of junction of its anterior and middle thirds. Although in both cases the gliosed area is limited to the dorso-medial part of
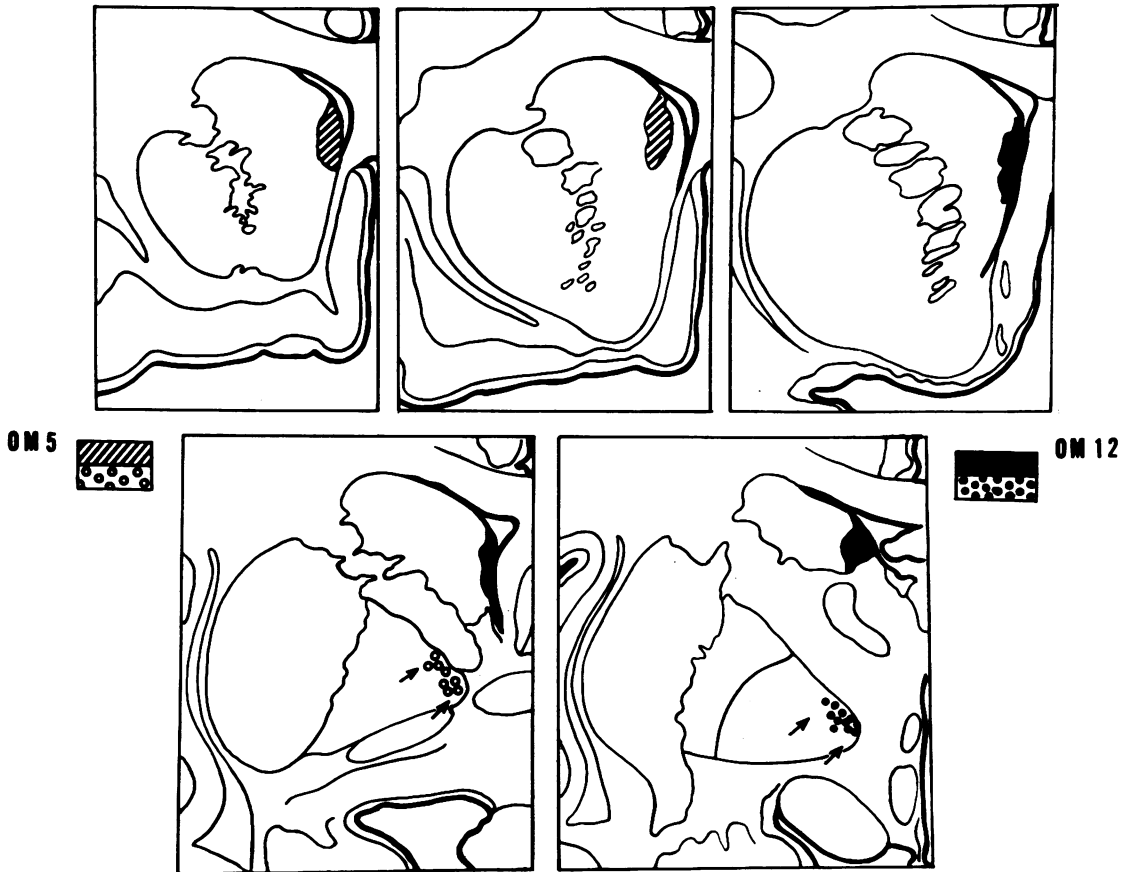

FIG. 9. *The caudate lesions in experiments OM 12 and OM 5(L) (shown in solid black and cross-hatching, respectively) and the ensuing gliosis (filled-in and open circles).*

the pallidum, that in OM 5 extends somewhat more ventrally than the narrow band-like area of gliosis in OM 12. Perhaps the most important feature of these experiments is not simply that the gliosis is at different antero-posterior levels in the globus pallidus but that it is found differentially in the two segments of the pallidum. Although we do not have lesions in all parts of the caudate (and, in particular, any confined to its body and tail), from many experiments with lesions in different parts of the head of the nucleus it is clear that there is a medio-lateral organization within the projection of this part of the caudate upon the dorso-medial sector of the pallidum; thus, a comparison of experiments OM 18 on the one hand, and OM 5 and OM 12 on the other, shows that the more lateral lesion in OM 18
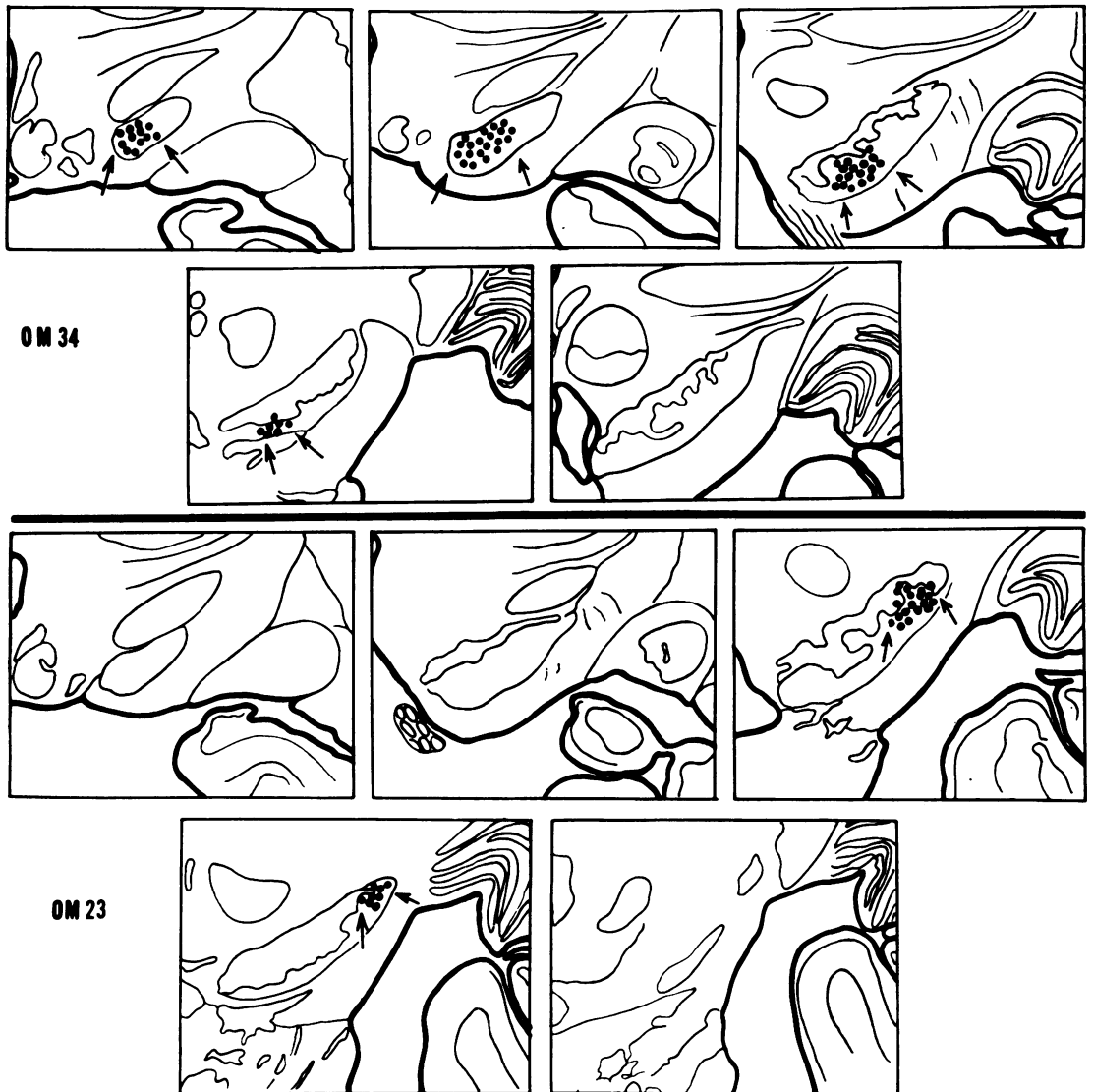
OM 34

OM 23

FIG. 10. *A series of tracings of equally-spaced sections through the substantia nigra in experiments OM 34 (above) and OM 23 (below) to illustrate the difference in distribution of the gliosis after a large lesion in the head of the caudate nucleus (OM 34) and following a lesion in the ventro-medial part of the putamen (OM 23), In each case the gliosis is indicated by coarse dots and the affected area marked by bold arrows.*

has resulted in gliosis situated further laterally in the pallidum than the two more medial lesions of the other experiments.

In some of the experiments which have been described the area of gliosis in the pallidum has extended as a band across most of its medio-lateral extent, but we have not observed gliosis occupying its full dorso-ventral extent after lesions restricted to either the caudate nucleus or the putamen. However, in a number of brains with large lesions involving both the caudate and putamen (together with the intervening part of the internal capsule) the whole dorso-ventral extent of either the external or internal segments shows gliosis. In those cases in which the lateral parts only of the caudate and putamen are damaged the external segment alone is filled with dense gliosis; after lesions which damage the medial parts of the caudate and putamen both pallidal segments show gliosis, possibly due to the interruption of fibres originating in more peripheral parts of the striatum.

The gliosis in the substantia nigra after lesions restricted to the striatum is less intense than that found in the globus pallidus, but in the majority of the experiments which have been used in this study foci of gliosis have been readily detected in different parts of the pars reticulata of the substantia nigra, and together these serve to confirm the general organization of the strio-nigral projection described by Szabo (1962). The findings in two experiments will be described and these clearly illustrate the difference in the projection of the caudate nucleus and the putamen upon the substantia nigra. In OM 34, in which the lesion has destroyed a large part of the head of the caudate nucleus (Fig. 7), quite severe gliosis is found in the anterior half of the substantia nigra. Anteriorly, the gliosis occupies the medial two-thirds of the cross-sectional area of the nucleus, but more posteriorly it decreases, to fill first, the medial half of the nucleus and then, an intermediate segment as shown in Figure 10. While there is slight gliosis in the pars compacta, the most marked change is seen in the pars reticulata extending throughout its whole thickness (Fig. 11). The findings in this experiment may be compared with those in experiment OM 23 in which the lesion is in the postero-medial part of the putamen, and gliosis has occurred in the most lateral part of the substantia nigra over rather more than the posterior half of the nucleus (Fig. 10); again, the gliosis is primarily in the pars reticulata, and at its maximum extent occupies no more than its lateral one-fifth. These

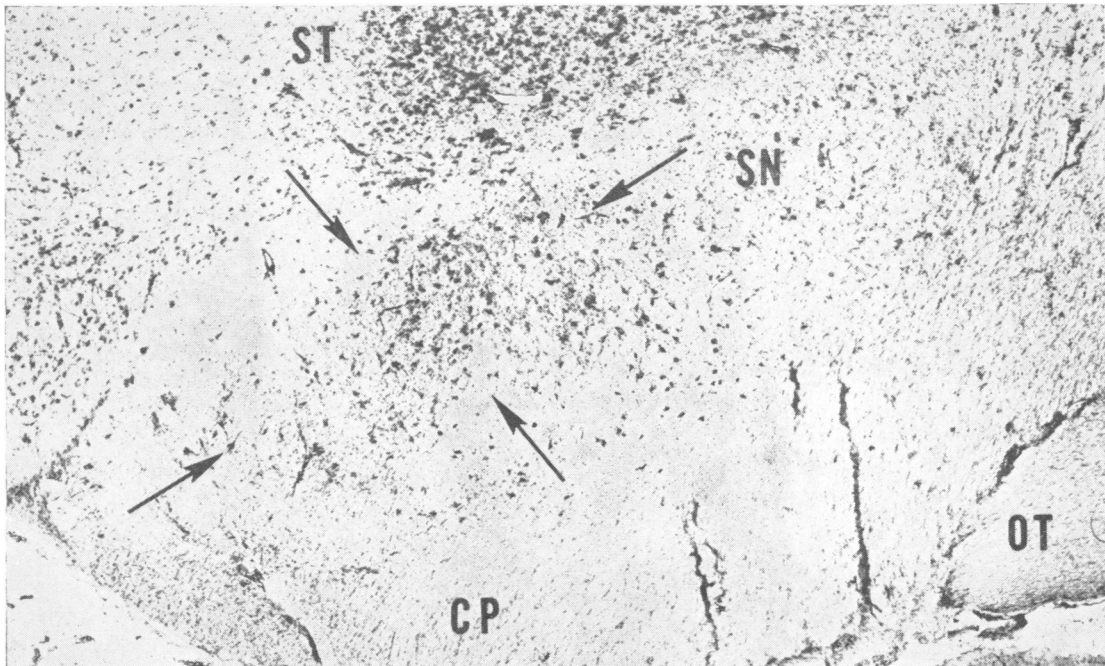

FIG. 11. *A low-power photomicrograph to show the extent of the gliosis (marked by arrows) in the rostral part of the substantia nigra in experiment OM 34. ST—subthalamic nucleus; SN—substantia nigra; CP—cerebral peduncle; OT—optic tract.* × 28.

two experiments by themselves indicate that in the striatal projection upon the substantia nigra there is a well-defined organization in both the antero-posterior and medio-lateral dimensions, and the findings in other experiments with lesions in different parts of the striatum are all consistent with this conclusion.

DISCUSSION

Before going on to discuss the present findings on the organization of the projection of the striatum upon the globus pallidus and its significance in regard to the afferent and efferent connexions of these basal ganglia, it is necessary first to assess the validity of the technique which has been used. As we have pointed out above, this study arose from observations which were made quite incidentally during the course of a study of the cellular degeneration in the thalamus after lesions in the striatum and all the material which has been used was in fact collected with that purpose in view. Had our primary intention been to study the efferent connexions of the striatum the method of choice would undoubtedly have been the axonal degeneration technique of Nauta (1957). The use of gliosis as an indication of fibre connexions may be criticized on the grounds of the relative insensitivity of the method and the impossibility of distinguishing between gliosis which is secondary to degeneration of fibres of passage and that which is found at the site of terminal degeneration. Readily detectable gliosis probably only occurs when there has been substantial fibre loss, and associated with

this is the added difficulty of delimiting with confidence the boundary between an affected area and the surrounding normal neuropil since the gradient of change is usually not sharp. For these reasons it is likely that the actual areas of termination of strio-pallidal fibres may be more or less extensive than our findings suggest, but with this qualification it may reasonably be concluded that the margin of error inherent in the use of this technique is not very great, because the gliosis in the globus pallidus after a striatal lesion is so intense and generally very sharply localized. Moreover, it is worth pointing out that there is remarkably close agreement between the present findings and those of other studies based upon the Nauta method (Johnson and Clemente, 1959; Voneida, 1960; Szabo, 1962; Nauta and Mehler, 1966).

The findings in this and earlier studies (Voneida, 1960; Szabo, 1962; Nauta and Mehler, 1966) are consistent in showing that the efferents from the corpus striatum project radially 'like the spokes of a wheel' (Papez, 1942) upon the globus pallidus and that within the strio-pallidal projection as a whole there is a considerable degree of organization. However, they are inconclusive as to the relationship of different parts of the striatum to the two pallidal segments, and two alternative possibilities must be considered. First, the projection may be organized upon a simple topographical basis, so that the two segments of the pallidum receive fibres from different parts of the striatum as shown in Figure 12A. Secondly, all parts of the striatum may project in an organized manner upon both the external and
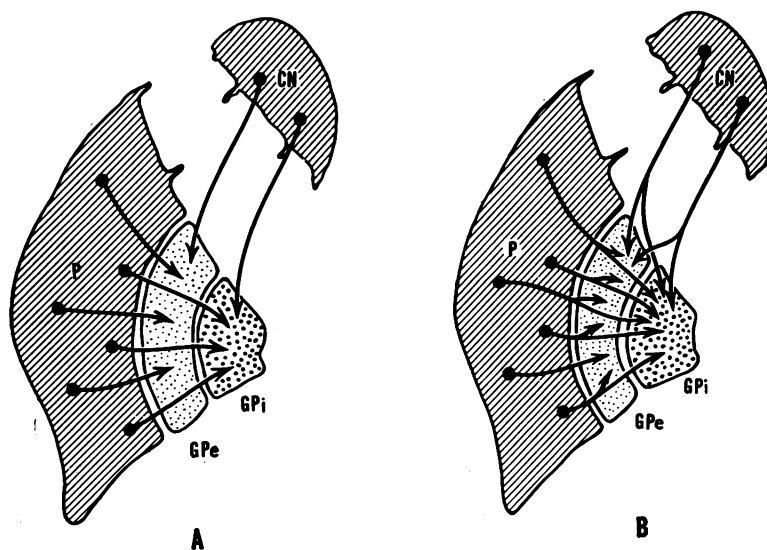

FIG. 12. *Diagram to illustrate the two possible arrangements of strio-pallidal fibres as discussed in the text. CN—caudate nucleus; P—putamen; GPe—external segment of globus pallidus; GPi—internal pallidal segment.*

internal segments as suggested in Figure 12B. In support of the first of these views are the observations that certain parts of the caudate nucleus and putamen project exclusively to either the internal or external pallidal segment. For example, lesions in the peripheral part of the putamen, as in experiment OM 21 of the present series, result in gliosis only in the external segment of the globus pallidus whereas lesions confined to the medial part of the caudate give rise to preterminal degeneration (Voneida, 1960; Szabo, 1962) or gliosis (experiment OM 12 of the present series) limited to the internal pallidal segment. The main reason for considering the second view is the finding that lesions in the putamen and in the greater part of the head of the caudate nucleus appear to result in preterminal degeneration in both segments of the pallidum (Szabo, 1962; Nauta and Mehler, 1966). Whether or not this extensive degeneration is due to the interruption of fibres from more peripheral parts of the striatum is difficult to determine, but it is significant that both Voneida (1960) and Szabo (1962) found degeneration limited to the inner segment when the lesions involved only the medial part of the caudate nucleus. Unfortunately, there is no report of the distribution of fibre degeneration in experiments with lesions in the peripheral parts of the putamen. It would be interesting to know if a lesion in the peripheral part of the putamen, similar to those in OM 8 and OM 22, would result in fibre degeneration only in the external segment of the pallidum, and if this is so, to determine with the Nauta method at what point in the latero-medial extent of the putamen a lesion would produce preterminal degeneration in the internal segment. It is clearly impossible with available neurohistological techniques to resolve the problem as to whether the central parts of the striatum project differentially upon the two pallidal segments or to both segments, but the observation that the gliosis occupies a progressively more internal position within the globus pallidus after more centrally placed lesions strongly suggests that these parts of the striatum project upon the pallidum in essentially the same manner as the peripheral portions.

The question of the relationship of the striatum to the two segments of the globus pallidus has been considered at some length because of the obvious cytoarchitectural differences between the internal and external pallidal segments, and because of the recent evidence that the two segments differ significantly in their efferent connexions. If cytoarchitectural variations reflect differences in connexions, as has been demonstrated in several other regions of the central nervous system, it would follow that if all areas of the striatum project upon both parts of the pallidum the significant factor underlying

cytoarchitectural differences between the two parts of the pallidum must be looked for in their efferent connexions. On the other hand, if the two pallidal segments are in fact connected with different parts of the striatum (and the balance of evidence seems to favour this position), this difference in the afferent connexions must be regarded as a contributory factor to the cytoarchitectural distinction. While this point must remain *sub judice* until more conclusive evidence becomes available, there is unequivocal experimental evidence that the two segments of the globus pallidus differ markedly in their efferent projection. The most detailed study of these connexions is that of Nauta and Mehler (1966) who have shown that the external segment sends fibres only to the subthalamic nucleus whereas the internal segment projects widely upon the thalamus and midbrain tegmentum. Depending upon which view of the organization of the strio-pallidal connexions proves to be correct it would follow that either the peripheral parts of the striatum may influence the subthalamus while the central region of the striatum plays upon the thalamus and midbrain tegmentum, or alternatively the whole striatum may act upon the entire pallidal projection field.

The ordered arrangement of the strio-pallidal projection fibres is only of interest when seen as a part of a larger system of similarly organized connexions involving the afferents to the corpus striatum on the one hand, and the further connexions of the globus pallidus on the other. From an anatomical point of view the striatum and globus pallidus may be regarded as lying at the centre of a complex interrelationship between the cerebral cortex and the thalamus, subthalamus, and midbrain tegmentum. For an understanding of the functional significance of the connexions between the striatum and the pallidum it is, therefore, necessary to consider briefly some of the recent evidence on the connexions of these basal ganglia.

Although the detailed relationship between the cerebral cortex and the corpus striatum has not yet been determined in the Primate brain, it is clear from work on lower mammals (Webster, 1961; 1965; Carman *et al.*, 1963; Carman, Cowan, Powell, and Webster, 1965) that the cortex is undoubtedly a major source of afferents to the caudate nucleus and putamen. Four features of this projection are of particular relevance in the present context. First, it is not limited to certain cortical areas (*e.g.*, the motor cortex or the so-called 'suppressor areas') but appears to be contributed to by the entire cerebral cortex; secondly, the fibres from the cortex converge in a well-organized topographical manner upon the striatum as a whole, so that cortical areas appear to be related to a medio-laterally disposed

band within the striatum often including parts of both the caudate nucleus and the putamen; thirdly, all parts of the caudate nucleus and putamen receive cortical afferents, and, fourthly, there is a bilateral projection to the striatum from the sensori-motor cortex. This means that different regions within the striatum are under the influence of cortical areas having distinctly different functions and this must be reflected also in the strio-pallidal projection.

The question of the nature of the relationship of the intralaminar nuclei of the thalamus and the striatum is still unresolved, but there is a substantial body of evidence to suggest that they form a second important source of afferents to the striatum (Mehler, 1966; Powell and Cowan, 1956, 1966). This thalamo-striate projection resembles that from the cortex in at least two respects: it is topographically organized and it is known that certain of the nuclei (notably the centromedian) send fibres into both the caudate nucleus and the putamen. At present, the significance of these connexions is rather obscure, but it may be important for an understanding of the strio-pallidal projection to point out that the intralaminar nuclei themselves receive fibres in an ordered manner from widespread areas of the cerebral cortex and that some of these nuclei are also connected with the dentate nucleus of the cerebellum (Mehler, 1966). Through these various pathways there is a considerable convergence of cortical, thalamic, and cerebellar influences upon the striatum. It follows from the nature of the strio-pallidal projection that there is even greater convergence of effects upon the cells of the globus pallidus, and because of the organized nature of these connexions, it is clear that parts of the globus pallidus (and probably even the two pallidal segments) are influenced predominantly by one or other area of the cortex or intralaminar nuclei of the thalamus.

One conclusion to be drawn from these studies is that the strio-pallidum is strategically placed to sample the activity of the entire cerebral cortex (through the cortico-striate connexions), to integrate this with the resultant activity of the intralaminar nuclei of the thalamus, and to affect in turn the activity of one component of the intralaminar system (the centromedian nucleus) and the motor area of the cortex (through the pallidal projection to the ventral nuclei of the thalamus). In this connexion it may be noted that the thalamic nuclei to which the internal pallidal segment projects are both closely related to the motor cortex, the ventral nuclei being reciprocally connected to the motor area while the centromedian nucleus receives a substantial projection from it (Astruc, 1964; Petras, 1964; Mehler, 1966; Powell and Cowan, 1966). Furthermore, it
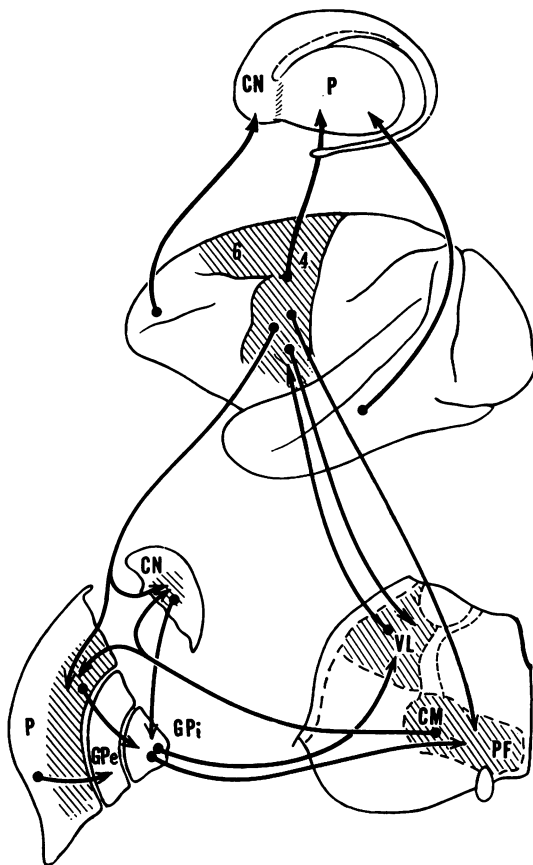

FIG. 13. *A diagrammatic illustration to show some of the major connexions between the cerebral cortex, striatum, globus pallidus, and thalamus. For sake of clarity the connexions with the motor cortex have been emphasized (see text) and those with the subthalamus, substantia nigra and midbrain tegmentum have been omitted. It should be pointed out that the cortico-striate projection in the upper part of the figure shows only its general topographical organization with respect to the striatum as a whole, and should not be taken to imply that any specific area of the cortex projects to either the caudate nucleus or to the putamen.*

seems very probable that both the centromedian nucleus and the motor cortex project upon those parts of the caudate nucleus and putamen which send their fibres into the internal pallidal segment. Some of these interrelationships are summarized in Fig. 13; although this shows some of the major interconnexions within the forebrain, the total system of connexions of the strio-pallidum is clearly much more complex as it includes an important descending influence upon the subthalamus and brain-stem.

SUMMARY

The projection of the corpus striatum upon the globus pallidus and substantia nigra has been determined by an analysis of the distribution of gliosis in these structures after a variety of lesions in the caudate nucleus and putamen. The strio-pallidal projection appears to be organized upon a rather simple topographical basis; 'peripheral' parts of the striatum project upon the external segment of the pallidum, but whether the more 'central' parts of the striatum project exclusively upon the internal segment or upon both segments cannot be resolved. The significance of this ordered projection is discussed in relation to other recent evidence on the connexions of the basal ganglia.

REFERENCES

Astruc, J. (1964). Corticofugal fiber degeneration following lesions of area 8 (frontal eye field) in Macaca mulatta. *Anat. Rec.*, **148**, 256.

Auer, J. (1956). Terminal degeneration in the diencephalon after ablation of frontal cortex in the cat. *J. Anat. (Lond.)*, **90**, 30-41.

Carman, J. B., Cowan, W. M., and Powell, T. P. S. (1963). The organization of the cortico-striate connexions in the rabbit. *Brain*, **86**, 525-562.

——, ——, ——, and Webster, K. E. (1965). A bilateral cortico-striate projection. *J. Neurol. Neurosurg. Psychiat.*, **28**, 71-77.

Johnson, T. N., and Clemente, C. D. (1959). An experimental study of the fiber connections between the putamen, globus pallidus, ventral thalamus, and midbrain tegmentum in cat. *J. comp. Neurol.*, **113**, 83-101.

Mehler, W. R. (1966). Further notes on the Centre Médian Nucleus of Luys. In *Thalamic Integration of Sensory and Motor Activities*, edited by D. P. Purpura, M. B. Carpenter, and M. D. Yahr. Columbia University Press, New York. (In Press.)

Nauta, W. J. H. (1957). In *New Research Techniques of Neuroanatomy*, pp. 17-26. Edited by W. F. Windle. Thomas, Springfield, Ill.

——, and Mehler, W. R. (1966). Projections of the lentiform nucleus in the monkey. *Brain Res.*, **1**, 3-42.

Niimi, K., Kishi, S., Miki, M., and Fujita, S. (1963). An experimental study of the course and termination of the projection fibers from cortical areas 4 and 6 in the cat. *Folia psychiat. neurol. jap.*, **17**, 167-216.

Olszewski, J. (1952). *The Thalamus of the Macaca mulatta*: An Atlas for Use with the Stereotaxic Instrument. Karger, Basel.

Papez, J. W. (1942). A summary of fiber connections of the basal ganglia with each other and with other portions of the brain. *Res. Publ. Ass. nerv. ment. Dis.*, **21**, 21-68.

Petras, J. M. (1964). Some fiber connections of the precentral cortex (areas 4 and 6) with the diencephalon in the monkey (Macaca mulatta). *Anat. Rec.*, **148**, 322.

Powell, T. P. S., and Cowan, W. M. (1956). A study of thalamo-striate relations in the monkey. *Brain*, **79**, 364-390.

——, —— (1966). The interpretation of the degenerative changes in the intralaminar nuclei of the thalamus. *J. Neurol. Neurosurg. Psychiat.*, in the Press.

Szabo, J. (1962). Topical distribution of the striatal efferents in the monkey. *Exp. Neurol.*, **5**, 21-36.

Voneida, T. J. (1960). An experimental study of the course and destination of fibers arising in the head of the caudate nucleus in the cat and monkey. *J. comp. Neurol.*, **115**, 75-87.

Webster, K. E. (1961). Cortico-striate interrelations in the albino rat. *J. Anat. (Lond.)*, **95**, 532-544.

—— (1965). The cortico-striatal projection in the cat. *Ibid.*, **99**, 329-337.