# Cerebellar Pathways to Ventral Midbrain and Nigra

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This study on cat and rat indicates that the cerebellar nuclei connect with a continuum of cells located on either side of midline in the ventral tegmentum of the midbrain. The following nuclei are located within this region: nigra, ruber, interpeduncularis, ventral tegmental (Tsai), and linearis rostralis. The nucleus fastigii projection is primarily ipsilateral to this region by way of a medial and dorsal pathway (accessory brachium conjunctivum). A greater number of these fibers terminates in medial as contrasted to lateral structures. The projections of nuclei interpositus-dentatus are primarily contralateral and become part of a lateral and ventral pathway through the brachium conjunctivum. Reduced-silver methods and horseradish peroxidase-treated materials furnish some evidence for a small Purkinje cell connection directly to the ventral tegmental area. Biochemical studies on dopamine levels in the forebrain indicate there is an increase ipsilateral to the cerebellar cortical lesion whereas a lesion in nucleus fastigii results in a decrease of dopamine levels in ipsilateral forebrain. Some cerebellar influences on catecholamine systems are discussed.

## INTRODUCTION

Cerebellar interaction with the functions of the extrapyramidal system are so widely recognized in the clinical and basic science fields that additional comments appear superfluous. However, surprisingly few studies have been made on cerebellar connections to ventral midbrain centers related to the extrapyramidal system. Of special interest is the ventral tegmental area and substantia nigra because of the intimate relationship of these centers to either fibers of passage or cellular activities of the monoamine system. The study is made more timely by the recent demonstration of cerebellar connections to the locus ceruleus (19). The present investigation

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utilizing the recently developed anatomical technique of horseradish peroxidase (15) labeling in conjunction with a silver-impregnation method (9) for detection of fine terminal degenerations was undertaken on cat and rat brains with the belief that a careful study of the ventral tegmentum might furnish new information relevant to cerebellar connections.

## MATERIALS AND METHODS

Twenty adult cat brains with lesions in cerebellar nuclei and/or cortex were studied after preparing the tissues with the Fink–Heimer I method (8). Four additional cat brains were prepared with the Fink–Heimer II method. Postoperative survival time ranged from 7 to 15 days. The material from animals with lesions was from ten cats with either unilateral or bilateral fastigial lesions, four cats with lesions in anterior and middle lobe vermian cortex, six cats with removal of nuclei interpositus and dentatus plus overlying cortex, and four cats with removal of nucleus interpositus plus pars intermedia cortex. Seven brains were sectioned along the parasagittal axis and the others were sectioned through the transverse axis of the brain stem. The precautions given by Heimer (11) on interpretation of potential artifacts have been very useful, especially so in the ventral area where there are numerous small vessels.

Degenerating terminals can be distinguished from stained cytoplasmic organelles resembling silver grains by the simple expediency of changing the depth of ×450 focus under the light microscope. The degenerating terminals appear to be attached to the surface of soma or dendrites whereas the "grains" are deeper in the cytoplasm. The cat brain is relatively free of these artifacts and they are even less troublesome in the rat brain. Tissues were prepared from 12 adult Sprague–Dawley rats of either sex, of which nine were stained by method I and three by method II. Animal groups were according to the following lesion sites: three, unilateral nucleus fastigii; three, one-half cerebellum; two, unilateral nucleus fastigii and nucleus interpositus; two, vermian cortex, lobules III through VII; two, nucleus interpositus and nucleus dentatus. Survival times ranged from 9 to 14 days.

To the above materials were added others obtained from the horseradish peroxidase technique of Lynch et al. (15) and Kievit and Kuypers (13). Each of 16 adult Sprague–Dawley rats was given a single unilateral injection of horseradish peroxidase via a stereotaxically oriented microsyringe (Hamilton) with 0.2 to 0.6 ml 10% aqueous horseradish peroxidase II (Sigma) and was injected during 30 to 60 min into either the ventral tegmental area or substantia nigra or the transitional area between them. Considerable care was taken to maintain peroxidase localization to the required site, and animals which did not meet these requirements were

eliminated from the experimental series. The restrictions were: (i) a large blood cot in the needle track, (ii) extravasation of horseradish peroxidase beyond the ventral tegmental area–substantia nigra site as shown by tan staining of cells and fibers, (iii) injection tract limited to between A 2.5 to 3.2 stereotaxic levels to avoid nucleus ruber, and (iv) evidence of peroxidase either in the cerebrospinal fluid or in the fibers of the cerebral peduncle. Such restrictions eliminated seven animals and emphasizes the need for caution in the use of this technique which is rapidly being adopted in many anatomical laboratories. The animals were anesthetized with Surital 36 to 72 hr after injection, and perfused through the heart with a solution containing 1% paraformaldehyde and 1.25% glutaraldehyde buffered to pH 7.4 for the later experiments and 2% paraformaldehyde and 2.5% glutaraldehyde buffered to pH 7.4 in the first ten animals. Frozen sections were cut at 30 $\mu$m and processed for observation with dark-field microscopy. The localizations of labeled Purkinje and cerebellar nuclear cells were mapped and plotted on enlarged drawings from sagittal and transverse sections.

Additional studies have been done to obtain data on the functional significance of these connections. Thirty male Sprague–Dawley rats weighing between 200 and 250 g were used in these studies on changes in dopamine levels following cerebellar lesions. Animals for sham-operated or cerebellar groups were anesthetized with chloral hydrate and immobilized in a stereotaxic apparatus. Sham-operated rats had left posterior fossa craniectomy with the arachnoid left intact. Other rats had electrolytic lesions of either the left vermian cortex (lobules IV, V, and VI) or vermian cortex plus nucleus fastigii. Direct current of 2.5 to 3.0 mA passed through a bipolar insulated stainless-steel electrode, tapered at the tip, was used to make the lesions. The extent of the lesions was verified by histological examination of Nissl-stained sections. Eight rats with damage to other cerebellar nuclei, structures to the right of the midline, or the brain stem were not included. Characteristically, the lesions involved dorsal and/or anterior nucleus fastigii. Rats were killed by decapitation 3 weeks after surgery. The forebrain was divided into left and right halves by a midsagittal cut. The brain stem and cerebellum were prepared for histological analysis. Forebrain halves were homogenized in iced 0.4 $N$ perchloric acid, and dopamine in the extract was separated by strong cation-exchange chromatography (17). Dopamine was analyzed by a standard fluorimetric assay (3).

## RESULTS

The anatomic data obtained from the cat are presented in detail and those obtained from the rat are presented for comparison with a lower species. There are two ascending pathways from the cerebellum to the

regions studied (Figs. 1A–D). A medial pathway arises from cells located in ipsilateral fastigial nucleus and a questionable one from vermian cortex, supposedly from Purkinje cells. A small contralateral component was present in some preparations, but there was considerable variation in the number of fibers involved within the group. The pathway leaves the cerebellum as fine myelinated fibers overlapping with dorsal one-fourth of brachium conjunctivum and sends short connections to the locus ceruleus. Before reaching the caudal margin of the inferior colliculus the degenerating fibers enter the accessory brachium conjunctivum by coursing dorsally into the ventral–lateral margin of periaqueductal gray area. In this locus they appear adjacent to and part of the dorsal noradrenaline pathway. They travel through this region to reach the level of the oculomotor nucleus where they descend through the region of linearis rostralis to reach the ventral tegmental area where degenerating terminals can be seen on soma and adjacent neuropile (see Figs. 2 and 3).

The second ascending pathway arises from cells in nuclei interpositus and dentatus and pass forward as coarse and medium-size myelinated fibers through the ventral two-thirds of brachium conjunctivum (Figs. 1A–D). They cross the midline at the level of the decussation and continue forward in brachium conjunctivum sending extensive degenerating terminals into nucleus ruber. However, fibers which are smaller in diameter occupy a ventral position and enter into dorsal ventral tegmentum area, substantia nigra, and nucleus interpeduncularis where degenerating terminals can be seen on intrinsic neurons. They overlap with terminations from accessory brachium conjunctivum. Also, like the latter, there are a few bilateral fibers which are present in approximately 20% of the animals. See below for additional details on sites of termination and how the rat differs from the cat.

*Terminations in Substantia Nigra.* Degenerating fibers resulting from lesions in contralateral nuclei interpositus and dentatus enter the medial and dorsal regions of substantia nigra (Fig. 2 A, B) in a limited region immediately lateral to ventral tegmental area. Degenerating terminals can best be seen in parasagittal sections between 3 and 5 mm lateral to midline in brains prepared from 8- to 12-day surviving animals. Scattered degenerating terminals can be found on plump spindle-shape cells (Figs. 2A and B) with a dorsal to ventro-medial orientation. Numerous nearby smaller cells have degenerating terminals along dendritic processes (Figs. 2A and B) and small-fiber degenerating granules may be scattered in the neuropile. Normal-appearing, very small myelinated fibers are randomly distributed in the field and large myelinated fibers are shown in medial lemniscus and in cerebral peduncle. Pars reticulata of substantia nigra was free of degenerating terminals except for one animal which had both a hemispheric
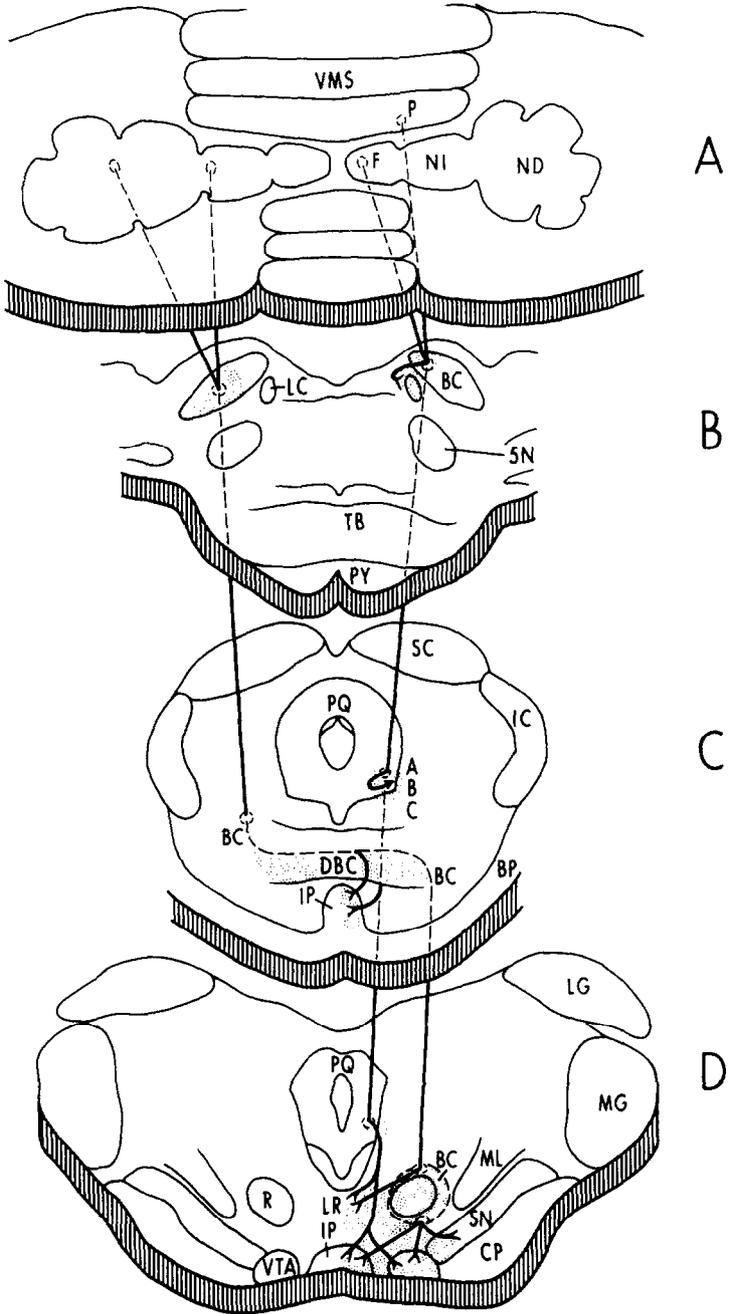
Fig. 1. Summarizing diagrams of cerebellar pathways studied in the cat; shaded regions indicate areas of degeneration. A—Outline drawing of dorsal view of cat

lesion and unilateral involvement of the inferior colliculus. The zone of degenerating terminals extended laterally into pars lateralis of substantia nigra and may partially explain why Carpenter (5) saw degeneration to that structure following cerebellar lesions. We have never seen degenerating terminals in substantia nigra which resulted from lesions limited to the cerebellar cortex, although the flocculo-nodular lobe and paramedian lobules have not been studied.

Lesions restricted to one nucleus fastigii can induce degeneration into a restricted region of pars compacta (substantia nigra) in the cat. We have not seen this in rat, nor have we seen this in any part of substantia nigra other than medial edge of pars compacta adjacent to ventral tegmental area. The projection from nucleus fastigii is considerably smaller than that from nuclei interpositus and dentatus.

*Terminations in Ventral Tegmental Area.* The ventral tegmental area (23) when studied for degenerating terminals following cerebellar lesions shows a heavier distribution than does substantia nigra. The nucleus fastigii projects ipsilaterally through accessory brachium conjunctivum to ventral tegmental area, and in two of the three cats with large lesions in the vermian cortex there were a few scattered degenerating terminals in ventral tegmental area neuropile supposedly arising from Purkinje cells and going directly there. Nuclei interpositus and dentatus axons project to the contra-lateral ventral tegmental area via brachium conjunctivum but in none of the brains studied were degenerating terminals as numerous as were those resulting from fastigial lesions. As expected, the fastigial projection in the cat is larger and more widespread than in the rat. In the latter animal (Fig. 2C) the most consistent changes are seen in the medial zone of ventral tegmental area adjacent to the oculomotor nerve fibers. It extends caudally and into the lateral parts of nucleus interpeduncularis.

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cerebellum showing Purkinje cell (P), nuclei fastigii (F), interpositus (NI), and dentatus (ND), and (VMS) vermis. B—Transverse section of brain stem at posterior 4.0-mm level showing the fastigial fibers overlapping dorsal one-fourth and the interpositus and dentatus fibers in the ventral three-fourths of brachium conjunctivum (BC). Synaptic terminals of degeneration were present in locus ceruleus (LC). 5N—fifth nerve; PY—pyramid; TB—trapezoid body. C—Transverse section at stereotaxic level AP zero, showing the fastigial projection fibers in the accessory brachium conjunctivum (ABC) at edge of periaqueductal gray matter (PQ) and the interpositus and dentatus fibers (BC) in a ventro-lateral position decussating to the contralateral side (DBC). Degenerating terminals were present in ventro-lateral parts of PQ and in lateral parts of nucleus interpeduncularis (IP). SC, IC—superior and inferior colliculi; BP—brachium pontis; LG, MG—lateral and medial geniculate body. D—Transverse section of brain stem at anterior 4.0-mm level showing areas of terminal degeneration in edge of PQ, nucleus linearis rostralis (LR), inter-peduncularis (IP), medial-caudal areas of substantia nigra (SN), and ventral tegmental area (VTA). Extensive changes in nucleus ruber (R) were not studied. A, ×4; B, C, D, ×6.
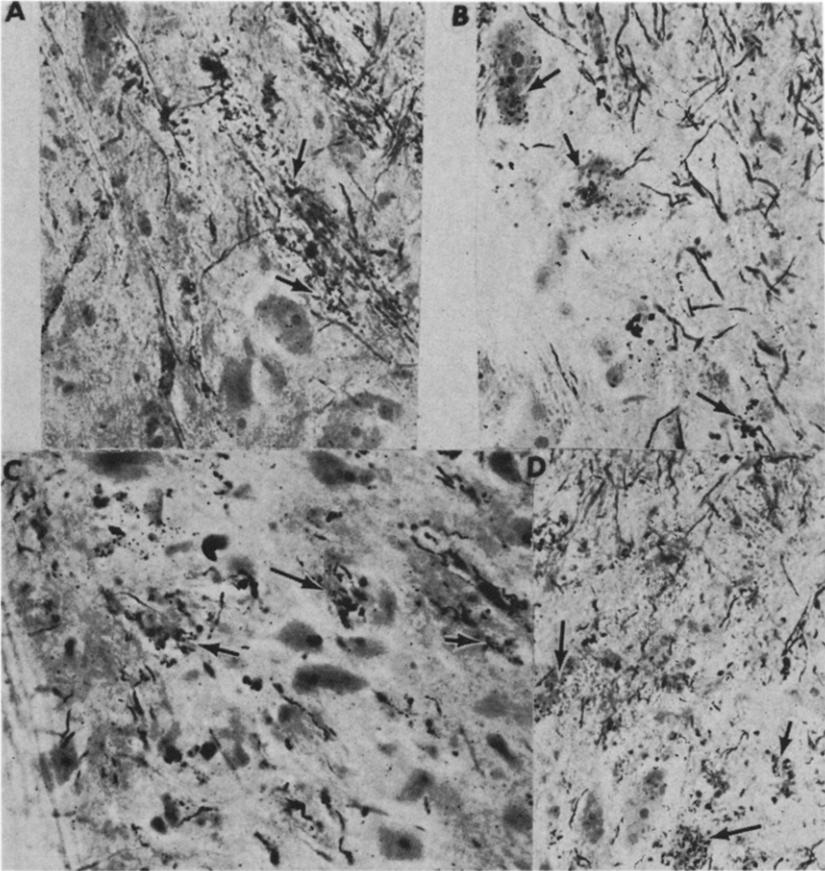
Fig. 2. A and B—Photomicrograph of degenerating fibers and terminals in sub-
stantia nigra. ×560. Cat, 12 days postoperative lesion in left dorsal one-half of
nuclei fastigii and interpositus plus overlying vermis and paravermis. Pars com-
pacta dorsal–medial margin, showing dark granules of degenerating fibers accom-
pained by small fascicles of normal fibers ipsilateral to lesion. Fink–Heimer I stain.
The cells in this section do not show degenerating terminals; however in B such
terminals are shown. This section is about 100 μm medial to A and is adjacent to
ventral tegmental area. C—Rat, ventral tegmental area, 11 days after bilateral nuclei
fastigii and interpositus lesion involving overlying vermis and paravermis. ×560,
Fink–Heimer I. Left margin shows myelinated fibers of left oculomotor nerve. Both
degenerating fibers and terminals are shown. D—Ventral tegmental area, 10 days
after unilateral nucleus fastigii lesion, which involved dorsal three-fourths of nucleus
plus overlying vermis. Cat, Fink–Heimer II. Arrows indicate degenerating terminals
on soma.

The multipolar cells of ventral tegmental area with their randomly
oriented dendrites (Figs. 2C and D) have varying sizes of degenerating
terminals on them and in the neuropile. Like substantia nigra, there are

degenerating terminals on the soma. However, caution need be used in studying this region because of the reticular fibers extending from the walls of fragments of small blood vessels which tend to contaminate the background. In the present material, cerebellar projections localized to subdivisions of ventral tegmental area were difficult to follow although cats
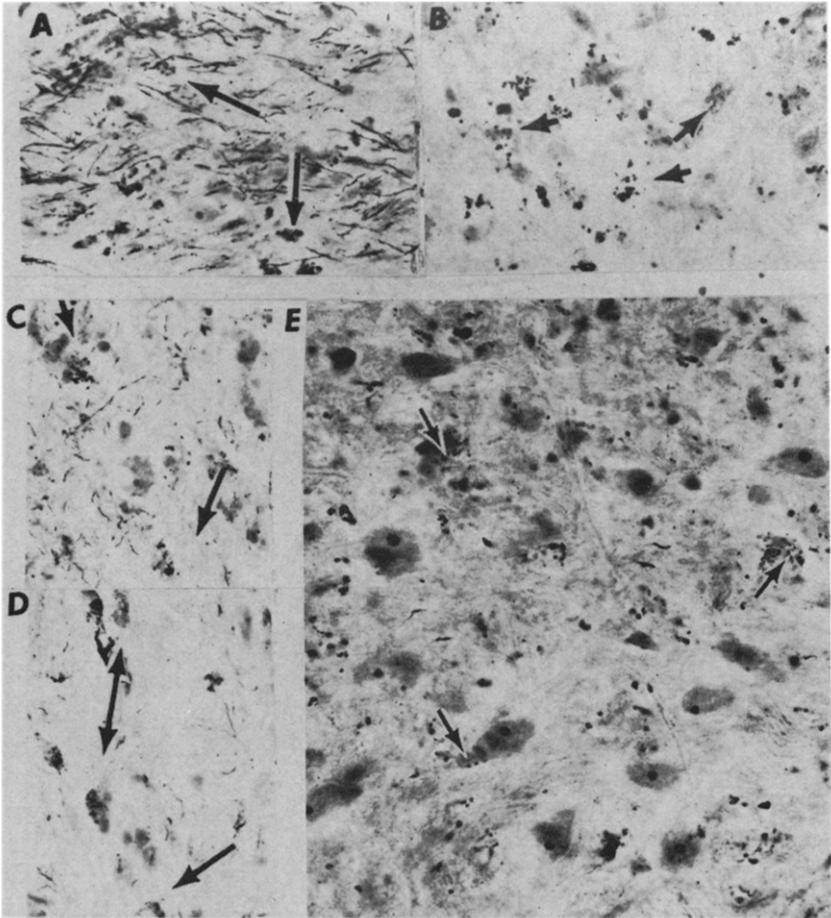


Fig. 3. A and B—Photomicrograph of degenerating terminals and fibers in nucleus interpeduncularis of cat with 12-day bilateral lesion in dorsal one-half of nuclei fastigii–interpositus involving overlying vermis and paravermis. A—pars lateralis showing normal fibers of habenulo-interpeduncular tract intermingling with the degeneration. B—Pars dorsalis. Arrows indicate location of degenerating terminals. ×280, Fink–Heimer I stain. C and D—Same preparation as A and B to show degenerating terminals on small cells in nucleus linearis rostralis. Small fibers course from dorsal (up in photo) to ventral in this nucleus. Fink–Heimer I stain. E—Nucleus linearis rostralis in rat. ×560. Same preparation as C. Left margin represents dorsal area of nucleus. Arrows indicate degenerating terminals.

with larger lateral lesions tend to have increased numbers of degenerating terminals on dendrites of laterally placed cells adjacent to and extending into medial boundaries of substantia nigra (Fig. 2 C, D). Allowing for this overlap, there was a dominant fastigial projection to ventral tegmental area and nuclei interpositus and dentatus projections to substantia nigra pars compacta.

*Terminations in Nucleus Interpeduncularis.* Parasagittal sections have proven especially helpful in the study of this nucleus. As judged by the density of degenerating terminals, some cells in all three cerebellar nuclei send connections to nucleus interpeduncularis with considerable overlap of terminal fields. There was a dominance of fastigial degenerating terminals (Figs. 3A and B) in pars dorsalis with very few resulting from nuclei interpositus and dentatus lesions, and the reverse condition was observed in pars lateralis. In the rat, pars lateralis was the most consistent site of degenerating terminals regardless of the lesion site. Degenerating terminals in pars medialis and the central part of pars dorsalis were consistently few in number even in cats or rats with destruction of all three nuclei. In no case was there evidence for a direct Purkinje cell projection. However, cells in pars lateralis upon which fibers from fasciculus retroflexus terminated also appeared to be in the receptive fields of cerebellar efferents although the latter fibers were greatly outnumbered by those from the retroflexus bundles. In keeping with the nomenclature of Ives (12), pars interfascicularis is considered part of nucleus linearis rostralis.

*Terminations in Nucleus Linearis Rostralis.* Taber et al. (22) have described nucleus linearis rostralis as the most anterior nucleus of the raphe group with cell bodies forming a thin band between the midline and the oculomotor axons. The cells have widespread ascending connections. Many of the fine fibers from ipsilateral nucleus fastigii traversing accessory brachium conjunctivum pass through this nucleus on their ventral course to ventral tegmental area. Some fibers terminate on the vertically oriented dendrites, but many more pass through and send collaterals to soma, especially those in ventral and anterior locations (Figs. 3C and D). After lesions of contralateral nuclei interpositus and dentatus, degenerating terminals can be seen in the neuropile between the cell columns (Figs. 3C and D) of nucleus linearis rostralis which extends caudally to the cephalic margin of the decussion of brachii conjunctivi where fine fibers, probably collaterals, leave the ventral margin of this decussation to pass among the cells. Projection fibers from nucleus fastigii tend to be more prominent in anterior nucleus linearis rostralis and pars interfascicularis. As shown in Fig. 3E, there are many degenerating terminals in the rat nucleus linearis rostralis following cerebellar lesions, but our material is not adequate to determine the total extent of this projection.
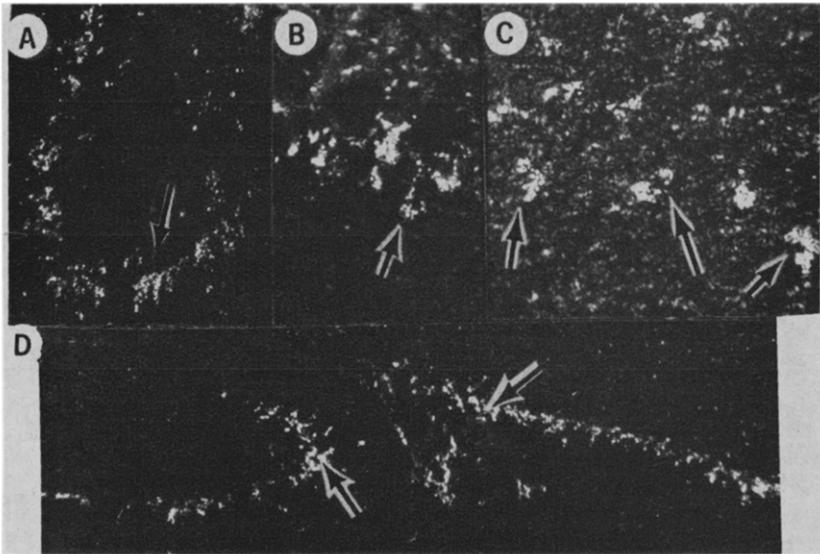
FIG. 4. Dark-field photographs of cerebellum of rat treated with horseradish peroxidase 3 days previously. Local injection into ventral tegmental area but spread to medial substantia nigra. A—Single row of labeled Purkinje cells in ventral part of anterior lobe folium. Arrow points toward cell body to molecular layer. ×140. B—Same preparation as A except ×280. Note label in dendrites as well as soma of adjacent Purkinje cell. C—Arrows point to large cells in nucleus fastigii. Rat treated as A. and B. D—Lower magnification (×105) showing single row of labeled Purkinje cells in vermian and hemispheric parts of lobule II ipsilateral to injection.

*Horseradish Peroxidase Studies.* The following studies on rats add supportive data to two aspects of the findings on the cat. Using the technique of labeling cell bodies with the reaction products of horseradish peroxidase according to the methods of Kievit et al. (13) and Lynch et al. (15), 16 Sprague–Dawley adult rats of either sex were injected and killed 1.5 to 3 days later for dark-field microscopical studies on the brain stem. Sham-operated animals were injected with equal amounts of saline under identical experimental conditions and at identical stereotaxic sites. Care was taken to avoid direct spread of horseradish peroxidase to any surface areas of brain stem. As shown in Fig. 4, a rim of labeled Purkinje cells was found in the deep folia of the anterior vermis. Nuclear or Purkinje cells in the contralateral hemisphere were not labeled. This indicates that unwanted spread of peroxidase to thalamic structures did not occur because the crossed nuclei dentatus–interpositus pathway was not involved.

These data can be interpreted to indicate retrograde transport of horseradish peroxidase from the ventral tegmental area–substantia nigra ipsilateral site via axon and axon terminals to the cell bodies and proximal

TABLE 1

Effect of Left Vermian Cortex or Left Fastigial Nucleus Lesions on
Forebrain Dopamine Concentration[a]

| Group (n) | Dopamine (nmol/g) | | Left vs right Significance (P) |
|---|---|---|---|
| | Left forebrain | Right forebrain | |
| Control (7) | 5.61 ± 0.16 | 5.57 ± 0.27 | n.s. |
| Sham-operated (6) | 6.19 ± 0.32 | 6.43 ± 0.61 | n.s. |
| Cortex (5) | 6.98 ± 0.31[b] | 5.48 ± 0.33 | <0.01 |
| Nucleus (4) | 5.49 ± 0.39[c] | 6.46 ± 0.41 | <0.05 |

[a] Rats were operated 3 weeks before being killed. Sham-operated rats had left posterior craniectomy without electrode insertion. Cerebellar cortical lesions involved lobules IV, V, and VI, mainly vermis overlying nucleus fastigii, where lesions were limited to the dorsal and anterior portions. After killing, the brain stem was transected at the mesencephalic–diencephalic junction and the forebrain divided into equal halves by a midsagittal cut. Shown are the mean I.S.E. dopamine concentrations in each forebrain half.

[b] $P < 0.01$ compared to control group (t-test).

[c] $P < 0.05$ compared to sham-operated group.

dendrites in the cerebellar cortex. Scattered cells in nucleus fastigii were labeled, which supports the degenerating terminal findings on the cat reported above, i.e., that both cortical and nuclear cells project directly to the ventral tegmental area. The data also suggest, but do not prove, a similar projection to substantia nigra. However, the degenerating terminal studies on the rat have failed to show substantia nigra projections either from cortex or nucleus. This discrepancy cannot be explained. Nor can the present horseradish peroxidase data clearly eliminate the possibility of involvement of nucleus A 10 because Ungerstedt (24) has pointed out that nuclei A 9 and A 10 are continuous.

*Biochemical Studies.* The biochemical studies summarized in Table 1 show changes in dopamine levels in both groups of operated animals. In animals with cerebellar cortical lesions, dopamine ipsilateral to the lesion was higher. By contrast, lesions of nucleus fastigii were associated with relatively lower dopamine on the side of the lesions. A curious side observation was the small increase in dopamine in sham-operated animals which proved to be statistically insignificant (Table 1).

## DISCUSSION

Numerous studies have been made on cerebellar projections (1, 2, 5, 6, 16) through the brachium conjunctivum following lesions of cerebellar nuclei, but as far as we are aware, none has utilized the advantages of

the Fink–Heimer methods which permit a study of terminal degeneration and enable the investigator to make a more detailed analysis of the areas. Such methods are especially useful where fine fibers or collaterals exist. Parasagittal rather then transverse sections have been especially helpful because in fortuitous cuts longitudinally coursing fibers can be followed through many sections. The recent studies of German and Bowden (9) are relevant to this study because these authors report staining of norepinephrine cell bodies in locus ceruleus of intact monkey with the Fink–Heimer method. This is seldom seen in the cat or rat, even in densely stained material. Personal communication with the authors indicates that they believe it exists in monkeys and man where there are increased amounts of pigmented granules in cells.

Additional study is necessary to sort out the small fibers in accessory brachium conjunctivum from the small fibers in the dorsal noradrenaline pathway at the ventral–lateral margin of periaqueductal gray matter. The cerebellar efferents tend to be larger, but as pointed out by Ungerstedt (24) there can be variability in fiber diameter in the noradrenaline pathway, and this would lead to overlap in fiber size within the accessory brachium conjunctivum fibers. Additional complexities arise since both the cerebellar and the noradrenaline fibers may synapse on periaqueductal gray cells, although we cannot definitely say upon the same cells. Cerebellar fibers reaching the periaqueductal gray area have been described by several workers (2, 6, 16). Earlier, Whiteside and Snider (25) gave electrophysiological evidence of such a projection.

In the present study, it is not possible to say precisely that cerebellar efferents synapse on so-called "5-hydroxytryptamine neurons." In nucleus linearis rostralis, degenerating terminals can be seen on both large and small cells, but more small than large cells were contacted and numerous small fibers of passage made it difficult to quantitate the number of contacts. The earlier paper by Brodal et al. (4) describes connections from the cerebellum to centralis superior and nucleus raphe pontis which extend caudally from the region of linear lineoris rostralis. Of special interest is the projection of nucleus fastigii to these nuclei as well as to nucleus reticularis tegmenti pontis. Recently Eller and Chan-Palay (7) have described a superior centralis (caudal extension of linearis rostralis) projection to the dentate nucleus.

An unpredicted finding was the predominance of fastigial efferents synapsing on cells in the ventral tegmental area while projections from nuclei interpositus–dentatus showed a preference for substantia nigra pars compacta cells which are known to be connected to the corpus striatum (neostriatal dopamine system). Assuming that the vermis represents an older area of the cerebellum, then a relay through ventral tegmentum (10)

to the oldest striatal area would not be surprising, and it might be predicted that the newer lateral hemispheres of the cerebellum would project through nuclei dentatus–interpositus to substantia nigra and thence to neostriatum. In the medial part of pars compacta numerous degenerating terminals were seen on plump spindle-shape cells of nigra which Schwyn and Fox (18), as a result of both light and electron microscopical study, believe give rise to the nigro-striatal fibers associated with dopamine transport. In view of the clinical interest in dopamine systems, these observations on the cerebellum may have considerable significance.

The biochemical studies which show an increase in forebrain dopamine concentrations after lesions of the cerebellar cortex are interpreted to indicate removal of cerebellar inhibitory influences on dopamine nuclei. In addition, the output of nuclear cells are known to be excitatory to efferent centers, the removal of which by means of a fastigial lesion could result in a decrease in dopamine concentrations in the forebrain in light of the anatomical studies which show a fastigial projection to ventral tegmental area in both the cat and rat and a projection to substantia nigra in the cat. This interpretation follows from the finding of Koob et al. (14) that lesions in ventral tegmentum reduce forebrain and nucleus accumbens dopamine concentrations and assumes that an excitatory influence is withdrawn from ventral tegmentum by a fastigial lesion. Not reported here are biochemical studies which show reduction in noradrenaline levels in the forebrain resulting from ipsilateral nucleus fastigii destruction (20). Such findings might be predicted from the demonstration of a cerebellar–ceruleus pathway (19). These biochemical studies suggest that cerebellar pathways to catecholamine neurons are functionally significant and may participate in the regulation of catecholaminergic activity in the brain.

Additional functional studies on these pathways have been made by Snider and Maiti (21) who showed that the effectiveness of cerebellar stimulation on the control of limbic lobe seizures was seriously impaired by pretreatmet of animals with 6-hydroxydopamine which induces chemical lesions in the noradrenaline and dopamine systems but causes no damage to intrinsic cerebellar neurons. This electrophysiological study, when combined with the biochemical observations presently reported, not only enhances the scientific merits of the morphological findings but also pioneers future investigations which may extend into clinical fields and may establish the cerebellum as a contributing center to catecholamine physiology.

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