SOME OBSERVATIONS ON SECONDARY ASCENDING AFFERENT SYSTEMS IN THE CENTRAL NERVOUS SYSTEM

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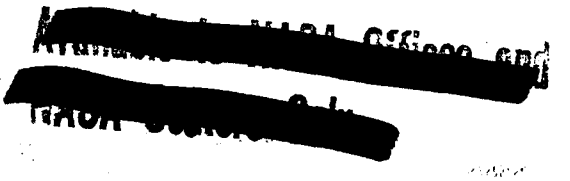
In recent years clinical findings following therapeutic stereotaxic lesions in man have cast serious doubt on the classical notion that the principal ventral posterior lateral (VPL) and medial (VPM) thalamic nuclei represent significant neural relays in what has been called the "central pain pathway" (CPP) 31. In certain respects these failures appear to mirror the results of earlier attempts to relieve pain by ablation of the post-central "sensory" cortex (e.g., 72, 66). Neurological and clinical neurophysiological observations made in such cases appear to suggest that these principal thalamic nuclei (i.e., VPL and VPM) subserve only an adjunctive function in the localization mechanism of the central "epicritic" pain pathway 16. Such data has therefore led investigators to seek other central anatomical foci for surgical intervention to alleviate various forms of deep pain or, as we have conveniently but perhaps erroneously 71 labelled them, "protopathic" pain.

In a previous report 38 we reviewed the attempts at surgical interruption of the so-called "pain tract" at various levels of the neuraxis in respect to anatomical findings in human cordotomy cases. In this report, and in previous studies of ascending spinal connections in primate and subprimate species 34 36 37, emphasis was placed on the remarkable phylogenetic constancy of the terminal patterns of ascending spinal projections found in mammals ranging from the marsupial to man. Morphologically homologous spino-bulbo-reticular, mesencephalic and diencephalic connections were demonstrated in all species examined. The only apparent interspecific spinal projection change that we observed was the complete absence of spino-olivary connections in man and the chimpanzee. In an initial report of experimental comparative neuro-



anatomical findings 34 39 we reported a striking phyletic increase in the number of fibers ascending in the more superficial classical spinothalamic tract (i.e., the neo-spinothalamic) in successively "higher" species in contrast with spinothalamic projections to the intralaminar region which course with the "medial spino-reticular system" 33 that Herrick and Bishop 19 labelled as the "paleo-spinothalamic tract." Figure 1 summarizes these findings and includes recent findings suggested by corresponding studies in sub-mammalian species (fig. 1a) now being carried out at the Walter Reed by Karten 20 and Ebbesson 15.

(Fig. 1, about here - 1/3 page)

The course and distribution of afferent projections to the mesensephalon.

Figure 1 (a to c) schematically demonstrate the medial, more central tegmental course of the paleo-spinothalamic pathway in the sub-primates in contrast with the completely dorso-lateral tegmental course of these fibers found in primates and man (figs. 1d and 1e). Although the terminal connections with the mesencephalon (dorso-lateral circumaqueductal gray and stratum profundum mesencephali) and diencephalon do not change, the apparent phyletic shift in the region of passage of the paleo-spinothalamic fiber projections might explain some of the interspecific differences encountered in functional studies of the systems in question (e.g., 12; 44; 26; 13).

In regards to topological functional differences in the mesencephalic central gray, Skultety 62 concluded that different functional deficits can be demonstrated in cases of lesions in the anterior and posterior regions, respectively, of the structure. The terminal degeneration observed in all of the species we have examined consistently demonstrate the largest number of fiber terminations in the more caudal intercollicular region (e.g., fig. 5 in 38) although some

connections continue to distribute as far rostral as the posterior commissure. Anatomical evidence suggesting the existence of both dorso-lateral and ventro-medial as well as anterior and posterior topological units in the central gray appears in Nauta's 47 demonstration of the "limbic midbrain area." We previously speculated on the possibilities these relationships present for a poly-synaptic CPP potentially available to relay "noxious" stimuli into "vegatative" and/or "limbic" systems 38. Studies in progress indicate that in the cat and rat ascending projections from the dorso-lateral central gray to the "intralaminar" region 47 46 tend to distribute to more medial "paralaminar" cell groups than the intralaminar connections observed in lesions of the ventral central gray and/or the central tegmentum. It is easy to conceive how perpendicularly orientated lesion electrodes directed at the central tegmental region or at ventral regions of the central gray in physiological studies might in passage disrupt the dorso-lateral central gray projections or their afferent fiber connections. These connections will be considered in more detail in a later communciation (see subsequent text).

At the present time the literature reveals little data to support a hypothesis that the dorso-lateral central gray contains any unique CPP mechanism. Valenstein 68, however, concludes from carefully controlled "escape reaction" studies in the rat that stimulation of corresponding dorsal mesencephalic regions demonstrate 90 percent or better "escape efficiency" whereas ventral central gray placements yield less than 90 percent efficiency and central tegmental sites usually less than 75 percent (N.B., 50 percent escape efficiency is neutral in Valenstein's experimental scale). Similarly, the idea still persists that vocalization on stimulation of the mesencephalic

central gray might reflect some kind of a pain mechanism response. In this regard it is of interest to mention studies based upon Shanzer and Wagman's 61 suggestion of utilizing the phenomena as a "physiological landmark" for locating the true Horsley-Clarke horizontal plane in anesthetized monkeys. In experiments in monkeys primarily designed to test the effects of spread of current in different types of electrodes Valenstein and Beer 67 corroborated Shanzer and Wagman's findings. Subsequent histological analysis revealed that the loci at which rhythmic vocalizations could be elicited with the lowest current intensities in bipolar stimulation lie in central gray positions (AP-Zero, lat .1 mm) at the level of or dorsal to the aqueduct. Histological examination further revealed that the sites necessitating increased current intensities occupied central gray regions ventral to the aqueduct and that points negative to even maximal stimulation occupy the central tegmental region.

Clinically, the frequent occurrence of disagreeable postoperative paraesthesias have led most neurosurgeons to abandon mesencephalic tractotomy. The very frequency of such paraesthesias, however, appear highly suggestive that the region contains neural mechanisms immediately relating to the CPP. In connection with White and Sweet's 72 evaluation that mesencephalic interruption of the CPP appears to offer potential value in relieving atypical head and neck neuralgias it might be mentioned that homologous terminal patterns of secondary trigeminal fiber connections to the mesencephalon (dorso-lateral circumaqueductal gray and stratum profundum mesencephali) can be identified in the opossum, rat, racoon and cat 40. It occurred to us, for instance, that experimental control cases demonstrating sites of convergence of secondary spinal and trigeminal pathway projections might present data leading to the identification of focal

points in neural mechanisms subserving the CPP. However, these same studies also demonstrated essentially homologous "trigemino-intralaminar" convergence patterns such as recently reported by Stewart and King 65. To complicate matters further, cerebello-fugal pathways have been found to project to the central gray substance and intralaminar thalamic region with a distribution which is surprisingly comparable with that shown by spinal and trigeminal projections 35 42. Nevertheless, it would be of interest to see what further physiological and behavioral studies involving the dorso-lateral circumaqueductal gray might reveal relative to the role of this region in CPP mechanisms.

The distribution of somesthetic afferent fibers in the posterior thalamus.

Currently, greater interest centers on certain caudally situated thalamic nuclei at the level of the meso-diencephalic transition which suggest possible neural relays in the CPP. Electrophysiological studies indicate that cells included in the so-called magnocellular nucleus of the medial geniculate (MGmc) 73 74 or a more inclusive group of posterior thalamic nuclei labelled as "PO" 54 receive impulses conveyed over secondary somatic afferent pathways such as the spinothalamic. These findings together with an increasing number of clinical reports 63 32 56 of beneficial pain relief from sterotaxic interventions in the corresponding meso-diencephalic area in man have prompted us to re-examine the region in question. Similarly, the reported relationships of certain nuclei in the same general region to the so-called "vestibular" cortex 2 as well as to the "second somatic sensory" cortex (SII) 75 relate immediately to current laboratory tasks. As subsequent speakers are expected to present physiological and clinical data bearing on these regions, I will limit my discussion primarily

to some anatomical observations that I have made on projections to the regions in question.

(Fig. 2, about here - 1/2 page each i.e., Full page)

In hemi-cordotomized cats and monkeys we have observed bilateral connections on cells lying in the region usually identified as the MGmc (Figs. 2c and 2g). It is our impression that the distribution of these connections corresponds more to the delimited, highly responsive, dorso-medial MGmc area indicated by Whitlock and Perl (73 and e.g., their Fig. 6 in 74) than it does to the more extensive "PO" region reported by the Johns Hopkins group 54. In control experiments, uncomplicated lesions of the nucleus gracilis in the monkey revealed connections with comparably situated large cells included in the MGmc region of the contralateral side. The finding of such spinal and lemiscal fiber convergence on these cells as well as on cytologically similar ventral posterior lateral (VPL) neurones led us to concur with Lewandowsky's 28 original interpretation that these "parageniculate" neurones represented only outlying caudal elements of the VPL 37. Although in his initial study of the simian dorsal funicular projections, Bowsher 6 did not specifically mention such connections his later comparison of spinal and lemniscal fiber distributions in the monkey 7 confirmed our observations regarding a dualistic distribution to the VPL as well as to the MGmc. However, it should be pointed out that Bowsher's 7 inclusion of significant spinal projections to the nucleus suprageniculatus (SG), lying dorsad to the MGmc, has never been observed by us in any species in any case. The late Dr. Olszewski 52 pointed out that his delineation of the MGmc and SG in certain macroscopic plates in his atlas was only approximate. However, following Olszewski's cytoarchitectural descriptions of the respective cell types and not literally accepting his pictorial borders of this nucleus, or certain other nuclei for that

matter, we have consistently found that degenerating spinal and lemniscal fibers terminate primarily on the VPL cell types present in the regions usually designated MGmc. We have never observed connections on the medium sized, more compact, oval, dark staining cells constituting the SG nucleus of most cytoarchitectural studies of the thalamus in the cat, monkey and man. Whereas anatomical and physiological evidence indicates that MGmc neurones are cortically dependent, the afferent and efferent connections of the SG are obscure 25.

It should be noted that Bowsher and I are essentially in agreement in the majority of our findings except for certain minor reticular and intralaminar connections in vaguely defined nuclear regions such as the SG already discussed. It should be apparent that our reported differences stem mainly from interpolations of cytoarchitectural atlas delimitations of nuclei rather than from actual differences in findings. I believe that our disagreement in respect to the SG, as well as certain other differences (e.g., connections to the nucleus centrum medianum - see subsequent text), stem from the same verbal communication or "atlas semantic" errors committed by myself (see 37, page 745) and others as a result of the labelling of heterogeneous cellular regions according to this or that atlas. Allotted time does not allow for further discussion of the real importance of these problems but we have repeatedly stated our concern with respect to the serious consequences to which these essentially semantic differences can lead to in initiating erroneous functional and clinical interpretations of anatomical and physiological data (see 38, page 50).

Evidence has recently been introduced that secondary trigeminal fibers also project bilaterally to the MGmc in the cat. Stewart, King and associates 64, 65 concluded that these connections originate only from the nucleus caudalis

trigemini. In view of the fact that they could only elicit potentials in the magnocellular region from stimulation of the caudal subnucleus, and that Carpenter and Hanna 10 failed to mention any such fiber connections originating from the more oral trigeminal nuclear subdivisions, Stewart and King's 64 conclusion seems logical. However, examination of the magnocellular region in a number of cases of lesions of the nucleus of the trigemino-spinal tract not involving the caudal nuclear subdivision reveal some fiber connections terminating in the magnocellular region in question 40.

(Figs. 3 a and b, about here - Full page)

The hiatal-like relationship of the MGmc region to the principal somesthetic thalamic nuclei is best demonstrated in the horizontal plane of section. Figure 3a depicts the passage (large dots) and terminal distribution (small dots) of fiber degeneration observed in Nauta silver sections in a case of unilateral antero-lateral spinal cordotomy at C_3 in the monkey (Case MST6; horizontal series, e.g., in 37). The cytoarchitecture of the region is revealed in a photograph (Fig. 3b) of the adjacent Nissl section (each 25 Nauta silver section in a series is routinely accompanied by a cresylecht violet preparation of an adjoining 50 section). Beginning at the level of the rostral half of the medial geniculate (Fig. 3a), terminal degeneration can be observed on cells intercalated in the degenerating spino-thalamic fascicles coursing through the MGmc region. On the contralateral side, similar but considerably less dense connections appear mainly on homologously located cells. Returning to the ipsilateral side, dense clusters* of terminal degeneration appear throughout the immediately contiguous region described by Olszewski 52 as the nucleus ventralis posterior lateralis, pars caudalis (VPLc). Owing to the plane of section and the rather distorted geometric

* Footnote[1]

shape of the VPL complex in the monkey there appears to be an interruption between the terminals found in the pars caudalis and those distributing to the pars oralis (VPLo). Adjacent sections, however, reveal the continuity of the spinal connections throughout contiguous regions representing the VPL complex.

Olszewski 52 based his division of the VPL on his observation that the pars caudalis contained more heterogeneous cell types than the pars oralis but that both subdivisions degenerate after (total) ablation of the postcentral gyrus (e.g., see 23, 55). Previous authors employing similar cytoarchitectural and experimental evidence have recognized homologous regions which appear under different labels. The VPLc of Olszewski's description, for instance, appears to include the greater part of Krieg's 22 nucleus ventralis posterior inferior (VPI). Disregarding the semantic differences in terms, it is of interest to recall Krieg's speculation based on the early evidence of a double cortical representation of the somesthetic projection systems. Krieg it appears was one of the first to consider the possibility that the predominently small-celled VPI division of the ventral posterior complex might represent the "protopathic" division of the somesthetic system and the large-celled VPL division the "epicritic." Krieg's contention was that a double cortical representation of the sensory projection systems would presume a double nuclear representation in the thalamus (i.e., VPL to SI, VPI to SII). Hassler and Reichert 18 supported such a notion but Hassler 17 recently concluded that extirpation of both sensory cortical areas in man (presumptive SI and SII areas) did not result in pain reduction.

As I interpret it, Hassler 17 based the major premise of his original conclusion principally on his Marchi observations according to which the

spinothalamic "tract" appeared to terminate mainly in a correspondingly restricted basilar VPI-like region (Hassler's V.c. pc) rather than throughout the more extensive VPL complex region that Le Gros Clark 27 and Walker 69 indicated or that Bowsher and I have both confirmed by means of selective silver impregnation studies in the monkey 7, 37 and man 5, 38. It appears, however, that both Bowsher and I have been remiss in not elucidating more clearly the magnitude of the VPL complex delineated with the more sensitive Nauta method 48. Furthermore, existing evidence indicates that no apparent differences exist in the areas of convergence of the spinal and lemniscal projections to caudal and oral segments of the VPL complex. Bowsher 7 states that lemniscal projections in almost complete dorsal funicular nuclei lesions fill the same entire rostro-caudal extent of the VPL that spinal projections cover. His controversial inclusion of "SG" connections in these cases clearly indicates to me that VPLc connections are included in his material. It is possible, however, that differences in synaptic characteristics such as described by Bowsher 7 might account for some of the differences obtained in electrophysiological studies of the region. Bowsher, however, states that the apparent synaptic differences seem to exist only in the principal and intralaminar thalamic distribution areas and that the synaptologies of spinal and lemniscal projections to VPL are identical 7,8. Personally, I will reserve judgement on these synaptic differences until the evidence is documented more fully. Another explanation of the reported differences in cellular potentials recorded in the VPL is the problem of levels of anesthesia, which is discussed in a recent article by Brooks 9.

(Fig. 4, about here - 1/2 to 2/3 page)

Examination of horizontal sections through the diencephalion of the cat (Fig. 4) demonstrates more fully the spatial relationship of the VPL and VPM nuclei to the medial geniculate body and to the intervening posterior thalamic region. The cellular heterogenuity of the latter region indicates one of the difficulties that Poggio and Mountcastle 54 encountered in trying to delimit their "PO" region in the cat. In regards to delineating the "PO" region by electrophysiological means, differences appear in the literature 21, 54, 73. Anatomical studies in the cat by the method of retrograde cell degeneration also appear to have failed to solve the problem due to a number of inherent limitations of the method 58, 30. Let us examine, however, additional evidence gained from antegrade fiber degeneration studies employing the selective silver impregnation methods on the cat.

Excepting certain unresolved differences with the authors in the interpretation of "intralaminar" connections reported by Anderson and Berry 1, their findings in regard to the distribution of spinal projections to the principal thalamic nuclei in the cat present data analogous to our observations. Their figure 12. 1, contrasting the distribution of spinothalamic connections in cases of cervical and thoracic cordotomies, respectively derived from series cut in the horizontal plane, clearly shows the continuity of spinal fiber terminations in cervical cases distributing throughout a zone extending from the MGmc levels to the rostral pole of the VPL (e.g., see Fig. 6b). Their figure 12 depicts a relatively narrow based posterior terminal region intercalated in the zone of passage of the spinothalamic projections extending from the MGmc level rostralwards to the level of the habenulo-interpeduncular tract (HP) and a larger oral zone

encompassing the principal VPL nucleus or pars lateralis of the ventro basal complex (VB) of Rose 57. The section in our figure 4 exhibits corresponding posterior and principal "VB" regions. Closer examination reveals that the denser-celled medial half of the posterior region containing prominent large cells corresponds remarkably well to the relatively narrow posterior terminal region demonstrated by Anderson and Berry 1.

We realize the inherent hazard of such apparently deductive evidence based only on interpretation of another author's figure. However, the Nissl section shown in figure 4 is from a case in which an attemped lesion of the claustrum destroyed the medullary pedicle of the anterior ectosylvian gyrus. The cortico-fugal degeneration in the case delineates a similar conical shaped PO region the apex of which ends in the MGmc. Moreover, evidence obtained from our transverse series (e.g., Figs. 2a to 2c) as well as other cortico-fugal series from cases involving restricted ablations of the SI and SII cortices (e.g., Nauta's Walter Reed collection, cases: CF - 73, 84, 85, 86) or incidental damage to the anterior ectosylvian gyrus (Mehler 40, cases: CLN 4, 6) consistently suggest a similar limitation to the "PO" somesthetic region based on the distribution of cortico-fugal fiber projections. Further evidence suggesting division of "PO" into medial and lateral regions appears in Moore and Goldberg's 45 study of inferior collicular nuclear projections in the cat. These studies confirm that the disputed lateral part of PO and the greater part of MGmc receive inferior collicular rather than spinothalamic connections. We based our labelling of these regions (Figs. 2a - 2c) on similar evidence obtained from control cases of lesions of the inferior colliculus and the auditory cortex (Nauta's Walter Reed collection; CTeg. 129, 152, 154, and CF 39).

In regard to differences in distribution patterns of projections from SI and SII to VB and PO respectively, the available data suggest that both cortical regions distribute fibers not only throughout VB but also to this somewhat more medially restricted PO region which extends caudally into a small zone corresponding to the dorsomedial region of the MGmc as it appears in transverse sections. Intra-cortical connections between the ipsilateral SI and SII regions as well as connections between these regions and their contralateral cortical homologues are suggested in many of the cases cited in the preceding paragraph. Auer's 4 study suggests comparable cortico-thalamic patterns and recently a similar study in the cat by Niimi and associates 51 corroborate these connections.

(Fig. 5a and b, about here - 1/2 - 2/3 page)

In their study of retrograde thalamic degeneration in "VB", Macchi and associates 30 indicate that regional groups of "essential" cells 58 (cortically dependent on SI or SII) and "sustaining" cells (dependent on SI and SII) exist throughout "VB" (PO is not specifically mentioned by these authors). They state that their findings provide evidence against Knighton's 21 earlier conclusions that only the caudal tip of VPM (i.e., MGmc or PO) projects to SII. Figure 5b shows a lesion, placed by means of an electrode directed across the midline from the contralateral side, which involves the most caudal part of the dorso-medial MCmc corresponding to the spinothalamic terminals shown in figure 2c. In this case the corticopetal projections that can be traced beyond the massive fiber degeneration ascending to PO and VB distributes significantly dense terminal degeneration to the deep layers of the ventral half of the anterior ectosylvian gyrus (AEG in fig. 5b) which corresponds to the SII area. Some degenerating fibers can be traced into the gray matter at the bottom of the coronal sulcus

but few, if any, terminals can be demonstrated in the SI region of the sigmoid gyrus. Control cases involving corresponding tectal and pretectal regions with concomitant damage to SG, limitans, pulvinar and/or the medial geniculate, but without involvement of the MGmc region in question, have to date not revealed projections to corresponding regions of the anterior ectosylvian gyrus. The distribution of corticopetal degeneration demonstrated in the latter case appears to support Knighton's 21 findings and, in part, those of Macchi and associates 30. Additional antegrade fiber degeneration studies are needed to clarify the complete mode of connections established by the thalamo-cortical projections from VB and PO suggested by retrograde cell degeneration studies.

(Figs. 6a to d, about here - 1/2 page)

Time restrictions prevented me from preparing a comprehensive re-evaluation of the distribution of spinal fiber projections to the posterior thalamic region in man. The data based on studies in man 17 suggest that subdivisions analogous to those demonstrated in the cat and monkey (Fig. 6) might also exist in man. With respect to the need for additional studies to establish the homologous nature of these connections we plan to re-examine our human spinal cordotomy series and compare the thalamic distributions in these cases with the distributions exhibited in recently acquired medullary cordotomy cases 41. A report of these findings will be presented in a later communciation 43.

Intralaminar afferents and connections of the nucleus centrum medianum.

Experimental evidence of spinal projections to the internal medullary laminar region of the thalamus were called to our attention by Le Gros Clark 27 and Walker 69 in their now classical Marchi studies of ascending projections in the primate. Originally both of these authors concluded that these projections

coursed around or through the nucleus centrum medianum (CM) and distributed to nuclei lying in or adjacent to the internal medullary lamina. Later we 37 corroborated such a course and distribution in comparable studies employing the recently introduced selective silver impregnation method of Nauta 48. In more detailed reports of findings in the monkey 37 and man 38 we reiterated our negation of spinal connections to CM in deference to the positive claims of other investigators employing the Nauta method in studies in man 5 and the cat 1. We attempted to rationalize our negative findings in our 1960, 37 report by pointing out the cytoarchitectural complexities of the CM and the vague boundaries the intralaminar nuclei have with each other as well as with the surrounding principal thalamic nuclei. In this difinitive report we stated:

> "Due to the disparity of opinion among authors in subdividing these groups and, in order to avoid introducing still another terminology, we have attempted to adhere as closely as possible to the scheme of subdivision followed by Olszewski(1952). According to the present findings the intralaminar distribution of spinal fibers is limited to a region encompassing certain small-celled clusters contained within the dorsolateral region of Olszewski's borders of the nucleus parafascicularis, the pars densocellularis and multiformis of the nucleus medialis dorsalis and throughout the nucleus centralis lateralis.... Such distribution essentially limits the significant terminal field of these spinal fibres to the nucleus centralis lateralis and to a number of caudally located cytologically similar cell clusters probably belonging to this nucleus. In order to clarify further the terminal nuclei in question, it should be noted that in none of the cases examined could terminal degeneration be demonstrated in the other intralaminar nuclear subdivisions recognized by Olszewski; viz. centralis superior lateralis, para-centralis or in the caudally situated centre median-parafascicular complex."

The reports of positive anatomical findings taken together with reportedly confirmatory electrophysiological evidence of spinal projections to the CM by Kruger and Albe-Fessard 24 appeared to strengthen Luys' 29 century old idea that the nucleus is a convergence center for all somatic impulses relayed to the thalamus. Subsequently, however, studies on the distribution of projections from the lentiform nuclei 49, 50 revealed that significant numbers of afferent connections of CM originate from the medial segment of the globus pallidus. We noted that these pallido-CM terminals delineate the CM from the nucleus parafascicularis as well as from the predominently small-celled clusters constituting the "intralaminar" nuclei to which ascending spinal, trigeminal and cerebellar projections distribute. In the cat projections of the entopenduncular nucleus -- the long suspected homologue of the medial pallidal segment -- literally outlines the small feline CM again differentiating the nucleus from the "intralaminar" cell groups which receive ascending projections 49. Additional evidence strongly suggesting non-somesthetic function of CM may be drawn from Petras's 53 demonstration that massive numbers of afferent connections with CM descend from the precentral gyrus. More complete documentation of the recent findings bearing of the CM will be reported elsewhere 39. Because of the increasing clinical interest in the CM as a possible focal point in the CPP; generated by Bowsher's 5 report that a component of the spinothalamic tract distributes to the CM in man, a final note of caution must be added.

In studies of the so-called pain tract in man 38 we demonstrated the phylogenetic constancy of the spinal fiber projections to the internal medullary lamina region. In the human these fibers terminate on para-, and intralaminar cell clusters lying dorsomedial to the main masse of the nucleus centrum medianum

exactly as demonstrated in the monkey and other species (see above). Some time ago Bowsher wrote me that he had re-examined his human material including new cases and confirmed that the degeneration of spinal origin is confined to the dorsomedial paralaminar region such as described above which Bowsher in 1957 labelled as "CM" according to Dekaban's 11 tentative delimitation of the nucleus. In other words, regardless of the label placed on the terminal cells in question, the important point is that no spinal or other secondary sensory fiber projection terminate in the large, small-celled nuclear masse, lying ventro-lateral to the internal medullary lamina which represents the true nuclear homologue of the mammalian CM.

In respect to the spinal fibers distributing to intralaminar cell groups we originally concurred with Bowsher 5 and others in the speculation that these elements might represent a neural relay for the more slowly conducting "protopathic" component of the central pain pathway but experimental studies reveal data contradictory to such a hypothesis. Recently, for instance, both Astruc 3 and Petras 53 reported that projections from the pre-motor cortex in the monkey distribute to the same para- and intralaminar cell groups which receive ascending spinal, trigeminal and cerebellar connections. Similarly, the literature indicates that cortical ablation studies have repeatedly demonstrated that the paralaminar cell groups in question (i.e., Olszewski's 52 pars denso-cellularis (MDdc) and multiformis (MDmf) of the nucleus medialis dorsalis) are cortically dependent upon the premotor cortical region 70, 60, 59.

In conclusion then, it appears that recent experimental data argues against the hypothesis that the nucleus centrum medianum or the central lateral, para-, and intralaminar nuclei represent significant neural relays in the central pain pathway. The possibility that CPP mechanisms might be represented by neural structures lying in the posterior thalamus or in the region of the meso-diencephalic transition, as suggested by neurophysiological investigations, appears to be more firmly supported and compatible with findings demonstrated in experimental neuro-anatomical studies.

* FOOTNOTE 1

It should be noted that the VPL terminal clusters, or delimited bursts of pericellular degeneration semi-diagrammatically illustrated in the case of the monkey have not been observed in the cat or other sub-primate species (see; Mehler et al., 37, 38). This more diffuse mode of termination of spinothalamic projections exhibited in the primate species including man might explain some of the paucity of thalamic cellular units reported by Whitlock and Perl 74.

CAPTION FOR FIGURE

Figure 1. Schematic representation of the course and distribution of ascending spinal fiber projections in: a. Submammalian species such as the frog (Ebbesson[15]) and pigeon[20] (Karten[20]). b. opossum. c. cat. d. monkey and e. man. Neo-spinothalamic system (interrupted black) vs. paleo-spinothalamic system (uninterrupted-outline).

CAPTION FOR FIGURE

Figure 2. Semi-diagrammatic representation of the course (heavy dots) and terminal distribution (fine stipple) of degenerating ascending spinal fibers following antero-lateral cordotomy at upper cervical levels in the cat (Figs. 2a to 2d) and monkey (Figs. 2e to 2h). The A-numbers to the right of the sections represented in figures 2a to 2d refer to the millimeters anterior to A-P zero in the Horsley-Clarke coordinate plane.

CAPTION FOR FIGURE

Figure 3. a. Semi-diagrammatic representation of the thalamic distribution of spinal projections exhibited in a horizontal section subsequent to subtotal hemi-section at C_2. Monkey, Case MST6. b. Adjacent section, cresylecht violet stain. Symbols as in preceding figure. The X in figure a identifies the marker hole self evident in figure b. See text for additional explanation.

CAPTION FOR FIGURE

Figure 4. Horizontal section through the mesencephalon and diencephalon of the cat brain at approximately zero in the Horsley-Clarke coordinate plane. Compare with figures 2a to 2d and figures 6a and 6b. Cresylecht violet stain. See text for additional explanation.

CAPTION FOR FIGURE

Figure 5. a. Distribution of corticopetal fibers in case CF 98. AEG: anterior ectosylvian gyrus. ASG: anterior sylvian gyrus RhS: rhinal sulcus. Cd: caudate nucleus. Put: putamen. CL: claustrum b. Lesion. See text for additional explanation.

CAPTION FOR FIGURE

Figure 6. Schematic diagrams summarizing the relationships exhibited in the horizontal plane of the ventral posterior lateral and posterior thalamic nuclear regions in: a. Cat; compare with figure 4. b. Distribution of spinothalamic projections (cross-hatched area) in the cat after Anderson and Berry's[1] figure 12. c. Monkey; compare with figure 3b. Generalized terminal area delineated by spinothalamic projections in figure 3a. Comparison of the findings suggest that a limited medial portion of the so-called magnocellular nucleus (mc) of the medial geniculate (MG) in both species appears to represent the initial terminus, or "porta thalami" (Hassler[17]) of the somesthetic projections which distribute to a caudal or posterior region almost as extensive as the principal nuclear region lying oral to the region in question. See discussion in text.

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ABBREVIATIONS IN ILLUSTRATIONS
FOR CHAPTER _____

BC	Brachium conjunctivum
CI	n. colliculi inferioris
Cl	n. centralis lateralis
CM	n. centrum medianum
CP	Commisura posterior
Cs	Central gray substance
Cun	n.cuneiformis
CSM	n.centralis superior medialis
D	n. Darkschewitsch
GL	n. geniculatus lateralis
GM	n. geniculatus medialis
H	Forel's field H
Hb	Habenula
HP	Habenulo-interpeduncular tract
IP	n. interpeduncularis
LD	n. lateralis dorsalis
Li	n. limitans
LP	n. lateralis posterior
mc	pars magnocellulais (MD or GM)
MD	n.medialis dorsalis
--dc	-----pars densocellularis
--mf	-----pars multiformis
--pv	-----pars parvocellularis
ML	Medial lemniscus
NR	n.ruber

Pcn n. paracentralis

Pf n. parafascicularis

PO n. posterior

Ppd n.peripeduncularis

Ppl n.papillioformis

Prt Regio pretectalis

Pul Pulvinar thalami

R n. reticularis thalami

SN Substantiae nigrae

S n. subthalamicus

TA Tegmental area of Tsai

Tgcm n.tegmentosus pedunculopontinus,pars compacta

VA n.ventralis anterior

VL n.ventralis lateralis

VPI n.ventralis posterior inferior

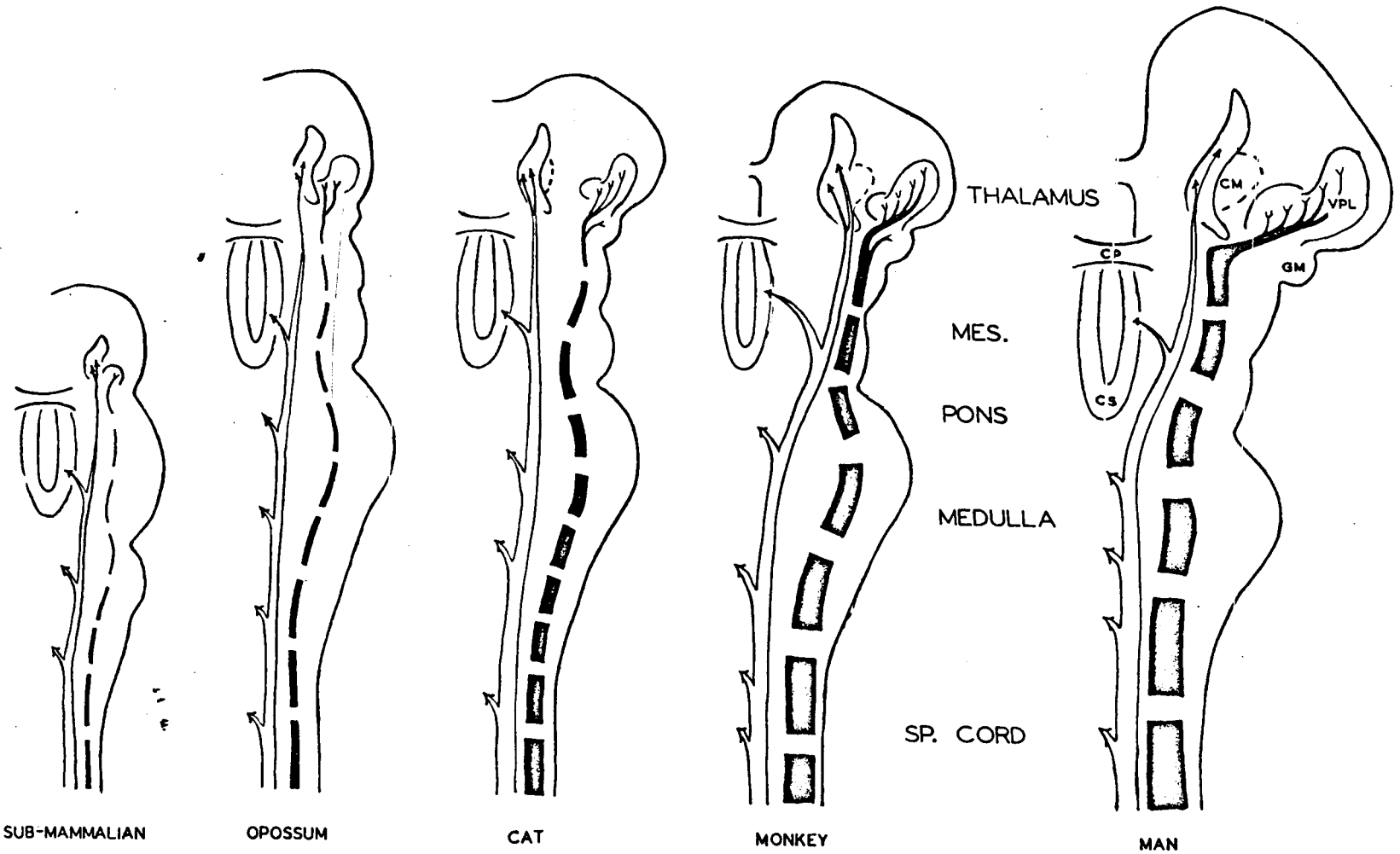
VPL n.ventralis posterior lateralis

---c ----- pars caudalis

---o ----- pars oralis

VPM n.ventralis posterior medialis

ZI Zona incerta



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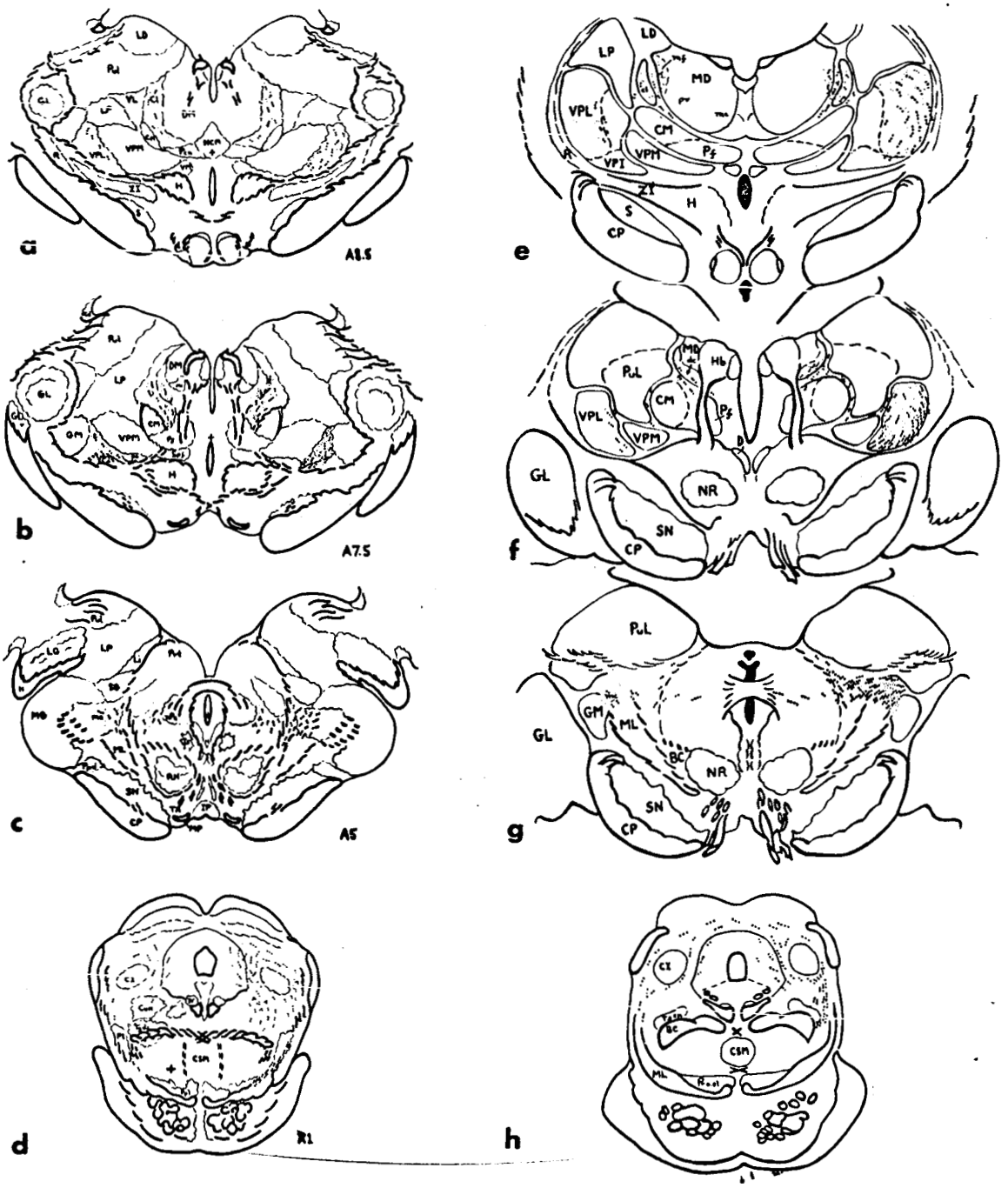

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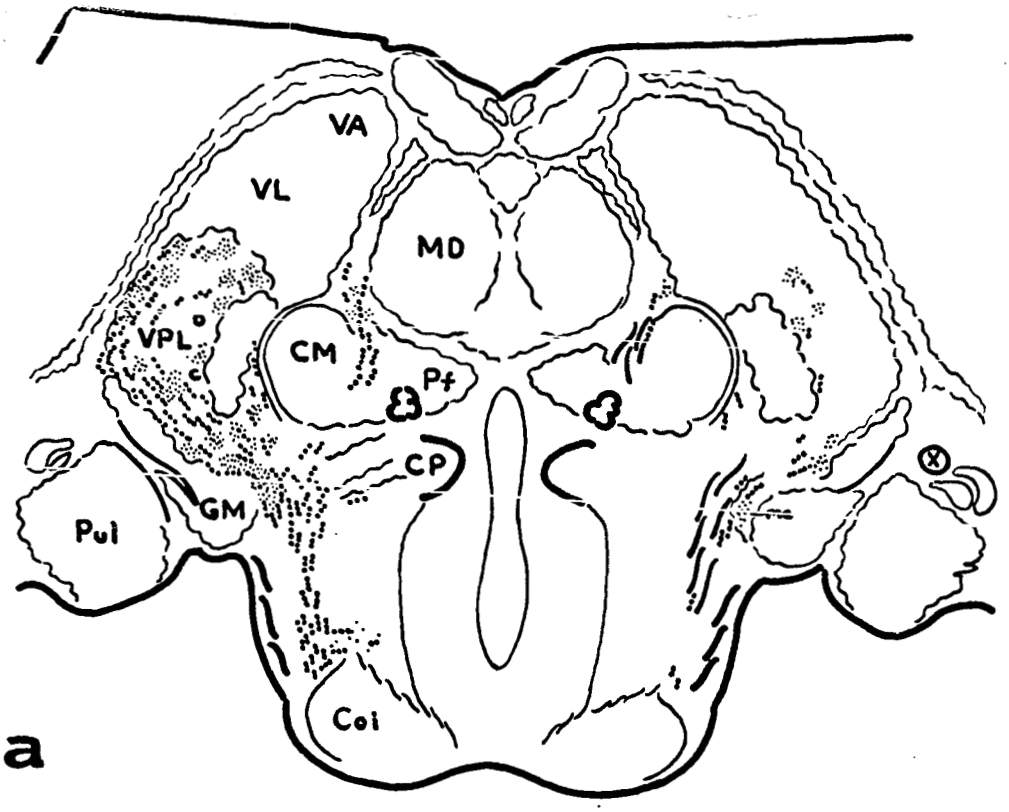

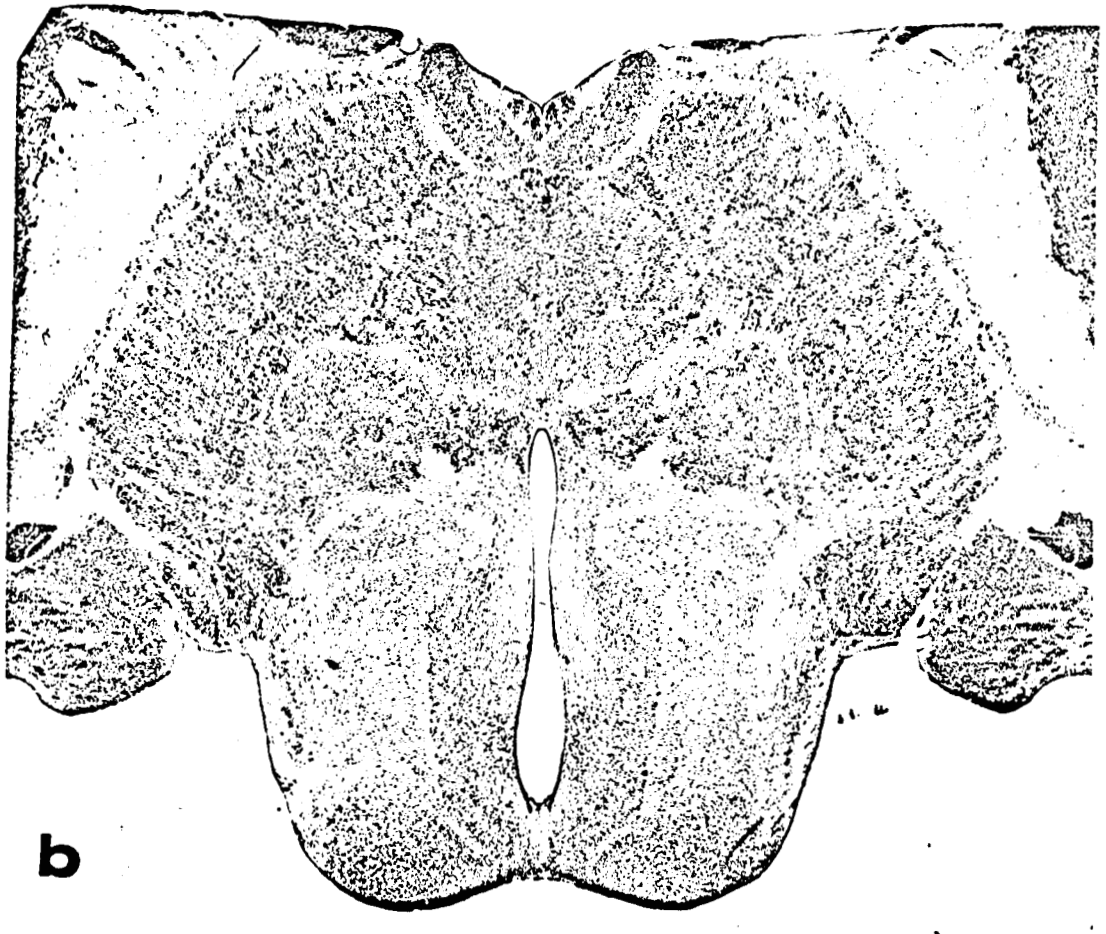

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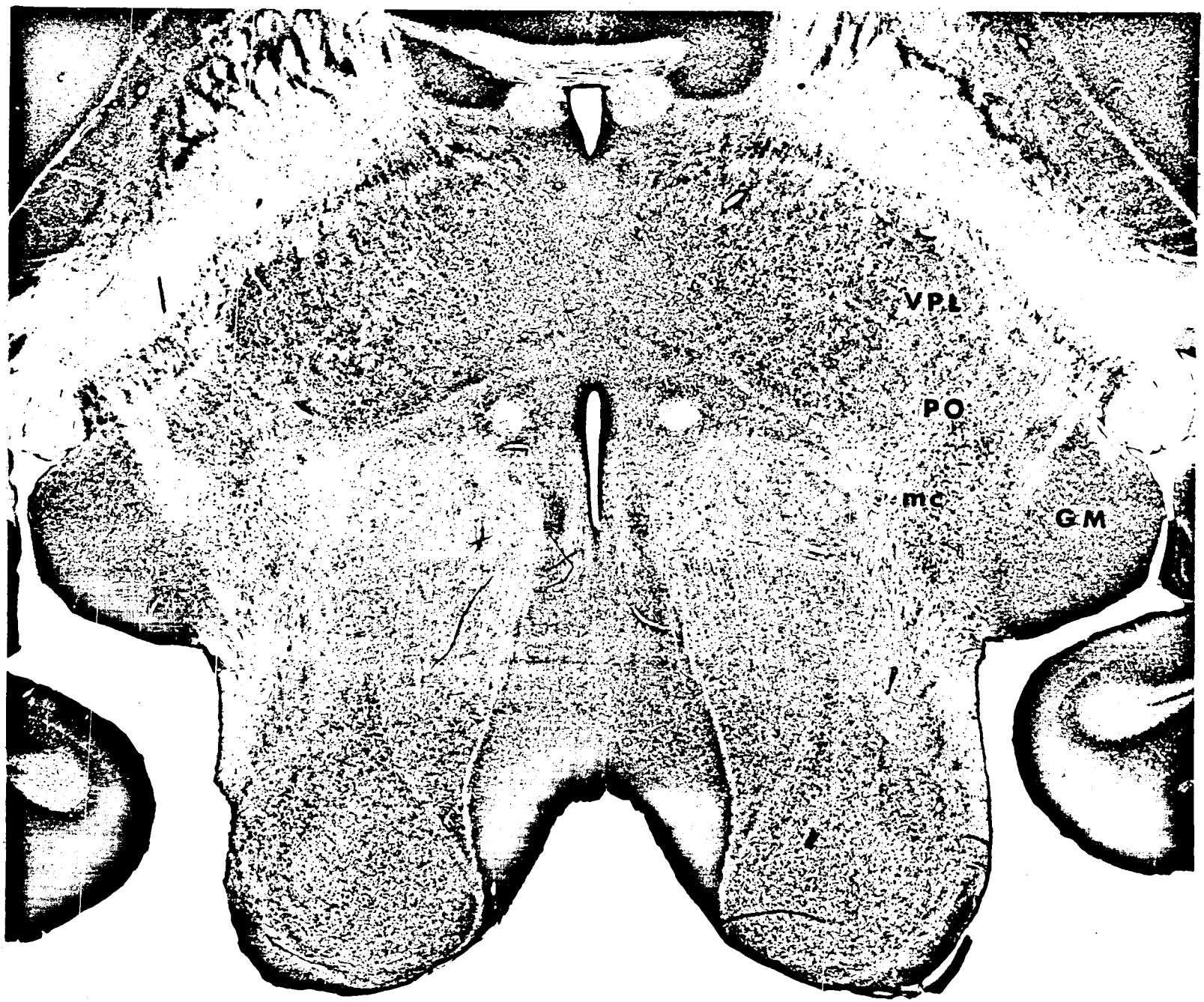
VPL
PO
mc
GM

Fig. 5

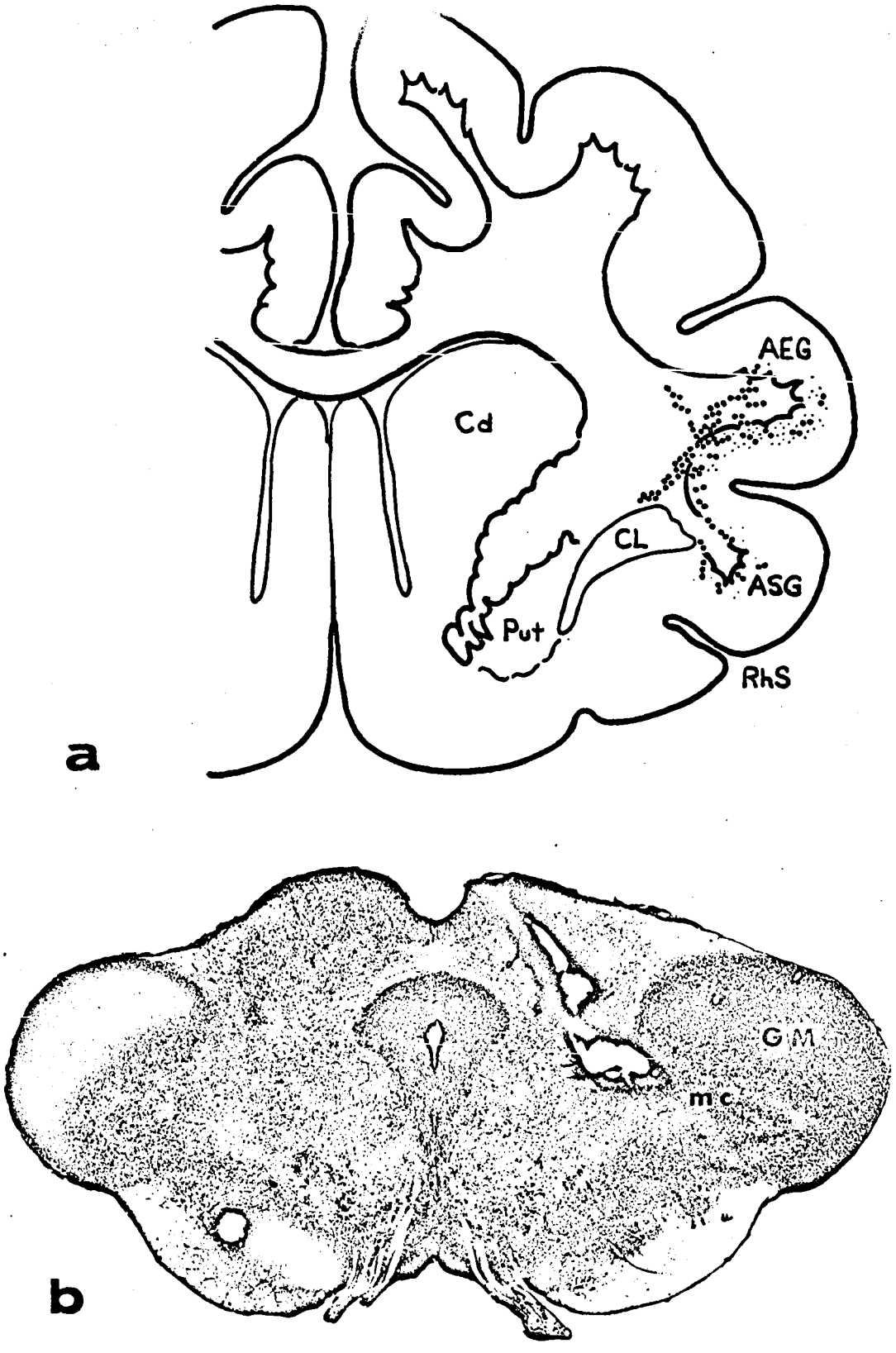

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Fig. 6