CERTAIN PHYLOGENETIC ANATOMICAL RELA- TIONS OF LOCALIZING SIGNIFICANCE FOR THE MAMMALIAN CENTRAL NERVOUS SYSTEM

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NINE FIGURES

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INTRODUCTION

Much has been written concerning cortical localization— its probable presence or absence, its degree, the basis of its representation, and those factors which underlie or determine it. In the following pages the author is venturing to con- sider this very interesting problem by stressing certain facts— some of them well known, others little thought of in this connection, still others new in certain details—which empha- size another phase of the underlying causes and suggest the inevitability, so to speak, of such an organization. This dis- cussion seeks to establish that, with respect to general ar- rangement, sensory and motor cortical localization patterns

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are predetermined in submammalian forms before differ-entiated cortex appears, since these patterns are both the result and the reflection of those laid down early in phylogeny in the primary centers of reception and origin of the sensory and the motor nerve roots. Such patterns are projected in orderly fashion on the higher centers by the fascicles of the connecting tracts, which retain, in passing from one center to the other, a specific functional arrangement. This arrange-ment is impressed on the nuclei of termination of ascending paths or on the nuclei of origin of descending systems. Obviously this development of localization patterns is a cumulative affair so that, in establishing cortical localization in man, there is a great ontogenetic repetition of the phylo-genetic pattern. In this progressive evolution from lower forms without laminated cortex to man, the first step lies in the appearance and maintenance of a specific arrangement at the primary level.

As a preliminary to the development of this discussion the writer wishes to stress his thorough appreciation of the fact that structure and function are inextricably related and develop hand in hand, so that one cannot correctly state that one precedes the other. If, in the following pages, structure is given preference over function it is done simply in the elaboration of an argument which depends principally on morphological relationships and with the full understanding that the two are coincident phenomena.

These hypotheses concerning neural organization have been developed in discussions with Dr. Elizabeth Crosby, who has been an unfailing source of inspiration and assistance in the accumulation, organization, and presentation of the evidence assembled here. The author acknowledges his very consider-able indebtedness to her for her generous help and penetrating criticism.

The microscopic material used to document the accom-panying discussion is in large part from the Huber Neuro-logical Collection of the Department of Anatomy of the University of Michigan. This material has been supple-

mented by series of primate brains (of the macaque and man) made available through a grant from the Horace H. Rackham School of Graduate Studies. The author wishes to express his sincere appreciation of the opportunities afforded by this grant as well as of material assistance in publication.

EVIDENCE FOR SPECIFICITY OF PATTERN IN THE AFFERENT CENTERS OF THE SPINAL CORD

Preliminary reconnaissance. As preliminary to the presentation of the material attention is directed to the well-known contributions of Coghill ('14, '16, '29) and of Herrick and Coghill ('15) which show the stage of development of the spinal reflex arc at the time of the first swimming movements in larval Amblystoma. These observers (see fig. 6 A) found the cell body of the typical afferent neuron to be intramedullary, the neuron itself being relatively non-specific in sensory function, since its dendrites, although intermyotomic in position, receive both exteroceptive impulses from the skin and proprioceptive from the developing somites. Such a neuron forms the receptive side of the crossed reflex arc, for its neuraxis ascends within the central nervous system and then synapses with intrinsic neurons which, in turn, convey the impulses by way of commissural fibers to nerve cells of higher and opposite levels of the spinal cord to come into relation with the cells of origin of efferent neurons. Obviously the sensory neurons of these larvae show a positional specificity from their intermyotomic relations but a lack of specificity in the kind of impulses which they carry.

The pattern described for these amphibian larvae finds representation in more differentiated form in adult cyclostomes such as petromyzonts, in which both intramedullary and extramedullary ganglion cells occur and in which distinct motor neurons appear to have developed (for documentation see Ariëns Kappers, Huber and Crosby, '36). Moreover, in passing, during embryonic development, from larval Amblystoma to adult forms, or in phylogeny from cyclostomes up through true fishes, various outstanding changes occur. Ex-

tramedullary sensory neurons form ganglia (fig. 6 B) on
the dorsal roots (although intramedullary and, in some cases,
supramedullary ganglion cells remain) and show increased
specificity since certain of them supply skin areas and others
are sensory to muscle, although there is not as yet much
differentiation in the sensory endings, except possibly in
certain higher amphibians. A segmental pattern of peripheral
distribution is well established and some of the fibers acquire
medullary sheaths (above cyclostomes). In reptiles and
birds (in which intramedullary ganglion cells persist only
in the embryos) and in mammals the extramedullary ganglion
cells show, with a greater differentiation in the sensory termi-
nations, a marked increase in specificity of function, and this
is reflected in the central arrangement of their neuraxes and
in the organization of the nuclei in which these neuraxes
terminate. Since the establishment of localization patterns
in primary centers of the spinal cord is obviously dependent
upon a specific distribution of the entering neuraxes of spinal
sensory neurons the presentation of evidence for such dis-
tribution is important.

Presentation of material. In the available material of the
frog spinal cord, each entering dorsal root (fig. 1) shows the
evident separation into a medial and a lateral division char-
acteristic of it in higher forms—the medial, made up of heavily
medullated fascicles, entering the dorsal funiculus directly,
and the lateral, consisting of finer medullated and unmedul-
lated fibers, taking up a position at the tip of the dorsal
horn. The outline drawings in figure 1, based on Marchi
preparations of a frog spinal cord in which the lower lumbar
ganglia on the right side had been destroyed, show a pri-
mordial fasciculus gracilis and the finer distribution of its
ascending fibers within the primitive nucleus gracilis, al-
though a very considerable proportion of these fibers do not
reach the medulla oblongata but end at various spinal cord
levels. In their termination the fascicles from these caudal
regions end caudomedially in the nucleus. In their course
forward the most caudal fibers of this fasciculus lie most

ABBREVIATIONS

AB. PYR.TR., aberrant pyramidal tract

AQ., aqueduct

BR.PONT., brachium pontis

CER.PED., cerebral peduncle

CH.SENS.N.V, chief sensory nucleus of trigeminal

COMM.POST., posterior commissure

CORP.TRAP., trapezoid body

D.E.N. or D.EF.N., dorsal efferent nucleus

D.SP.CER.TR., dorsal spino-cerebellar tract

DEC.RUB.SP.TR., decussation of rubro-spinal tract

DEC.SEC.FIB.V(CH.), decussating secondary fibers of trigeminal from chief sensory nucleus

DESC.RT.V, descending root of trigeminal

DIST.MED.LEM.(CUN.), distribution of cuneate component of medial lemniscus

DIST.MED.LEM.(GRAC.), distribution of gracile component of medial lemniscus

DIST.SP.TH.TR.(L.), distribution of lateral spino-thalamic tract

DIST.V.SEC.ASC.TR.V, distribution of ventral secondary ascending tract of trigeminal

DORS.HORN GR., dorsal horn gray

DORSOLAT.FASC., dorsolateral fasciculus

EXT.CAPS., external capsule

EXT.CUN.N., external cuneate nucleus

F.S. or FAS.SOL., fasciculus solitarius

F. + N.CUN., fasciculus cuneatus and nucleus cuneatus

F.+ N.GRAC., fasciculus gracilis and nucleus gracilis

FAS.SOL., fasciculus solitarius

FASC.CUN., fasciculus cuneatus

FASC.GRAC., fasciculus gracilis

FASC. + NUC.GRAC., fasciculus gracilis and nucleus gracilis

FIMB., fimbria

FORN., fornix

GENU VII, genu of facial nerve

H, head representation, in motor cortex and in cortico-spinal tract

HAB.PED.TR., habenulo-peduncular tract

HABEN., habenula

HIPP., hippocampus

INF.CER.PED., inferior cerebellar peduncle

INF.COLL., inferior colliculus

INF.OL., inferior olivary nucleus

INT.ARC.(CUN.) or INT.ARC.FIB.(CUN.), internal arcuate fibers (cuneate component)

INT.ARC.FIB.(GRAC.), internal arcuate fibers (gracile component)

INT.CAPS., internal capsule

L, lower extremity representation, in motor cortex and in cortico-spinal tract

L.RET.N., lateral reticular nucleus

L.TECT.SP.TR., lateral tecto-spinal tract

L.VEST.N., lateral vestibular nucleus

LAT.DIV.DORS.RT., lateral division of dorsal root

LAT.LEM., lateral lemniscus

LUMB.DORS.RT., lumbar dorsal root

M.L.F., medial longitudinal fasciculus

M.VEST.N., medial vestibular nucleus

MAM.PED., mammillary peduncle

MAM.TH.TR., mammillo-thalamic tract

MAM.TH.TR. + MAM.TEG.TR., mammillo-thalamic and mammillo-tegmental tracts

MAX-MAND.FIB., maxillo-mandibular fibers

MED.DIV.DORS.RT., medial division of dorsal root

MED.LEM., medial lemniscus

MED.LEM.(CUN.), medial lemniscus (cuneate component)

MED.LEM.(GRAC.), medial lemniscus (gracile component)

MES.RT.V, mesencephalic root of tri-
geminal

MO.N.V, motor nucleus of trigeminal

MO.N.VII, motor nucleus of the facial
nerve

MOTOR DECUSS., motor decussation

MOTOR N., motor nerve

N, neck representation, in motor cortex
and in cortico-spinal tract

N. + DESC.RT.V, nucleus and descend-
ing root of the trigeminal

N.DESC.RT.V, nucleus of descending
root of the trigeminal

N.GEN.LAT.P.D., dorsal part of lateral
geniculate nucleus

N.GEN.LAT.P.V., ventral   part   of
lateral geniculate nucleus

N.GEN.MED., medial geniculate nucleus

N.GRAC., nucleus gracilis

N.IV, nucleus of trochlear nerve

N.XII, hypoglossal nucleus

NN.V, trigeminal nerve

NN.VII, facial nerve

NN.VIII, acustic nerve

OL.SP.TR., olivo-spinal tract

OP.CH., optic chiasm

OP.TR., optic tract

OPHTHAL.FIB., ophthalmic fibers

PONT.GR., pontine gray

POST.COMM., posterior commissure

PYR., pyramid

RAD.MEYN., radiations of Meynert

RUB.SP.TR., rubro-spinal tract

RUB.SP.TR. + L.TECT.SP.TR., rubro-
spinal tract and lateral tecto-spinal
tract

SEC.FIB.V(CH.), secondary fibers of
trigeminal from chief sensory nucleus

SENS.DEC., sensory decussation

SENS.NEUR., sensory neuron

SP.TECT.TR., spino-tectal tract

SP.TH.TR.(L.), (lateral) spino-thala-
mic tract

STR.MED., stria medullaris

SUB.NIG., substantia nigra

SUP.COLL., superior colliculus

SUP.COLL.COMM., superior collicular
commissure

SUP.OL., superior olivary nucleus

TECT.TEG.TR., tecto-tegmental tract

TERM.DIST. OF ASC.SENS.SYS., ter-
minal distribution of ascending sen-
sory systems

TERM.FIB., terminating fibers

TERM.MAX-MAND.FIB., terminating
maxillo-mandibular fibers

TUB.ACUS., tuberculum acusticum

U, upper extremity representation, in
motor cortex and in cortico spinal
tract

V.L.VEST.SP.TR., ventrolateral vesti-
bulo-spinal tract

V.SEC.ASC.TR.V, ventral   secondary
ascending tract of the trigeminal

V.SP.CER.TR., ventral spino-cerebellar
tract

V.SP.CER.TR. + SP.TECT.TR + SP.
TH.TR.(L.), ventral   spino-cerebellar
tract + spino-tectal tract + spino-
thalamic tract (lateral)

VENT.N.D.TH., ventral   nucleus   of
dorsal thalamus

dorsomedially and are added to laterally and ventrolaterally, as various observers (for example, Bok, '28, and Ferraro and Barrera, '35) have found to be the case in mammals. Preparations of this type demonstrate that, even in tailless amphibians, there is a direct projection of dorsal root fibers from lower extremity levels upon the medulla oblongata, which is in accordance with the appearance in phylogeny of a primordial nucleus gracilis in these forms.   Moreover, in
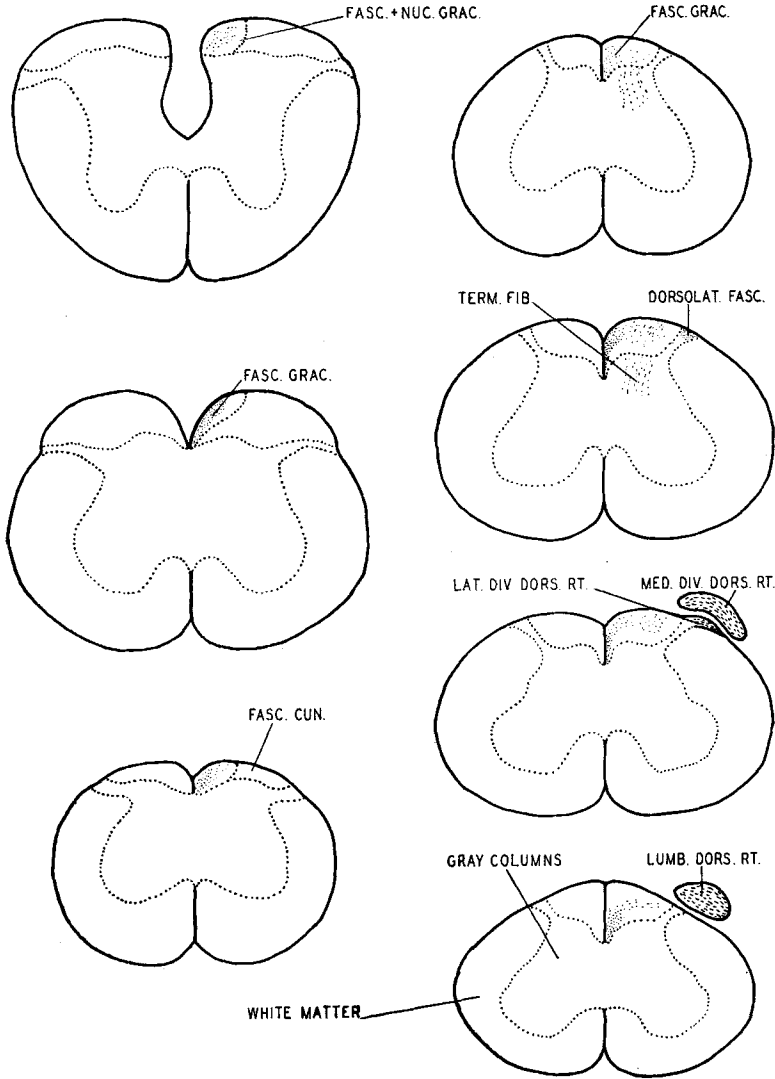
Fig. 1 A series of outlines of selected levels through the spinal cord and lower medulla oblongata of the frog, Rana pipiens, to illustrate the position and the distribution of degenerated fibers after section of right upper lumbar roots. Marchi preparations. × 17.5.

its early appearance this primordial fasciculus gracilis exhibits the same orderly arrangement of its fibers in course and the same caudomedial to rostrolateral termination of its fascicles which were indicated in the experimental results of Ferraro and Barrera ('35) on the homologous tract of the macaque. Study of Marchi series following a low thoracic hemisection of the rat spinal cord shows likewise an orderly medial position of degenerated fascicles in the fasciculus gracilis and in the most medial part of the fasciculus cuneatus above the level of the lesion and a distribution, beginning mediocaudalward, in the nucleus gracilis and the most medial part of the nucleus cuneatus. The evidence presented, in conjunction with the descriptions in the literature, indicates also that there is a progressive increase, in passing from submammals to lower mammals and from lower mammels to higher mammals, in the proportionate number of root fibers passing from lower levels of the body through the dorsal funiculus to terminate in the dorsal funicular gray of the medulla oblongata.

Silver preparations of the frog spinal cord (fig. 6 D) demonstrate the unmedullated and the thinly medullated fibers of the lateral division of the dorsal root which enter the spinal cord to constitute the dorsolateral fasciculus. This fasciculus is best developed at the levels of the enlargements but does not show a progressive increase caudorostrally, indicating that, as in mammals, there is no consistent forward accumulation. Marchi preparations of the frog spinal cord, following cutting of the lumbar roots, permit the tracing of thinly medullated fibers (fig. 1) within the dorsolateral fasciculus for $2\frac{1}{2}$ mm. above the level of the lesion. The number of such fibers is not large in the frog and the Marchi sections, of course, do not demonstrate the unmedullated components of the tract or those endogenous to the spinal cord. Ranson's ('13, '14) study of Lissauer's tract in the cat and Foerster's ('27) consideration, based on clinical material, of the course of pain impulses within the human spinal cord indicate that the fibers (which Ranson regards as chiefly

unmedullated) carrying such pain impulses terminate almost immediately upon entrance to the nervous system. The report of May ('06), substantiated, then and later, by a considerable body of clinical data from various sources, appears to show that temperature impulses follow rather closely the course of pain impulses in mammals, so that the thinly medullated fibers of the lateral division of the dorsal root, which are believed to provide the pathway for such temperature (and possibly some pain) impulses, are regarded also as being relatively short in these forms. From the preceding account it is evident that the frontal extent, at the lumbar levels considered, of the entering root fibers in the dorsolateral fasciculus is much greater in proportion to the total length of the spinal cord in the frog than appears to be the case in the mammalian material in which this system has been studied. This indicates that the longitudinal area of termination of such fibers within the substantia gelatinosa becomes reduced in passing from lower to higher forms. This reduction results in the appearance of a more specific functional pattern (approaching though not reaching that of a segmental arrangement in man) in the substantia gelatinosa of higher forms than in that of the amphibians considered. Such a pattern determines for the form the degree of specificity of conduction to brain levels over secondary ascending paths. It should be said finally that the results presented here for the frog are not in complete accordance with those given by Leszlényi ('12), who found no considerable amount of dorsal root fibers entering the dorsolateral fasciculus in the reptilian, avian, and mammalian material available to him for study, with the possible exception of the human preparations. His work was based on Pal-Weigert series.

EVIDENCE FOR SPECIFICITY OF PATTERN IN THE AFFERENT CENTERS OF THE BRAIN STEM

Preliminary reconnaissance. The detailed distribution of entering sensory components of the cranial nerves is known

only for certain of these nerves and only for certain forms. As an example of a primary brain stem receptive center in which a specific localization pattern has been determined, at least for man, the nucleus of the descending root of the trigeminal has been selected. Various observers have studied the peripheral distribution of the trigeminal (for example, Cushing, '03, '04, and Gerard, '23). The analysis of the nucleus of the descending root is based on three types of evidence: clinical (Dejerine, '14), comparative (van Valkenberg, '11, and Woodburne, '36), and that made available through the intensive study of Golgi preparations (Windle, '26, '27; and others).

Dejerine demonstrated that segmental divisions of the descending root of the trigeminal nerve in man show a pattern of peripheral loss to which the term 'onion peel' (for example, see Brock, '37) has been generally applied, and a comparison of his results with the known peripheral terminations of the human trigeminal nerve has led clinical neurologists in general to accept the following distribution of the central fibers. The central neuraxes of maxillo-mandibular fibers from the perioral-perinasal regions are conceded to end at pontine levels. Ophthalmic fascicles from around the eyes, maxillo-mandibular fibers with peripheral distribution to the cheek, and impulses carried from chin regions by mental branches of the mandibular, are believed to terminate through the central neuraxes of their respective neurons at upper medullar levels. Finally, impulses from the forehead and top of the head, by way of the ophthalmic branches and the auriculotemporal branch of the mandibular nerve, from the region of the cheek, by way of the maxillary bundles, and from regions of the jaw (except the angle) by way of mandibular fibers, are thought to reach the most caudal regions of distribution of the trigeminal fibers over the descending sensory root. Consideration of this pattern of central distribution indicates that impulses carried by fibers from all three divisions of the trigeminal nerve reach all excepting the pontine portion of the nucleus of the descending root, this latter area being

chiefly, at least, a region of ending of the central neuraxes of neurons distributing peripherally through maxillo-mandibular fibers.

A series of observers, among whom may be mentioned van Valkenberg ('11) and Woodburne ('36), have presented evidence, based on normal material, that the ophthalmic division in many submammalian and mammalian forms lies ventral to the maxillo-mandibular division behind their common level of entrance to the brain stem in their course through the central nervous system, and that this ophthalmic division extends caudal to the maxillo-mandibular, being traceable to the cervical cord, in which region it overlaps sensory fibers of upper cervical segments. Herrick ('30) found that the fibers of the ophthalmic division myelinate earlier than those of the maxillo-mandibular in larval Amblystoma. A considerable number of workers have demonstrated in a wide range of submammals and mammals (including man) the presence of sensory fibers to the nucleus of the descending root of the trigeminal from the facial, the glossopharyngeal, and the vagus nerves, which enter this nucleus near the plane of entrance to the brain of the respective nerves. Evidence that such fibers distribute behind their level of entrance (except of the indirect type such as that afforded by Dejerine's cases) is not at present available. From the present descriptions in the literature, anatomic evidence appears to be lacking in many forms for the distribution of maxillo-mandibular fibers to levels caudal to approximately the plane of entrance of the vestibular fibers.

Presentation of material. Before the present article was begun, the writer had convinced himself that, in general, van Valkenberg's ('11) allocation of ophthalmic fibers to the more ventral portions and maxillo-mandibular fibers to the more dorsal portions of the descending root of the trigeminal was applicable to a wide range of submammalian and mammalian forms. It seemed desirable to establish in some form easily available for experimentation a more detailed pattern of distribution of the descending root fibers of the trigeminal

along the lines recognized for man, if perchance such a pattern exists, since this is a necessary prerequisite for the determination of the functional fascicular arrangement in the secondary paths arising from the nucleus of the descending root. The first question which arose in determining the pattern distribution of the primary trigeminal root fibers concerned the possible presence, or the absence, of any maxillo-mandibular fibers in the caudal end of the brain stem. For the consideration of this problem serial sections of rat material stained in pyridine silver and similar series stained in iron haematoxylin were consulted. On the basis of such normal material maxillo-mandibular fibers in small number were traced caudalward to the beginning of the cervical cord, although the great majority of the maxillo-mandibular fibers ended approximately at the caudal level of the motor facial nucleus or slightly behind this. The small, most caudal component of the maxillo-mandibular division is its most dorsal portion and lies throughout pontine levels, at the dorsal tip of the descending root, separated from the ophthalmic fibers by the remaining maxillo-mandibular fascicles. It has not been possible to determine whether it includes both maxillo-mandibular or only mandibular bundles. As the main part of the maxillo-mandibular fascicles distributes to the nucleus of the descending root of the trigeminal, the root itself decreases in size and this small dorsal, caudal component and the ophthalmic bundles approach each other, so that, at the most caudal levels of the medulla oblongata, the descending root, even in normal material, appears to be composed chiefly of a dorsal tip of maxillo-mandibular origin and a much larger portion of ophthalmic origin.

This distribution, based on a study of normal material, has, up to the present, been tested on only two operated rats. The results are summarized in the series of outline drawings in figure 2, drawn directly from the preparations made of rat brain number 23. In this rat, a lesion was made which involves the upper tip and the lower tip of the descending root of the trigeminal as it surrounds the nucleus of the
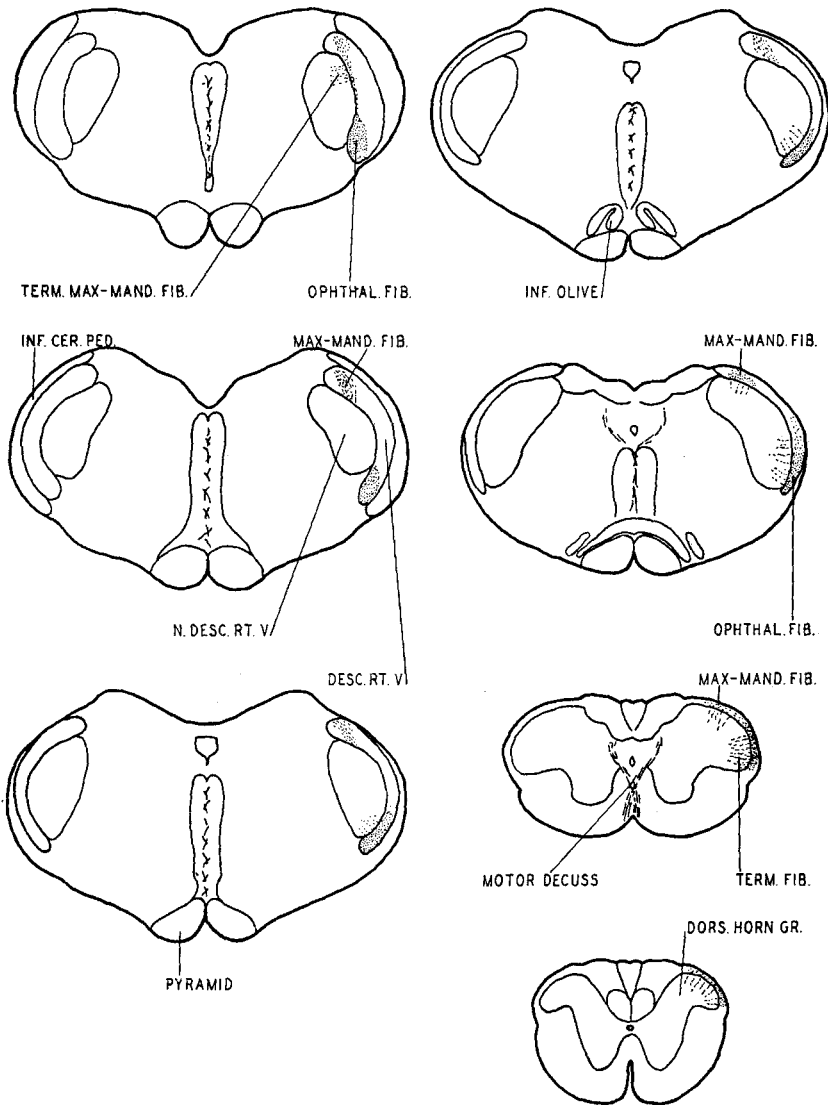
Fig. 2 A series of outline drawings through the brain stem of the rat (Mus norwegicus) showing the distribution of certain of the fibers of the descending root of the trigeminal nerve following lesion of its most dorsal and most ventral fibers just caudal to their entrance into the brain. Marchi preparations. × 6.75.

descending root at levels just caudal to the chief sensory nucleus, in an effort to show the distribution of the portions of the descending root which pass farthest caudalward. At upper levels of the brain stem, behind the level of the lesion, degenerated areas appear in the dorsal and ventral portions of the descending root. Between these two portions are the normal fibers of the root which have not been affected by the cut. As the sections are followed caudalward, the degenerated areas approach each other until, at the lower levels of the medulla oblongata, near its transition to the spinal cord, degenerated fibers are found throughout most of the extent of the descending root, although not all of the fibers are degenerated. These results confirm those obtained from the study of normal material and indicate that the maxillomandibular fibers of the dorsal tip of the descending root of the trigeminal pass to lower levels of the medulla oblongata, and that the majority of the maxillo-mandibular fibers in the rat end in pontine regions. In rat brain number 24 a small lateral portion of the descending root was cut at uppermost levels of the medulla oblongata in regions to which some of the more caudal fibers of the maxillo-mandibular had been traced. Fibers degenerated for only a short distance caudal to the lesion, indicating that this component of the maxillomandibular division terminates at upper levels of the medulla oblongata.

THE DEVELOPMENT OF LOCALIZATION PATTERNS IN CERTAIN AFFERENT THALAMIC CENTERS

Preliminary reconnaissance. Many observers have studied, in normal or in experimental material, the great secondary ascending systems to the thalamus. Most of the experimental studies have either selected one system for observation or considered the complex as a whole, so that the interrelations of the various tracts to each other have received little emphasis. However, an example of such an analysis, based on clinical material, is found in the classic work of Dejerine

who has shown the relations of these systems to each other as they pass toward the dorsal thalamus in man.

Studies of the detailed organization within any one of these ascending systems are also rare. Outstanding among such studies is that of Foerster ('27). He analyzed the lateral spino-thalamic system in human clinical material, finding that this bundle, followed caudorostrally, shows an orderly arrangement of its component fascicles, those carrying pain impulses from lower body levels lying most ventrolaterally in the fasciculus and being added to along their inner border, level for level, in regular fashion, so that the bundles carrying impulses from upper body regions lie most dorsomedially in the tract. This is an outstanding example of a known detailed functional pattern in a secondary ascending system.

Various observers (for literature, see Ferraro and Barrera, '35 a; Ariëns Kappers, Huber, and Crosby, '36; Walker, '38) have differentiated between the gracile and the cuneate components of the medial lemniscus by the device of destroying one portion, usually at its nucleus of origin. Thus Ferraro and Barrera traced the gracile component following experimental lesions in the macaque, and established its position at various levels in the medial lemniscus. Such an analysis is excellent but needs to be continued in much greater detail if the localization pattern found in the nucleus gracilis and the nucleus cuneatus by these observers and also reported here (see p. 218) is to be followed to its projection on the ventral nucleus of the dorsal thalamus.

The dorsal and ventral secondary ascending trigeminal systems, dorsal and ventral portions of the trigeminal lemniscus, have been studied by various workers (Wallenberg, '05; Dejerine, '14; Le Gros Clark, '32; Woodburne, '36; and others) and the course of such fibers as distinct from that of other secondary ascending systems has thus been established. Particular attention has been given to the experimental study of that portion arising from the chief sensory nucleus of the trigeminal (Wallenberg, '05; Le Gros

Clark, '32). None of these analyses approaches in complete-
ness of detail those available for the primary trigeminal
centers.

The terminal distribution of the various ascending sensory
systems within the dorsal thalamus has been studied by
numerous observers and space permits here the quoting of
only a very few of the many papers dealing with this subject
(for bibliographies see the Ariëns Kappers, Huber, and
Crosby text, '36; and, for primates particularly, the recent
book of Walker, '38). Some of the outstanding contributions
on the terminations of these ascending systems in the rodent
brain are those of van Gehuchten ('01) and Wallenberg
('05) on the secondary ascending tracts of the trigeminal in
the rabbit, Le Gros Clark's ('32) study on the distribution
of the medial lemniscus and the trigeminal component of
the chief sensory nucleus to the ventral nucleus of the dorsal
thalamus of the rat, and the account of Quensel and Kohn-
stamm ('07) on the projection of the spino-thalamic tracts
on the rat thalamus. More detailed study of the distribution
of these systems within the ventral nucleus of the dorsal
thalamus is obtainable for higher mammals. Von Economo
('11), Walker ('38), and others have carried the secondary
trigeminal tracts to the nucleus arcuatus or nucleus ventralis
posteromedialis in the monkey, although Papez and Rundles
('37) believed they could trace the dorsal division of this
system outside of the ventral nucleus to the centromedian
nucleus in this primate. Ranson and Ingram ('32) found the
medial lemniscus to terminate chiefly in the pars externa of
the ventral nucleus in carnivores, and Ferraro and Barrera
('35 a), Le Gros Clark ('36), and Walker ('38) carried this

Fig. 3 Drawings of successive transverse levels (A to F) through the medulla
oblongata and lower pons regions of the rat (Mus norwegicus) brain. These
drawings form the first part of a series (figs. 3 to 5) designed to show the
relations in course of certain of the ascending sensory systems, particularly the
components of the medial lemniscus, the spino-tectal and spino-thalamic tracts
and the ventral secondary ascending tract of the trigeminal. Weil preparations.
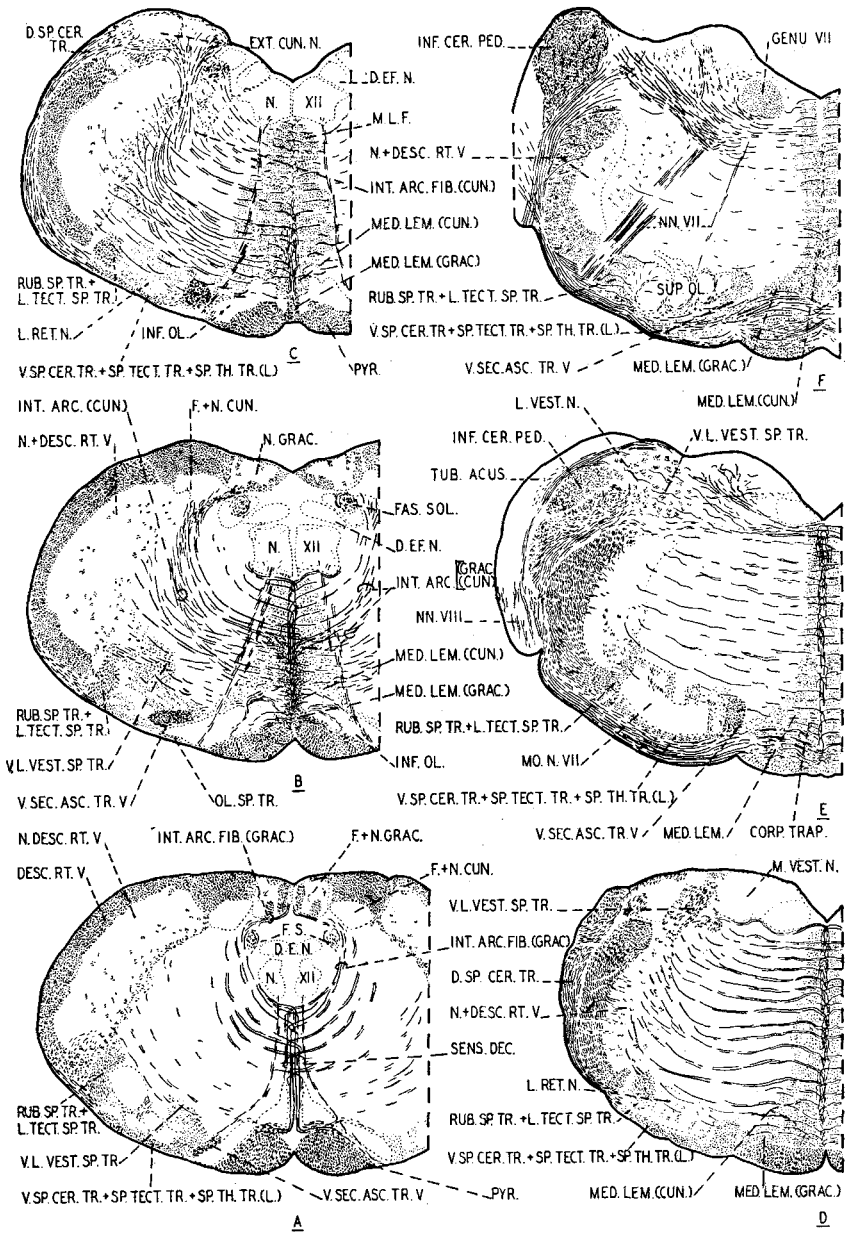× 10.5.

Figure 3

system to the posterior part of the ventral nucleus in higher primates.

Presentation of material. Normal material of the rat brain, stained by the Weil method, permits documentation for this form of the relative positions of the great ascending sensory systems in their course from lower levels of the medulla oblongata to their termination in the ventral nucleus of the dorsal thalamus, in a pattern for this rodent which is directly comparable, except for slight differences in tilt, to that described by Dejerine ('14) for man. These tracts are labelled in figures 3 to 5 and require no detailed description. Certain facts about these relations need emphasis and each system will be considered separately and particular points stressed.

In the formation of the medial lemniscus in the rat, the internal arcuate fibers arise successively, as followed caudorostrally, from the caudomedial portion of the nucleus gracilis (fig. 3 A), from the frontolateral portion of that nucleus and the caudomedial portion of the nucleus cuneatus (fig. 3 B), and then from the frontolateral part of the main cuneate and from the external cuneate nucleus (fig. 3 C). (This arrangement is in accordance with that described by Ferraro and Barrera, '35 a, in the macaque.) Such fibers cross at about their level of origin and pile up serially to form the medial lemniscus (fig. 3, A to C) in the interolivary space immediately dorsal to the pyramid. There the most ventral portion of the medial lemniscus carries fibers arising from the caudomedial portion of the nucleus gracilis (that portion which receives impulses from the lower extremity) and the dorsal tip of this lemniscus is occupied, at such interolivary levels, by those fascicles of the cuneate component which are conveying impulses from the upper extremity and the neck. This pattern shows very clearly on the normal primate material, and particularly on the human material available for study, and moreover has been verified for the caudomedial portions of the nucleus cuneatus on available experimental material of the rat, prepared by the Marchi method. As the
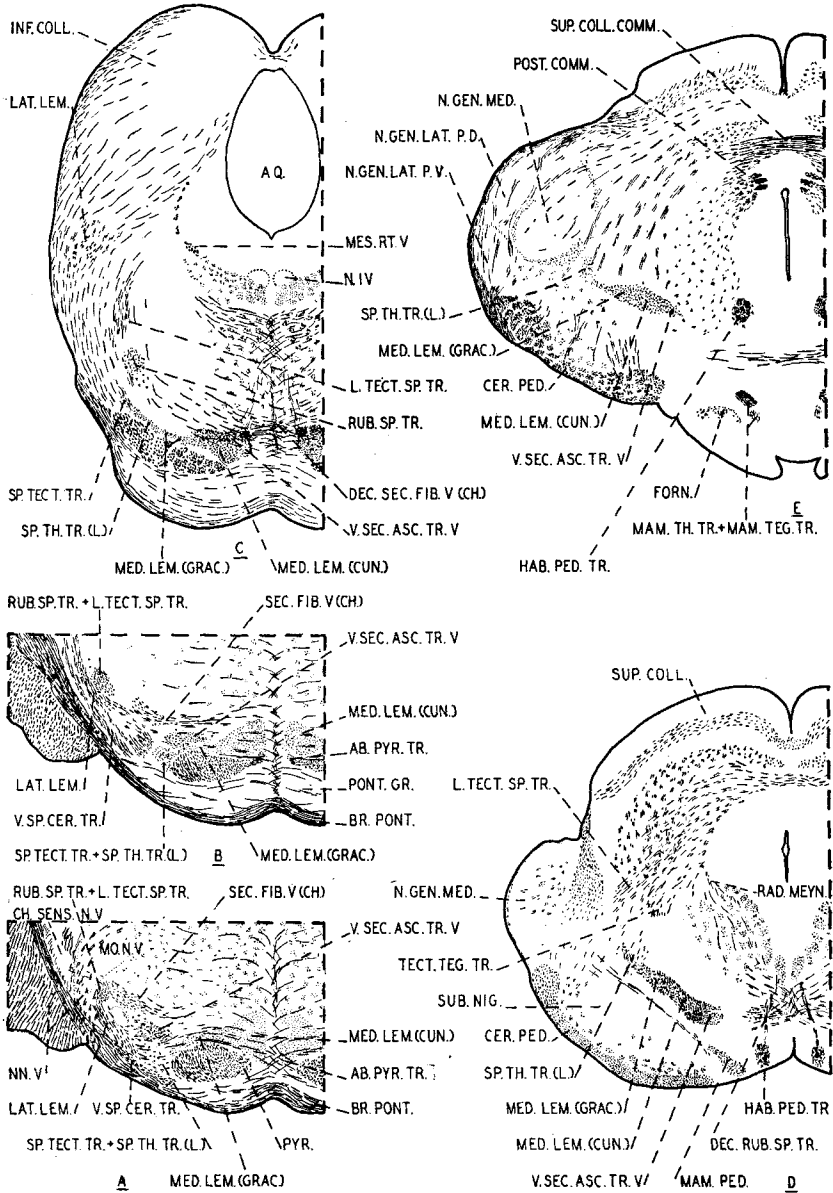
Fig. 4 (See figs. 3 and 5.) Drawings of transverse levels (A to E) through upper pons and midbrain. Rat material. Weil preparations. × 10.5.

medial lemniscus shifts from a vertical to a horizontal position (fig. 3 F) in the pons, it is not possible to follow individual fascicles nor to be certain that there are no intermingled secondary trigeminal fibers (see p. 237). Moreover, there appear to be gustatory fibers accompanying both components, the final termination of which is not known. However, the gracile component shifts so that it is lateral and slightly ventrolateral to the cuneate component, with its most ventral and ventrolateral portion occupying a lateral position. Similarly the upper tip of the cuneate component remains medial in the bundle. In this shift lateralward first the gracile component (fig. 3 F and fig. 4, A and B) is ventral to, and later the cuneate component (fig. 4 B) underlies, bundles of the ventral secondary ascending tract of the trigeminal, in relations essentially similar to those described by Dejerine for man, and the three components proceed forward in these relations with the trigeminal component gradually increasing in size dorsomedially by the addition of fibers from the nucleus of the descending root of the trigeminal until planes near the upper border of this nucleus are reached. Le Gros Clark ('32) pointed out from degeneration material that the main portion of the medial lemniscus in the rat enters the ventral nucleus from its ventral and lateral aspects to terminate in the nuclear gray, although a small portion passes by way of the medial medullary lamina to the dorsomedial portion of the ventral nucleus. Le Gros Clark's lesions appear to include in a varying amount (depending upon the site of the lesion) fascicles of the secondary ascending tract from the nucleus of the descending root of the trigeminal, the trigeminal lemniscus described by him arising only from the chief sensory nucleus. Figure 4, D and E, shows the positions of the gracile and cuneate components of the medial

Fig. 5 Drawings of successive transverse levels (A to C) through the thalamic levels of the rat brain. They form the third part of the series illustrated in figures 3 to 5. Weil preparations. × 10.5. Figures A′, B′ and C′, drawn from pyridine silver preparations, show certain details of fiber termination for the respective levels of A, B and C. × 12.
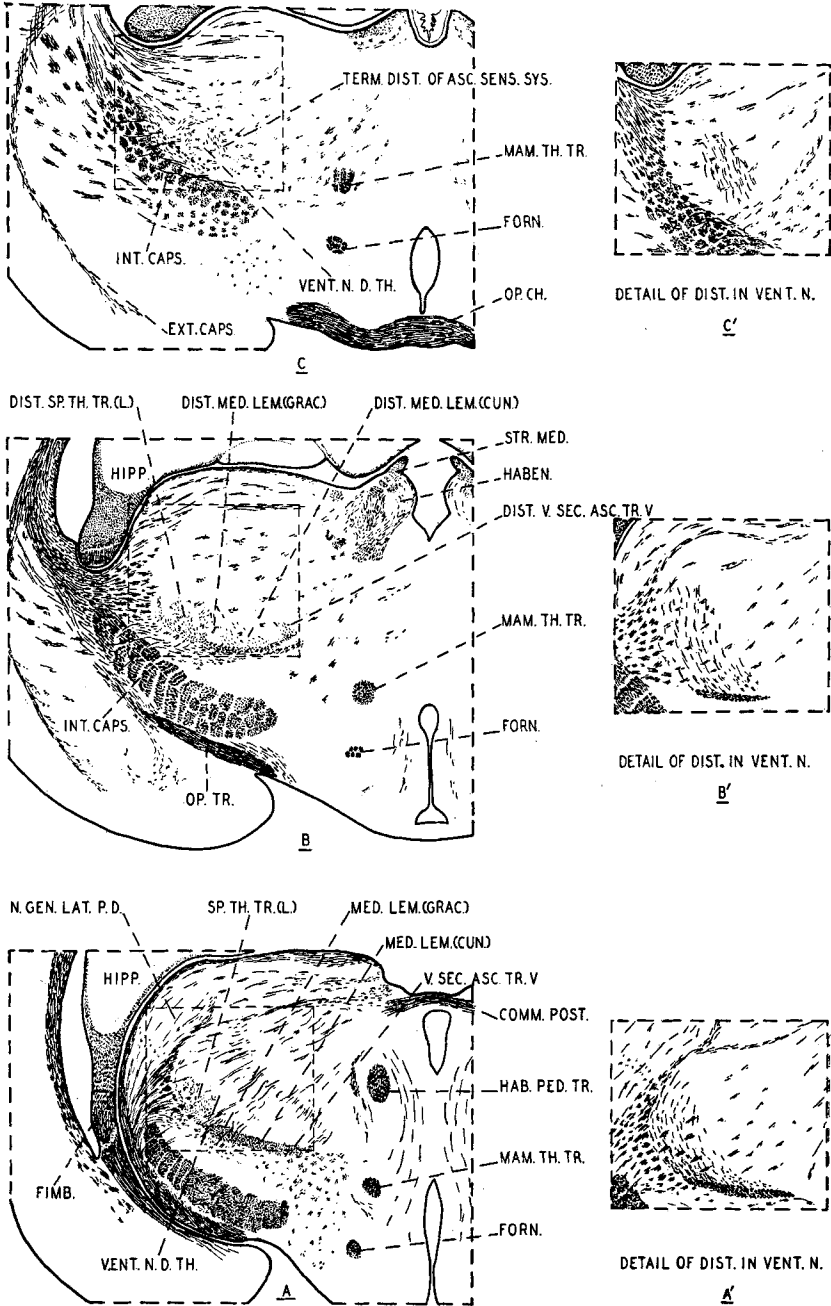
Figure 5

lemniscus as they approach the ventral nucleus. They enter
this nucleus laterally and ventrally (fig. 5), as Le Gros Clark
found to be the case in his material, and here distribute so that
the gracile component passes primarily to dorsolateral por-
tions of the ventral nucleus (fig. 5 A and B), with the lateral-
most fibers, those carrying impulses from lower extremities,
reaching the outer and upper part of the area. The cuneate
component (fig. 5) distributes more medially, primarily to
intermediate portions of the nucleus, although its fibers over-
lap to some extent those of the gracile component laterally
and the terminal fibers of the ventral secondary ascending
tract of the trigeminal (fig. 5) medially which ends in the
more medial and in general the more frontal parts of the
area (fig. 5 C').

Mention has been made of the fact that as the medial
lemniscus shifts lateralward the fasciculus gracilis underlies
the ventral secondary ascending tract of the trigeminal in
upper pons levels (fig. 4 B) and the cuneate component under-
lies this trigeminal system as lower midbrain levels (fig. 4 C)
are attained. The course of the ventral secondary ascending
tract of the trigeminal is shown in figures 3 to 5, and many
of the details of its pattern formation are obvious in normal
material. From the caudal end of the nucleus of the descend-
ing root of the trigeminal fascicles can be traced across
the midline and into a position along the medial border of
the lateral spino-thalamic tract lateral to the olivary complex.
These bundles are added to successively, medially and dorso-
medially, as the series is followed forward through figure 3,
A to E, so that the ventral secondary ascending tract of the
trigeminal shows at least a general pattern arrangement, with
the fibers arising from the lower caudal end of the brain (and
hence concerned with conveying impulses from forehead, ear,
and cheek regions) lying lateral and ventrolateral to those
bundles carrying impulses from eye and upper nose regions.
These latter are added to dorsomedially by fibers mediating
sensations from the alar regions of the nose and from the
mouth which cross directly from the pontine portion of the nu-

cleus of the descending root. As the chief sensory nucleus (fig. 4 A) is approached, a special bundle arises (fig. 4) which crosses the midline and joins the ventral secondary ascending tract of the trigeminal on its medial border. This bundle, which has been described by Wallenberg ('05) in the rabbit and by Le Gros Clark ('32) in the rat—both of these descriptions being based on experimental material—can be readily identified in normal rat preparations and can be traced from the chief sensory nucleus to the frontomedial portion of the ventral nucleus of the dorsal thalamus, a result essentially in agreement with that of Le Gros Clark. In addition to the secondary trigeminal system here described, there is a dorsal secondary ascending tract of the trigeminal in rodents (Woodburne, '36) which follows a special course and which will not be considered here. Moreover, it is not possible in normal material to be certain whether or not there are further secondary trigeminal fibers intermingled with the gracile and the cuneate components of the medial lemniscus.

The normal material permits the tracing of the lateral spino-thalamic tract (figs. 3 to 5) forward to the thalamus, although it is possible to differentiate it from ventral spino-cerebellar and spino-tectal systems only as these turn off to their regions of termination. In the preparations at present available it was followed primarily to the lateral and intermediate portions of the ventral nucleus.

The preceding discussion indicates that in the rat there is the beginning of the establishment of a localization pattern within the ventral nucleus, based, as Wallenberg ('05) long ago predicted, on the arrangement of the ascending systems as they approach the thalamus. Thus in a broad sort of way the dorsolateral portions (particularly caudally) are concerned with impulses from the lower extremities, the intermediate portions with impulses from the upper extremities and the neck, and the medial and frontal areas with impulses from head regions. In the rat this pattern is not clear cut. There is overlap of terminal fibers and accordingly an intermingling of stimuli.

THE THALAMO-CORTICAL PROJECTION OF THE VENTRAL NUCLEUS

The present writer has nothing new to offer on the thalamo-cortical connections. The following brief references to a few of the pertinent papers dealing with such connections are included here in order to suggest the manner in which the thalamic localization pattern is projected on the cortex.

Le Gros Clark ('32) found that the dorsal and lateral portions of the ventral nucleus are connected with the dorsal part of the parietal cortex and the medial and ventral portions of this nucleus with the ventral part of this cortex and with the insular area in the rat. Elliot Smith ('10) had stressed the fact that thalamo-cortical fibers follow the shortest possible course to the cortex and Le Gros Clark's ('32) work offers confirmation of this and indicates that "their topographical distribution in the cortex is directly dependent upon their topographical position of origin in the thalamus."

Various observers (Polyak, '32; Walker, '34, '35, '36, '38; Le Gros Clark and Boggon, '35; Crouch and Thompson, '38; and many others) have considered the interconnections of the ventral nucleus and the cortex. On the basis of retrograde cellular atrophy after cortical ablation, Walker ('34) established four major areas within the macaque dorsal thalamus, a dorsolateral area concerned with impulses to the cortical centers for lower extremities, succeeded ventromedially by a region concerned with impulses to the cortical centers for trunk and then for upper extremities, and, most frontomedially of all, with impulses to the cortical centers for the head. Waller ('34) was not successful in obtaining such a clear cut pattern in the rat.

In the present paper a localization pattern has been described within the ventral nucleus of the rat dorsal thalamus, on the basis of the terminations of the ascending sensory systems, which is obviously in line with the thalamo-cortical studies of Le Gros Clark and Walker quoted in the preceding paragraph. That the pattern is not so clear cut in the rat as in the macaque, as Waller's work would tend to indicate is the case, is to be expected. Probably there is much more

terminal overlap of distribution of the ascending systems in the subprimate than in the primate, and certainly there is a lack of the high intranuclear differentiation of the ventral nuclear complex of the rat such as characterizes the homologous complex of the macaque.

Additional examples. Before terminating this brief discussion of the afferent systems some mention should be made of the visual and auditory systems. The pattern arrangement in fiber tracts and nuclear centers of the visual system (as a result of the work of a large group of observers, Minkowski, '20; Brouwer and Zeeman, '25; Brouwer, '27; Polyak, '33; Lashley, '34; Le Gros Clark and Penman, '34, and others) is too well known to need further discussion but knowledge of the auditory system is largely lacking. The work of Crowe, Guild and Polvogt ('34) has shown that the basal portion of the cochlea is concerned in the recognition of tones of higher pitch. Fibers from the basal turn form the outer layer in the cochlear trunk and those from the apical portion lie in its center. It is generally conceded that the auditory fibers end in the dorsal and ventral cochlear nuclei and Polyak described the ventral cochlear nucleus of the bat as consisting of a thick, folded, dorsal large-celled portion, which receives fibers from basal parts of the cochlea, and a smaller, folded, smaller-celled ventral portion, which receives fibers from the apical portions of the cochlea. Granting that this localization pattern has comparable representation in other mammals (a supposition yet to be proved), there is need of evidence as to the manner of the projection of tones of higher pitch (as distinct from tones of other pitch) through the lateral lemniscus to the medial geniculate and from there to the auditory cortex. Obviously the anatomic basis for cortical recognition of tones of different pitch is a function not only of the cochlea but also of every level of the nervous system through which the auditory impulses are relayed to the cortex.

THE ESTABLISHMENT OF THE LOCALIZATION PATTERN IN PRIMARY EFFERENT CENTERS

Preliminary reconnaissance. In embryonic tailed amphibians at early swimming stages (Herrick and Coghill, '15; see also fig. 6 A) the efferent fibers are merely collaterals

of longitudinally conducting paths, the non-specificity of their impulses being indicated by the fact that a number of such collaterals, passing to as many different somites, arise from a single descending fiber. The motor neurons of these larvae then show specificity in the type of impulse which they carry but are non-specific in their central origin and arrangement. Whether the most primitive responses in embryos of higher forms are total responses of the Coghillian type, as Angulo y Gonzales ('35 and elsewhere) and Hooker ('36) believe, or specific responses, as Windle ('31, '34) and his co-workers (see bibliography) hold, the mechanism in these larval Amblystoma appears to provide for total responses. In passing from such embryonic to adult forms or from cyclostomes to higher forms, there is a grouping of the motor neurons indicated by the gradual establishment of longitudinal columns of gray within the ventral horn associated with the innervation of functional groups of skeletal muscles (for literature, see Ariëns Kappers, Huber, and Crosby, '36). The number of studies of longitudinal sections of the spinal cord of various vertebrates is exceedingly small. Sections of this type are found in the 1926 paper of Terni on the marginal nuclei in Sauropsida and in John Franklin Huber's ('36) contribution on the avian cord, and mammalian sections of this type are illustrated in papers by G. Carl Huber ('27) and by Murray ('29). Undoubtedly there are others in the literature.

Presentation of material. In figures 6 to 8, the longitudinal columns of gray formed by the somatic efferent neurons are shown for the spinal cords of the cyclostome, the tailed amphibian, Necturus, the frog, the turtle, the snake, and the

Fig. 6   A. A diagram based on the Herrick and Coghill ('15) report showing the reflex arc within the central nervous system associated with the early swimming movements in larval Amblystoma. (By permission.)

B. Drawing of a longitudinal section of the spinal cord of Petromyzon marinus unicolor. Pyridine silver preparation. $\times$ 37.5.

C. Drawing of a longitudinal section of the spinal cord of Necturus maculosus. Toluidin blue preparation. $\times$ 37.5.

D. A composite drawing based on a toluidin blue transverse section of the spinal cord of the frog (Rana pipiens) through the cervical enlargement, supplemented as to detail from pyridine silver preparations of the same region. $\times$ 23.
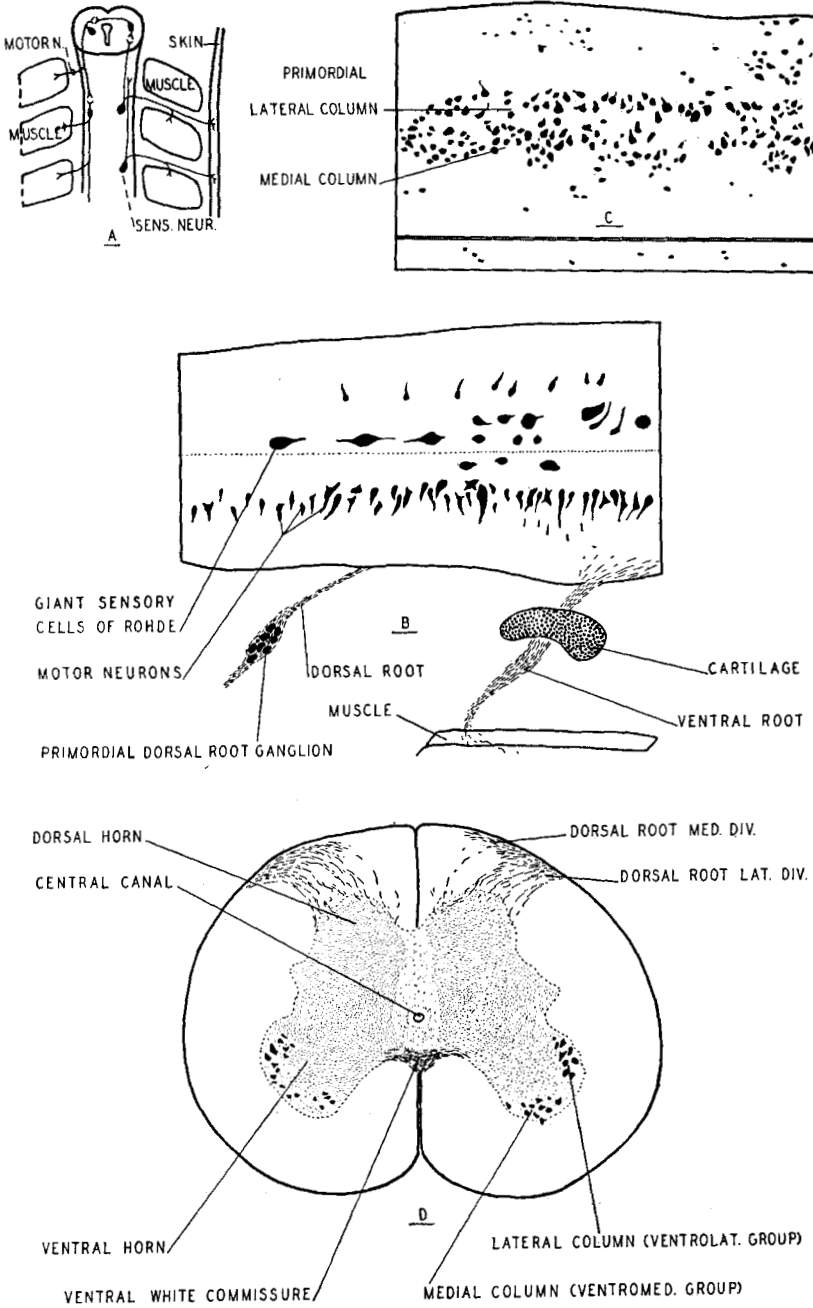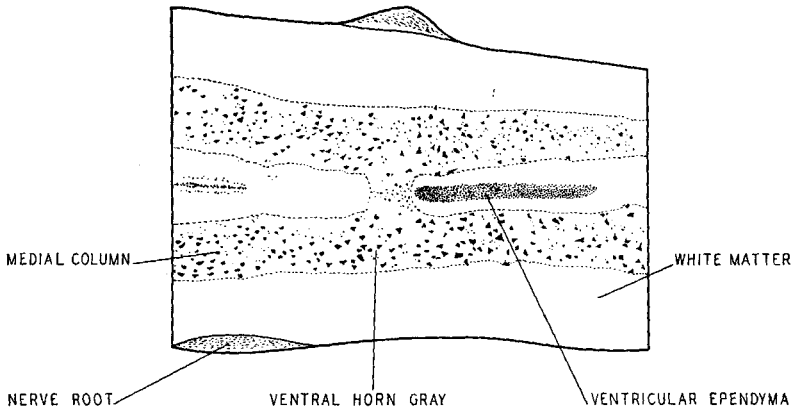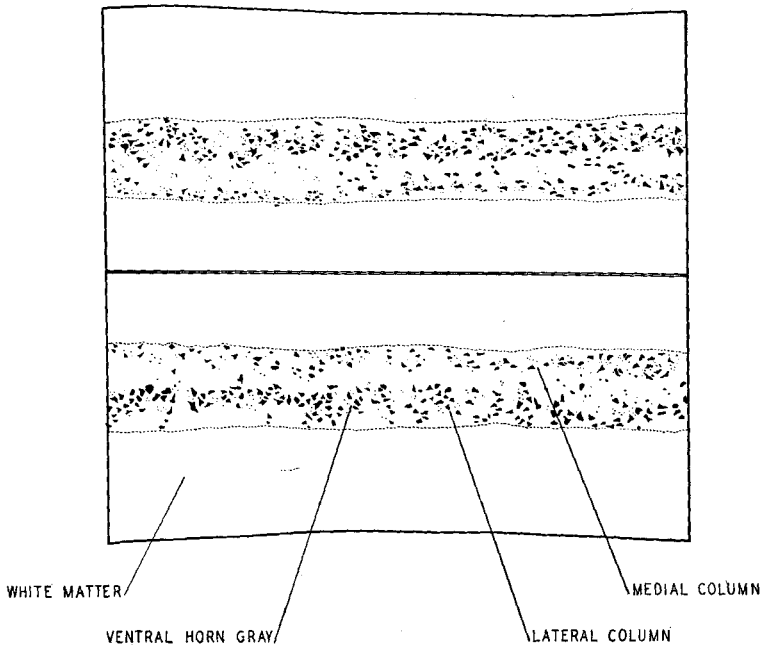
Figure 6

rat. These illustrate only a few of the types of vertebrate spinal cord consulted in preparing this paper, both cross and longitudinal series being available.

The ventral horn neurons are difficult to distinguish and show no special arrangement in cyclostomes (fig. 6 B). In all forms above cyclostomes, with such rare exceptions as the turtle, which has almost no motor neurons in the thoracico-lumbar region (in correspondence with the almost complete lack of trunk musculature), there is a longitudinal column which is to be regarded as homologous throughout to the ventromedial column of mammals, being concerned un-doubtedly in all forms in the innervation of trunk musculature. A lateral column, present throughout the enlargements, is found from tailed amphibians (figs. 6 C to 8) to mammals, including man, in all forms which have extremity musculature, the outstanding exception here being found in the snake spinal cord (fig. 7 A), in obvious correlation with the lack of fore- and hind-limbs. Suggested by certain groupings in reptiles such as the alligator, clear cut at certain levels and indistinct at others in the avian enlargements (see also John Franklin Huber, '36), and present throughout the mammals consulted, are two subdivisions of the lateral column—a ventrolateral and a dorsolateral (figs. 7 B and 8 A)—associ-ated, as Bok ('28) has shown, with the innervation of shoulder and pelvic girdle musculature and with arm, wrist, and hand and leg, ankle, and foot musculature respectively. The retro-dorsolateral column, concerned with supplying muscles of fingers and toes, is best differentiated from the dorsolateral in primates. A like specificity can be demonstrated in the efferent centers of the cranial nerves. This brief résumé illustrates that progressive differentiation in the efferent columns of the central nervous system is correlated with the progressive specialization in function of the muscle groups in the animal under consideration and that this degree of differentiation sets the limits of specificity of response for the whole efferent arc.

MEDIAL COLUMN

WHITE MATTER

NERVE ROOT

VENTRAL HORN GRAY

VENTRICULAR EPENDYMA

A

WHITE MATTER

MEDIAL COLUMN

VENTRAL HORN GRAY

LATERAL COLUMN

B

Fig. 7 Drawings of longitudinal sections of the spinal cords of the garter snake, Thamnophis sirtalis (A) × 34.5, and of the turtle, Chrysemys marginata (B) × 23, to show the ventral efferent columns. Toluidin blue preparations.

DORSAL HORN

DORSAL FUNICULUS

VENTRAL HORN

LATERAL FUNICULUS

VENTRAL FUNICULUS

LATERAL COLUMN (DORSOLAT. GROUP)

MEDIAL COLUMN (VENTROMED. GROUP)

A

LATERAL COLUMN (VENTROLAT GROUP)

VENTRAL HORN GRAY

WHITE MATTER

INTRINSIC NEURONS

MEDIAL COLUMN (VENTROMED. GROUP)
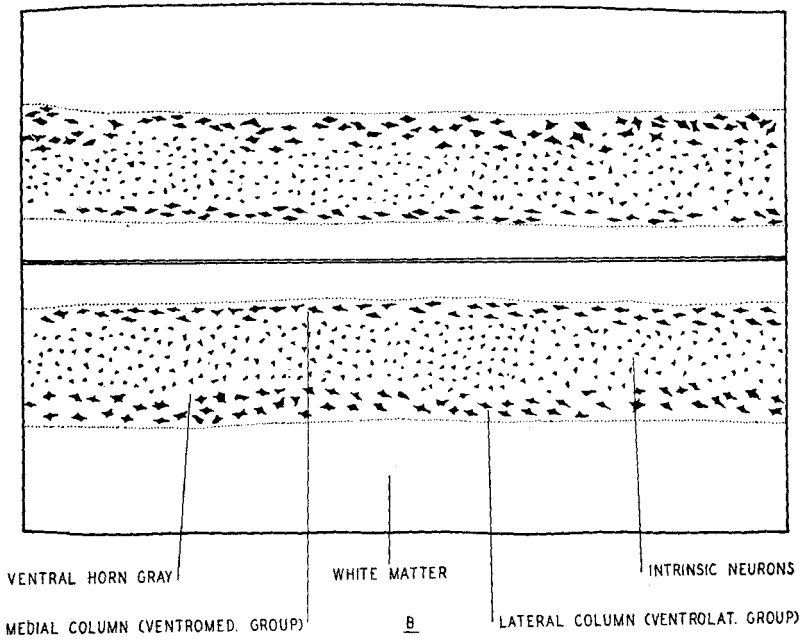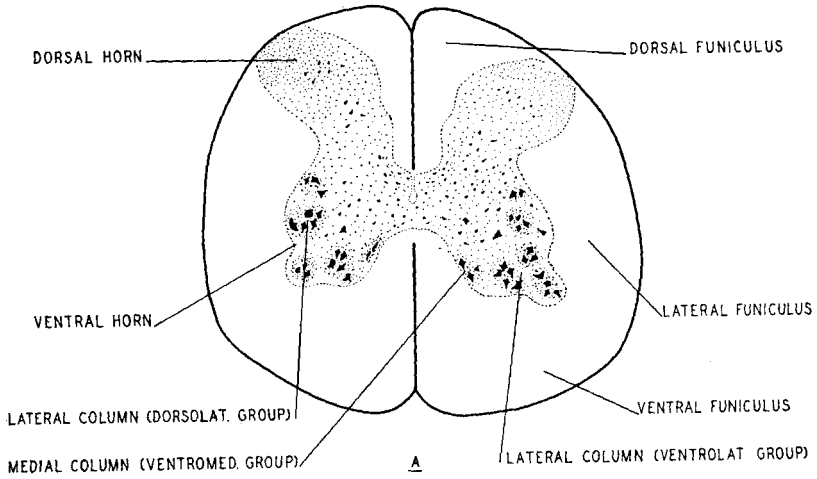
B

LATERAL COLUMN (VENTROLAT. GROUP)

Fig. 8   Drawings of transverse (A) and longitudinal (B) sections of the spinal cord of the white rat, Mus norwegicus.   Toluidin blue preparations. $\times$ 21.5.

THE ESTABLISHMENT OF THE LOCALIZATION PATTERN IN THE EFFERENT CORTICAL CENTERS

Preliminary reconnaissance. Just as specificity develops progressively within the efferent columns, so there is a gradual superposition upon them of the paths from higher centers. The way in which these paths are established in phylogeny and the development of localization patterns in higher sub-cortical areas by the projection back upon these areas of the organization within the primary efferent centers through the orderly arrangement of the interconnecting paths have been discussed recently (Crosby and Woodburne, '38) and need not receive further consideration here, but some attention will be given to the finer organization of the cortico-spinal system.

The cortico-spinal tracts and the pattern of motor cortical localization have been studied in a great range of mammals including man, and the recent paper on the macaque brain by Levin and Bradford ('38), consulted in conjunction with any of the larger neuroanatomical or neurophysiological texts, will provide adequate references (Ariëns Kappers, Huber and Crosby, '36; Fulton, '38; and many others). There is no need for reviewing this literature here, such articles as are particularly pertinent for the problem in hand being referred to in connection with the following description. But it should be emphasized that, although the course of the cortico-spinal tract from the cortex to the spinal cord is comparatively well understood for various mammals, the arrangement of the constituent fascicles within the tract has received much less attention. It is this organization within the tract (already discussed briefly in a preliminary report, Crosby and Woodburne, '38) which will be considered in the following account, since such an analysis seems desirable as a basis for understanding cortical localization.

Presentation of material. Lesions were made in the rat cortex and material was prepared by the Marchi method with a view of determining the arrangement of the fascicles of this tract throughout its course from higher to lower centers.

The motor fields in the rat cortex are indicated in figure 9 A, following Lashley's ('31) work in which these areas were plotted. The pattern of distribution of the fiber bundles arising from the several areas is illustrated in figure 9, which was drawn as a composite from ten series of Marchi preparations made following limited cortical lesions. Figure 9 B shows that, as the fascicles pass through the caudate-putamen complex, those from head and neck cortical centers lie ventral to the bundles from upper extremity centers and these in turn lower than those supplying fibers to the centers for lower extremity muscles. As the fascicles swing into the base of the midbrain (fig. 9 C) those from head and neck centers lie medially and are succeeded mediolaterally by bundles from upper extremity centers and then by those from lower extremity centers. At such midbrain levels certain fibers of the head component pass off from the main bundle as an aberrant pyramidal tract (fig. 9 C) which terminates around cranial nerve nuclei. Similar fascicles are given off in the pons region. Within the basilar part of the pons the fibers of the peduncle are broken into separate fascicles by the intermingling bundles of the ponto-cerebellar tract and, when they reunite in the pyramid, their arrangement is not so clear as at midbrain levels although still a general pattern may be seen of the type indicated in D of figure 9, in which the fibers to efferent neck centers override those to the efferent centers of upper and lower extremities. In the motor decussation (fig. 9 E) the upper fibers of the pyramid cross first and, after such decussation, arch into the dorsal funiculus and ultimately come to occupy its ventromedial area. The

Fig. 9 A series of drawings to illustrate the relations in course of the components of the cortico-spinal system of the rat (Mus norwegicus). Republished by permission from the University of Michigan Hospital Bulletin, vol. 5, 1938. (A) is a diagram of the dorsal surface of the rat cortex. The regional localization here is from the account of Lashley ('31). The drawings (B) to (F) are based on a study of Marchi preparations and show the localization of the components in course—(B) at telencephalic levels through the caudate-putamen complex, (C) through the cerebral peduncle, (D) through the pyramid of the medulla oblongata, (E) at the level of the motor decussation, and (F) through the upper cervical cord.
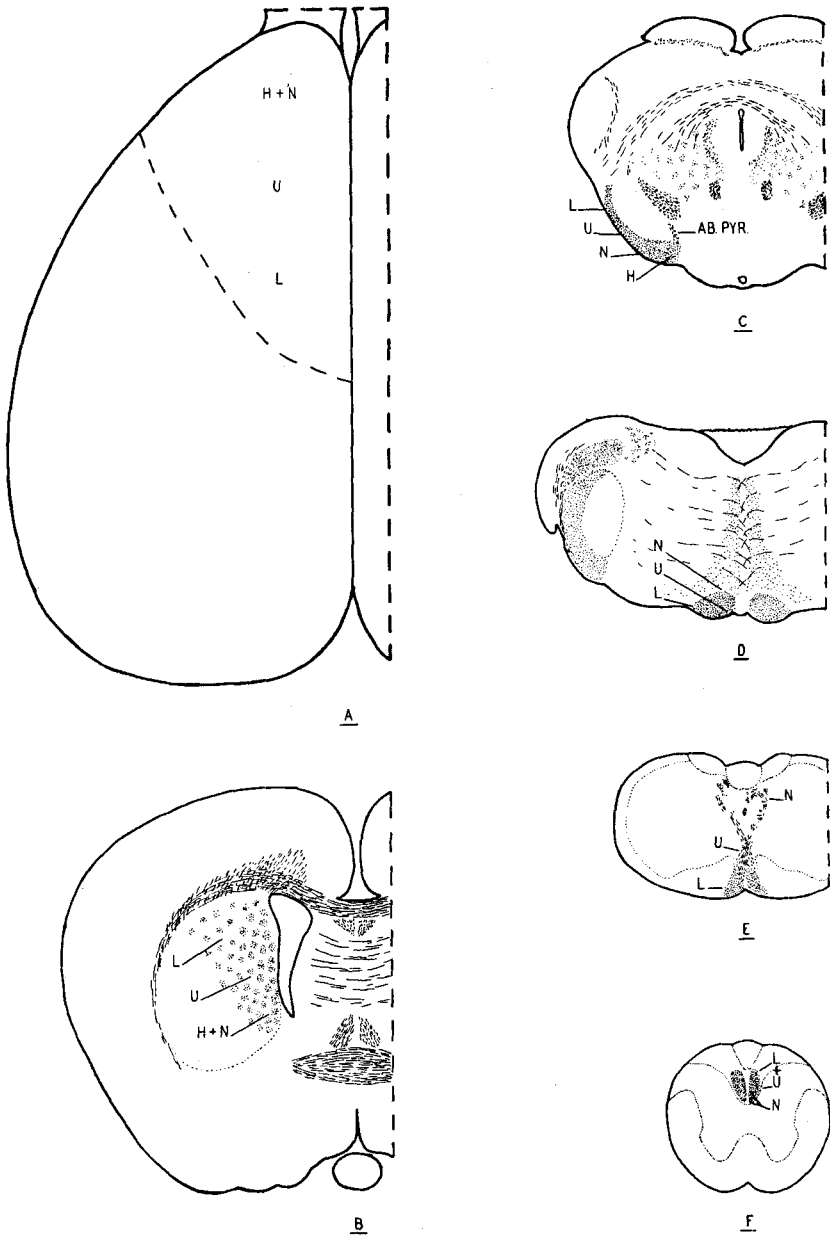
Figure 9

next fibers to cross are those for the upper and then for the lower extremity and these pile up in regular fashion. Within the cord (fig. 9 F) those fibers passing to the neck levels are given off first and end around motor centers to neck musculature. In this way the fasciculus loses successively ventrally and ventromedially, with the most dorsolateral fibers passing as far as the ventral horn neurones of the lumbosacral enlargement in this rodent.

In the foregoing discussion evidence has been presented that the centers of the adult rat cortex concerned with certain specific voluntary movements are connected by fascicles which show an orderly arrangement in their course and which terminate within the spinal cord and brain stem on the appropriate motor centers for producing movement in accordance with the established pattern. Just what does this mean from the standpoint of phylogenetic or ontogenetic development? It is clear that the primitive efferent pattern is established by the nuclei of origin for the motor neurons to the muscle, that is, by the lower motor neurons, consequently any tract terminating on such neurons can increase or modify or inhibit a reflex contraction of the muscles which they supply or can initiate voluntary contraction of them but cannot of itself affect the movement of other portions of the body. Thus fibers from the cerebral cortex to efferent centers supplying neck muscles by their connection with these efferent centers take on the function of upper motor neurons associated with neck movements. Others, by virtue of their spinal cord connections, become associated with the innervation of the extremities, and so on down the list. In this way cortical neurons of the cortico-spinal paths reflect the specificity and type of function of the lower motor neurons with which they are connected. Since there are more lower motor neurons than there are cortical neurons, it is obvious that the specificity of the upper motor neuron will usually be less and never more than that of the lower motor neuron. Since the connection between the cortical upper motor neuron and the spinal cord lower motor neuron is according to a definite

arrangement, with the fibers from a given region of the cortex running together and maintaining this relation throughout their course to their termination in a restricted region of the spinal cord, a regional localization pattern is established in the cortex. It is obvious that this cortical localization, then, is a reflection of a very primitive spinal cord localization which antedates the appearance of any motor cortex, and that its degree of specificity in any mammal is dependent upon the specificity of distribution of the lower motor neuron and the proportionate number of cortico-spinal fibers to such a lower motor neuron. Moreover, it is evident that this localization pattern is a function of the complete neuron arc and is not inherent in the cortical gray as such. Any change, then, in the peripheral pattern of innervation, either phylogenetically or by experimentation, will modify the complete pattern and change that of the cortical localization in the animal concerned.

Additional examples. The foregoing discussion has emphasized the principles of determination of efferent cortical localization, the pattern arrangement of the cortico-spinal tract being cited as an example of a system showing a rather precise functional localization which impresses on the cortex the functional pattern determined by its termination on the primary efferent centers of the spinal cord. Additional data, based on the study of normal material, is at hand with regard to functional patterns in other efferent systems. The arrangement of the tecto-spinal paths and the localization in the superior colliculus have been discussed in a previous paper (Crosby and Woodburne, '38) and an analysis of the rubro-spinal tract and red nucleus has also been made. In the red nucleus of mammals such as the rat the more fronto-laterally arising fibers cross first to reach the lateral portion of the descending rubro-spinal tract and are succeeded in orderly fashion by more mediocaudally arising fibers which decussate later and then occupy the medial portion of the descending tract. Having once joined the system the bundles proceed in parallel arrangement to the spinal cord, in which region the medial fibers terminate first and are succeeded by progressively more laterally running fibers. Thus the rubro-spinal tract shows a pattern from lateral to medial. Further

experimental documentation of these functional localization patterns in the efferent centers and fiber paths of the brain has been begun for both rat and monkey and will receive attention in a later publication.

DISCUSSION

It is hoped that the problems of finer localization within nuclei and the pattern organization of fiber paths in course may interest an increasing number of those observers who deal primarily with experimental material. Many of the series prepared for the consideration of various other problems would undoubtedly give evidence of such organization in both nuclear masses and fiber bundles. Further knowledge of such functional components of both centers and tracts would be of value from the standpoint of the finer anatomy of the nervous system. Such data would also be useful to the clinician in determining the direction of spread of pathological processes in the brain and in more accurately locating the levels of the lesions.

The conclusions presented in this final recapitulation are to be regarded as offering primarily a basis for further discussion. It is evident that specificity in its development appears first in the peripheral neuron as a whole, whether the afferent or efferent nerve cell be considered, and that this specificity is indicated both by the degree of development of the neuron itself, including its termination, and by the nuclear arrangements established by the central grouping of neurons functionally related. These limits of specificity set by the motor and sensory centers and their related fibers in the spinal cord and brain stem regions mark, for a given animal, the limits for any specificity either on the reflex or conscious plane for the region so innervated, unless it receives an overlapping innervation from some other portion of the nervous system. The specificity of the primary neuron, whether it be motor or sensory, sets, then, the limit of specificity for the whole conduction arc. For this given arc there can be no greater specificity and there is usually less in the higher centers than in the primary neuron.

Ascending paths formed as neuraxes of primary neurons or arising from secondary or tertiary neurons, which receive their impulses from primary neurons, tend to be formed by the accumulation of neuraxes carrying like impulses. As is well known the peripheral nerve tends to bring in all the sensory impulses from a region and to carry motor impulses to that region but at spinal cord levels and brain stem levels a sorting of impulses occurs, so that they are redistributed into paths within the central nervous system in accordance with the kind of impulse carried. But the arrangement goes further in that the secondary paths accumulate in such orderly fashion that the impulses of a given kind arrange themselves in a regional or segmental pattern, not only the kind of impulse but the region of stimulation of this impulse being reflected on the higher centers by the arrangement of the fascicles of the ascending path. For example, the more lateral part of the lateral spinothalamic path carries not only pain but pain from the caudal part of the body (Foerster, '27).

Since the pattern of localization of specific impulses in space is inherent in the organization of the major ascending paths their nuclei of termination have impressed upon them a similar pattern the perfection of which is dependent upon: a) the orderly termination of the fascicles of the ascending tract; b) the discreteness of their termination (which in turn is to a considerable extent a function of the size and cellular content of the receptive nucleus, a large and well-differentiated nucleus of termination providing the possibility of a decreased overlap of the terminating fibers); and c) the differentiation within the nucleus of reception of secondary subdivisions which still further decrease the possibility of terminal overlap. The increased differentiation within the ventral nucleus of the dorsal thalamus in primates, in contrast with the differentiation of the homologous nucleus of the rat, illustrates these points. Since there is seldom or never a one to one relationship between the neuraxes of the ascending path and the neurons of the secondary centers—although this is approached in the optic system

(Brouwer, '27; Polyak, '32; Lashley, '34; and many others)—
there is a constantly decreasing specificity of localization in
the ascending system with each area of synaptic exchange.
It should be kept in mind that it is the specificity of the cortex
of which we are aware, although all such specificity of localiza-
tion within the cortex is consciously projected to the pe-
riphery of the body.

Similarly, on the efferent side, the localization patterns
established in higher centers—whether these be motor cortex,
tectum, or red nucleus—are reflections of patterns established
at the primary motor levels which are projected back on the
secondary centers by the orderly arrangement of the de-
scending paths. The pattern in the higher efferent centers
then is usually less clear cut and less specific than that of
the primary centers and under no circumstances can it become
more specific.

Following the laws established for other nuclear centers,
the patterns of cortical localization in the sensory and motor
projection areas are the inevitable end-products, phylo-
genetically and ontogenetically, of the localization patterns
of subcortical centers, which have been impressed on these
cortical areas by the orderly arrangement of the fascicles
of the cortico-petal and cortico-fugal paths. Cortical ap-
preciation of sensory impulses—as made possible through
the sensory projection areas—has inherent in it not only the
kind of impulse but the localization of the impulse in space.
Sensations are not only experienced; they are immediately
localized. Thus one does not usually experience simple pain,
but specific pain in the finger or other region stimulated.
For pain, temperature, and general tactile sensibility both
the quality of the impulse and its localization in space are
end-products of the orderly arrangement of the paths and
of the localization patterns established in all the regions of
synapse over which the impulses pass from the primary
receptive centers to the sensory projection areas of the cortex.
Probably in the cortical appreciation of vision and hearing
there is essentially the same dependence upon both the kind

of impulses and their orderly localization in space, as determined by the arrangement in nuclei and fiber paths involved in the conduction. This appreciation of what the impulse is and where it is characterizes the functioning of projection cortex. The patterns of the projection areas of the cortex, then, whether these areas be motor or sensory, are the logical outcome of the connections with lower centers and increase in specificity in passing from lower to higher mammals and through primates to man. Such specificity makes for precision in reception and response but reduces that other desirable factor of cortical function, the variability of response.

Associated with these cortical projection areas, which show a localization pattern, are bordering cortical zones dominated for the most part by the projection areas along which they lie but, in lower mammals, showing little or no specific functional localization. With the increase of specificity of the projection areas, in passing from lower to higher mammals, apparently there is an increased specificity of pattern in these primary association areas, impressed upon them probably by the more localized projection areas. Thus in the premotor area of man various centers, including those concerned with coordinate movements of the eyes, cortical regions which affect sympathetic functions, and areas, the destruction of which interferes with speech, have been described. That these functions are in terms of their fiber connections and are not inherent in the gray matter has also been established by various types of studies. In any event it is evident that there is a tendency toward the establishment of a functional pattern in the primary association regions in man. Compensating, whether by chance or not, for this preempting of the primary association centers by the projection areas through their connections and so serving to overcome the tendency of a pattern furthering stereotyped responses, a new cortical development occurs through mammals and reaches its maximum in man in the large frontal, parietal and temporal secondary association areas, which, through the richness of their con-

nections and their distance in terms of synapses from the primary and secondary receptive centers of the brain stem, are under the continued domination of no one type of receptive center but shift in their pattern of correlation and response with the ebb and flow of impulses passing through them from other cortical areas. Any pattern established must be transient in character and vary from instant to instant. In general, then, as soon as the bounds of sensation as such are left behind and perceptions and patterns are to be dealt with, the cortical areas immediately involved are those of association rather than projection cortex and the more abstract the material to be considered the farther removed will the cortical area be from the dominance of any single projection area.

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