THE TRACT OF LISSAUER AND ITS POSSIBLE RELATION TO THE PAIN PATHWAY

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I. INTRODUCTION

The tract of Lissauer has long been associated with pain, but the exact pathway of this important sensation has been far from clear.

If the fibers carrying pain are "unmyelinated and small myelinated fibers" as physiological experiments have indicated (Gasser, 1937-1943; Adrian, 1932, Erlanger (1937) and if these fibers separate out at the root entrance zone, occupy the "lateral division of the dorsal root" and then enter the tract of Lissauer (Ranson and Billingsley, 1916), how far do they travel within this tract before terminating? What is the course of the fine fibers in Lissauer's tract? Are there any long fibers in this tract to account for discrepancies in the level of analgesia following anterolateral chordotomy? These questions are disputed and point out the need for study of this tract and its relation to pain.

The usual statement that "pain fibers" end within one or two segments after entering the cord has been challenged by several investigators. It has been suggested that these fibers may ascend for as many as three to five segments before terminating. Indeed, the idea that at least some of the pain fibers may have an uncrossed or direct pathway to the ipsilateral thalamus has often been expressed. This concept seems to have resulted from observations on patients who had return of pain following cord hemisection, failure to relieve certain

types of unilateral pain by chordotomy, and the fact that animals often show no evidence of analgesia following cord hemisection.

The anatomical studies that were made on Lissauer's tract during the last century were inadequate to answer these questions, being limited largely to gross description of normal or autopsy material stained by the Weigert or Marchi methods. The unmyelinated fibers, which were later shown to be very numerous in Lissauer's tract, did not stain by these two methods and received little attention until Cajal (1906) and Ranson (1912) studied the tract with reduced silver methods.

Most of what we know of the normal structure of Lissauer's tract was described by these two men. Ranson's studies, both physiological and anatomical, are the basis for our present concept of the relation of Lissauer's tract to pain.

In addition to studying the normal structure of Lissauer's tract and its physiological relation to pain, Ranson studied the extent of degeneration following section of this tract, but only in what he terms a "negative" way. That is, he allowed several weeks for degeneration to occur following a lesion and considered <u>complete disappearance</u> of fibers as evidence of degeneration, when stained with silver. That is similar to the way in which degeneration of myelinated fibers is determined by the Weigert method.

The work of Glees (1946), Hoff (1932), Gibson (1937) and others have shown that degenerating fibers and terminal endings may be traced without waiting for the fibers to completely disappear. These methods of directly tracing degeneration of fibers depend upon the fact that the axons and terminal endings of both myelinated and unmyelinated fibers show swelling, fragmentation, varicosities, or vacuolization during the early stages of degeneration which can be stained with silver and identified. Errors of interpretation may occur with these methods unless rigid criteria of degeneration are followed and the experiments well controlled, but they seem to be more sensitive than the older method of waiting for the fibers to disappear and have the advantage of being applicable to both the myelinated and unmyelinated fibers in the same section.

The Marchi method has also been shortened by the Swank-Davenport modification and has consistently demonstrated staining of degenerating myelin after less than six days in the cat, and can be used as a partial control for the silver methods.

This study was therefore planned as follows: 1) To review critically the evidence relating Lissauer's tract to the spinal pathway for pain,and 2) apply these newer direct method to determine the composition of Lissauer's tract, including the extent of degeneration within this tract following (a) section of the tract and (b) section of single and multiple posterior roots.

II. HISTORICAL REVIEW

In 1885 Heinrich Lissauer, a German neurologist, described the tract which bears his name in a short article in the Neurologisches Centralblatt. This article is reproduced in Figure 1 and is translated as follows:

"Observations on the Pathological Anatomy of Tabes and Course of Fibers in the Human Spinal Cord."
By H. Lissauer (From the Pathological Institute of Leipzig.)

In preparations of the human spinal cord which are stained by the Weigert hematoxylin-potassium ferrocyanide method, the following behavior of a part of the posterior roots can be seen; the fibers under consideration always collect themselves on the outside of the roots near the point of entrance into the spinal cord; the bundles which are formed this way and which are formed only by fine fibers, turn laterally immediately arter they enter the pia; and it seems that they direct themselves toward the lateral funiculus. But they turn vertically and are collected in one layer which is situated on the tip of the posterior horn between the posterior and lateral funiculi. This layer (which from topographical point of view is partly identical with the apex cornu posterioris of other authors) is pierced by the compact posterior roots in the vicinity of its medial border. On cross sections it is characterized by its uniform composition of fine longitudinal nerve fibers and is distinct from the

bordering white substance. After a longer or shorter period of vertical ascent these fine fibers penetrate into the gelatinous substance or the deep layers of the posterior horns. After these fibers change their direction from vertical to horizontal, they become interwoven and their course is extremely complicated, so that the following of these fibers is seldom possible for long distances.

In 12 cases of tabes dorsalis, except in one initial case, we found changes in the fine fibers; these changes were most clearly seen in the area of fine fibers described above which lies between the lateral and posterior funiculi. Here- quite a long distance from the posterior root entrance - we could see in these cases degeneration of various degrees, this degeneration has such a long sharp border at the margin of the lateral funiculi that no doubt exists about the systemic nature of the process. This degeneration can be seen even in the early stages of Tabes. Two cases of early tabes have been studied (one with slight lateral sclerosis). In these cases we found in the middle upper lumbar cord on the tip of the posterior horn a small field of degeneration which spread out and was identical with the fine fibers described above. At the same time we saw degeneration of the center of the posterior funiculi which was independent of the other degeneration. So it seems that those fine fibers whose destination is the posterior horn and which are situated between the posterior and lateral funiculi form a special systemic unit. This unit seems to be degenerated in some

stages of Tabes.

" The fine fibers in the anterior layers of the posterior horns are not spared in the process of the disease, but degeneration of these is, in general, not so striking as in the described peripheral field. So we can assume that the process in the posterior horn advances from the periphery toward the base."

From this study of Weigert stained material, Lissauer apparently believed that all of the fibers of this tract were of exogenous origin and therefore entered the cord from the posterior roots. He was, however, only describing the myelinated fibers in the tract and his apparent lack of knowledge of the unmyelinated fibers led him to an erroneous conclusion, as will be shown.

In fact, Nageotte (1903), made a similar error when he described the case of a man who had a metastatic tumor involving all the nerve roots of the cauda equina up to, and including, the fourth lumbar, without causing any evidence of degeneration of the fibers of Lissauer's tract. Using only the Marchi method of study, he concluded that all the fibers of Lissauer's tract were of endogenous origin. He, also, was apparently unaware of the unmyelinated fibers in this tract.

Nageotte's observations would seem to directly contradict Lissauer's observations except that the methods of study were different. Nageotte's results could be restated to say that

when the dorsal roots were destroyed by tumor, there was no degeneration of the myelinated fibers of Lissauer's tract as determined by the Marchi method. Thus, his conclusion that all the fibers of Lissauer's tract were of endogenous origin was no more justified than the apparent conclusion of Lissauer that they were all of exogenous (posterior root) origin.

Using the same Marchi method, other contradictory articles began to appear concerning the degeneration following destruction of posterior roots by pathological processes. Collier and Buzzard (1903) found small areas of degeneration in Lissauer's tract following posterior root section. They reported in a case with a cauda equina lesion: "Lissauer's tract contained a few very fine degenerated fibers which rapidly disappeared at higher levels." In a case with a lesion of the third lumbar posterior root they found that "the region of Lissauer's tract presented very few degenerated fibers even at a level immediately above the entry of the third lumbar root."

Sottas (1893) and Sibelius (1905) found "small areas" of degeneration in Lissauer's tract following dorsal root section, using the same Marchi method.

Many other authors reported cases with extensive lesions of the posterior roots and spinal cord, but most of these make no mention of degeneration in Lissauer's tract by either the Marchi or Weigert-Pal methods and we must assume that evidence of degeneration was lacking or very slight in these cases.

None of these authors mention the unmyelinated fibers of Lissauer's tract and apparently were unaware of their existence.

Cajal (1909) carefully studied the normal microscopic anatomy of the posterior roots and zone of Lissauer in numerous young animals and embryos. He used various staining methods, especially the Golgi, methylene blue of Ehrlich, and his own numerous silver methods. His descriptions and drawings were extremely detailed and accurate. He saw two types of fibers in the dorsal roots; (1) large, "internal", early myelinated fibers destined for the posterior columns and (2) fine, "external", poorly myelinated fibers which entered the marginal zone of Lissauer. His concept of the spinal cord is reproduced in Figure 2.

Cajal showed that the dorsal root fibers bifurcate soon after entrance and that the fine fibers ascend or descend in the zone of Lissauer "for short distances" giving off numerous branches along the way (Fig. 3). He stated that he was unable to follow these fibers to their exact terminations, but that the branches seemed to disappear among the cells of the substantia gelatinosa Rolandi and neighboring gray matter. Cajal agreed with the suggestion of Lenhossek (1895) that these fibers were "sensory in function" but did not specify the sensation of pain. He further described processes of marginal cells and cells of the substantia gelatinosa as contributing to the zone of Lissauer (Fig. 4).

From 1912 to 1916 Ranson and his co-workers made the most extensive studies of Lissauer's tract which have ever appeared. These studies have formed the basis for the direct association of Lissauer's tract with pain transmission and will be considered in detail.

In 1912 Ranson began by studying the dorsal roots with a new pyridine silver method which he had modified from a method of Cajal. He found that when the dorsal roots were stained by this method, the fine fibers were much more numerous than had been previously reported. This was apparently due to the fact that they were unmyelinated and would not stain by Weigert or Marchi methods. He traced these unmyelinated fibers of the dorsal roots to their origin in the spinal ganglia and found that they arose as the central process of a small spinal ganglion cell. He also found that the peripheral process of the same cell was often larger than the central process. This observation seems to have received little attention in later years, but is important if we are to consider the relationship of fiber diameters to function.

In 1913 Ranson stated that the intraspinal destination of the unmyelinated fibers of the dorsal roots was essentially unknown. He studied serial sections of pyridine silver stained spinal cords of cats and described in detail the topographical differences in Lissauer's tract at different levels. He described the way in which the non-medullated fibers of the

dorsal roots separate out in bundles at the root entrance zone, at first occupying the periphery, and then taking the "path of least resistance" in coursing laterally to join the tract of Lissauer. He called attention to the constricting band of pia which surrounds the entering rootlets or "fila radicularia", the pial band extending into Lissauer's tract and dividing it approximately into halves, and the connective tissue septa within the dorsal roots along which many of the bundles of unmyelinated fibers run at the zone of entrance into the cord.

He concluded, in regard to Lissauer's tract, "the ascending fibers must be relatively short — otherwise there would be a steady increase in size from lower to higher levels in the cord — the tract seems rather proportional in size to the entering rootlets. There is a marked decrease in going from lower lumbar into thoracic and again from lower cervical to upper cervical regions."

On the eventual termination of the fibers of Lissauer's tract he wrote, "the non-medullated fibers — run for short distances in this tract in an ascending direction chiefly and then pass forward into the substantia gelatinosa. The close relation of Lissauer's tract to this peculiar substance which caps the posterior horns, the fact that fibers can be seen passing from one into the other, and the fact that there is no other apparent outlet for the fibers of Lissauer's tract indicated that the substantia gelatinosa is the probable nucleus

of reception of these non-medullated fibers." Curiously, in discussing the intraspinal course of the unmyelinated fibers, Ranson did not comment on the bifurcation of these fibers at the root entrance zone, which had previously been so clearly described by Cajal (1909).

In 1913,Ranson made certain deductions regarding the function of Lissauer's tract, "so far as the function of the non-medullated fibers is concerned, their course within the cord shows that they can have little or nothing to do with the afferent impulses received from muscles and joints which travel up the posterior funiculus. This does not necessarily include muscle and joint pain. Their early termination within the gray substance would agree with the course of the sensations of pain and temperature and probably also with that of touch. But there are, of course, no data on which one would care to hazard a guess as to their function, beyond the statement that they can have little or nothing to do with those sensations which are known to travel directly upward in the posterior funiculus."

In 1914, Ranson extended his studies by sectioning the posterior roots in nine cats and tracing the resulting degeneration by Weigert-Pal, Marchi, and pyridine silver methods after periods of degeneration which varied from 14 to 17 days. Regarding the limitation of this technique he wrote, "the degeneration of the non-medullated fibers cannot be followed in so definite a way as that of the medullated fibers since

we have no stain for degenerating axons similar to the Marchi for degenerating myelin. It must be studied in a negative way just as the degeneration of medullated fibers is studied in Pal-Weigert preparations, i.e., we have only the disappearance of the fibers as evidence of degeneration." As stated in the introduction, it has since been shown that silver methods may be used to trace degeneration of fibers directly during the early phases of degeneration when fragmentation, vacuolization, swelling, distortion and bouton changes are occurring, but these criteria had not been established when Ranson was doing his experiments.

Ranson found the following from these experiments of cutting dorsal roots:

(1) Marchi — degeneration in part of the medial division of Lissauer's tract at the level of root section and one or two segments above. (2) Weigert-Pal — reduction in number of medullated fibers in the medial part of Lissauer's tract at the level of root section. (3) Pyridine silver — reduction in the number of fine fibers in the medial division of Lissauer's tract for one or two segments.

From these experiments he concluded: "the tract of Lissauer in the lumbosacral region of the cat's cord consists of two parts, approximately a medial and lateral half. The fibers of the lateral half, both medullated and non-medullated, are of endogenous origin. The fibers of the medial half, both medullated and non-medullated, are in part endogenous and in part exogenous."

Ranson also studied the cross section appearance of Lissauer's tract in man, monkey, cat, rabbit, squirrel, rat and guinea pig and found the same general structure in all. He found great numbers of non-medullated fibers entering the tract from the dorsal roots in all animals studied. However, there seemed to be no relation between the size of the substantia gelatinosa and the size of Lissauer's tract. In the rat and guinea pig, the substantia gelatinosa was found to be excessively developed, but the tract of Lissauer was poorly developed. No satisfactory explanation has ever been offered for this phenomenon. Ranson, like Lissauer and Cajal, was unable to definitely trace the unmyelinated fibers of Lissauer's tract beyond the substantia gelatinosa.

The theories of Head and his co-workers (1905-1906), which received wide acclaim, seem to have greatly influenced the work of Ranson during this period. Head performed an experiment in which he cut a cutaneous nerve in his own forearm and observed and recorded in detail the return of cutaneous sensation to the denervated skin. He also made extensive observations on patients with peripheral nerve and spinal cord injuries. His observations led him to theorize that sensation could be divided into three groups which he summarized as follows:

" I. Deep sensibility, capable of answering to pressure and to the movement of parts, and even capable of producing pain

under the influence of excessive pressure, or when the joint is injured. The fibers, subserving this form of sensation, run mainly with the motor nerves, and are not destroyed by division of all the sensory nerves to the skin.

"II. Protopathic sensibility, capable of responding to painful cutaneous stimuli, and to the extremes of heat and cold. This is the great reflex system, producing a rapid and diffuse response, unaccompanied by any definite appreciation of the locality of the spot stimulated.

"III. Epicritic sensibility, by which we gain the power of cutaneous localization, of the discrimination of two points, and to the finer grades of temperature, called cool and warm."

Head further maintained that "protopathic" and "epicritic" sensations must depend on separate, anatomically distinct, sets of nerve fibers.

These observations led Ranson (1915) to suggest that the course of the unmyelinated fibers of the dorsal root which enter Lissauer's tract were in "exact agreement with the fibers conveying protopathic sensation."

In 1915, Ranson and von Hess performed further experiments in support of this theory. They made various lesions in the spinal cord of cats, consisting of hemisections, bilateral destruction of the tract of Lissauer and the substantia gelatinosa. These animals were tested by physiological methods for

vasomotor responses and other responses to painful stimuli such as struggling and withdrawal. The painful stimuli used were pricking, pinching, and stimulation by needle electrodes. They reported: "it was found that while bilateral destruction of the tract of Lissauer and the substantia gelatinosa at the level of the first lumbar segment of the cat's cord did not interfere in any way with the perception of pain in the hind limbs, it entirely eliminated the pressor vasomotor reflex from stimulation of the sciatic nerve. Now, the vasomotor reflexes are distinctly protopathic in that they are produced almost exclusively by pain and temperature sensations. The evidence presented showed that the tract of Lissauer and the substantia gelatinosa formed a path for the conduction of afferent impulses involved in the reflex vasoconstriction due to painful sciatic stimulation. It seemed probable to us that the tract of Lissauer and the substantia gelatinosa Rolandi formed an apparatus for the reception and intersegmental conduction of painful afferent impulses. Some impulses from this apparatus passing over to the spinothalamic tract would reach the cortex and find expression as conscious pain, while other impulses received in this apparatus would ascend within it, producing pain reflexes. So far as the evidence goes, this work proves the theory that the unmyelinated fibers conduct protopathic sensation, in that it shows the portion of the cord in which these fibers run and terminate forms part of a protopathic reflex arc."

It is important to note that in spite of the theoretical interpretations which were made, these animals showed no loss of the usual responses which we consider to indicate pain, such as withdrawal or struggling, only a reduction of the pressor vasomotor response from sciatic stimulation. There was no evidence, therefore, that section of Lissauer's tract would abolish pain in the cat. In fact, Ranson suggested that this phenomenon may indicate that pain is bilaterally conducted in the cat's cord.

In 1916, Ranson and Billingsley performed further experiments to prove that pain was carried by these unmyelinated fibers. To understand the experiments we must first review what they mean when they speak of "medial" and "lateral" divisions of the dorsal roots. They defined these divisions as follows: "We shall speak of the bundle of unmyelinated fibers that turns ventrolaterally into the tract of Lissauer as the <u>lateral</u> division of the root, and to the myelinated fibers that run over the substantia gelatinosa into the cunate fasciculus as the medial division." This is an important distinction because (as shown in Figs. 5, 6 and 7) the unmyelinated fibers are not in a lateral position throughout the dorsal root. Only after entering the cord do they turn ventrolaterally into Lissauer's tract, and as will be pointed out later, their course varies with the level of the cord. Unfortunately, the concept that these fine fibers occupy a lateral position throughout the dorsal root seems to have found its way into most of the textbooks of neuroanatomy.

The technique of their experiments is outlined as follows: Adult cats. Preliminary laminectomy from L_5 to S_1 performed 5 to 10 days before the experiment to allow the animals to recover from the loss of blood and shock of this operation. Ether anesthesia. Wound in skin and muscles opened and dura exposed. Tracheotomy. Ether bottle connected and rather light grade of anesthesia was maintained. Carotid cannula and connections for tracing blood pressure. Placed on animal board with lower thorax and abdomen free to move during respiration. Dura opened. Cord and roots kept flooded with warm normal saline except during stimulation. Ligature passed around the left seventh lumbar nerve, tied, and the nerve cut distally. Ventral root cut near the ligature. Dorsal root gently raised by the ligating thread and electrodes applied close to the ligature. Faradic stimulation fifteen seconds with the secondary coil at 5. Result: Good rise in carotid blood pressure; increased rate and depth of respiration; some struggling. A very small cut along the lateral side of the root in the direction of the arrow shown at A (in Fig. 8). Root stimulated as before. Result: No struggling; no change in respiration; no change in blood pressure. A study of serial sections showed that the lateral division of the root, as defined above, was completely severed with practically no injury to the medial division. When the medial division was severed (at least 75% of the fibers by histological estimate) as shown by line B in Figure 8, stimulation of the root produced

increased blood pressure, changes in respiration and struggling just as before the lesion.

These experiments have been outlined in detail as they are repeatedly quoted in the literature as the evidence that pain is transmitted by the unmyelinated fibers of the lateral division of the dorsal roots and the tract of Lissauer. So far as I know, these experiments have never been repeated.

Ranson interpreted his results as follows: "We have shown that the afferent impulses producing struggling, increased rate and depth of respiration and the pressor vasomotor reflex are conducted along the lateral division of the dorsal root and not along the medial division. Now, practically, all of the fibers in the medial division are myelinated and the great majority of those in the lateral division are unmyelinated. Our results may, therefore, be restated as follows: The reflexes mentioned are abolished when a majority of the unmyelinated fibers have been divided. The conclusion cannot be avoided that the afferent impulses bringing about these reflexes are mediated by unmyelinated fibers. Struggling and the changes in respiration and blood pressure which have been described have always been regarded as reflexes produced by painful afferent impulses and we believe that we may safely conclude from our experiments that the unmyelinated fibers, although in the nature of things this can never be absolutely proven by animal experiments."

In later years, Boring (1916), Trotter and Davies (1909) and others failed to confirm the experiments of Head and psychologists generally discredited the idea of two separate "epicritic" and "protopathic" systems of nerve fibers. Furthermore, anatomists such as Woolard, Weddell and Harpmann (1940) have failed to find any anatomical evidence to support these two separate systems of fibers which Head had postulated for the skin. In 1931 Ranson reviewed his work and was questioned about the interpretation of his results in view of the failure to confirm Head's work. Ranson stated that he understood that Head's work had been questioned, but that if there were anything to Head's theory of two separate systems of fibers then his own experiments would seem to furnish anatomical basis.

Regardless of the theories involved, it seems that the evidence certainly favors the unmyelinated fibers and the Lissauer zone as being at least a part of the pain pathway.

Physiologists have contributed much to our knowledge of which fibers are concerned in the transmission of pain, especially Adrian (1932), Bishop, Heinbecker and O'Leary (1933), Erlanger and Gasser (1937), Lewis (1942), and Gasser (1943). These investigators have shown that pain is transmitted by relatively small fibers in the peripheral nerves and dorsal roots and have added support to the findings of Ranson. The findings of these authors may be summarized as

follows:

(1) The compound action potential of a nerve shows three main waves; A, B, and C. The A wave is the largest and consists of at least four components called alpha, beta, gamma and delta.

(2) The distribution of fibers within nerves of the same species are remarkably constant, and hence velocities are likewise constant. For practical purposes the velocity can bedescribed by a constant times the axon diameter, i.e., the larger fibers have the greatest velocity of conduction.

(3) Pain producing stimuli yield action potentials in which spike composition seems to be of small delta A and slow C fiber origin. Conduction in the non-medullated fibers is one to two meters per second. It has been suggested that this may account for the observation that pain consists of a "fast" and a "slow" component.

(4) When a nerve is asphyxiated, the largest fibers are blocked first (A and B fibers) and the smallest (C fibers) are blocked last. Clinically, asphyxia of a nerve produces loss of touch, cold, warm and pain in that order. Cocaine, on the contrary, blocks C fibers first and the larger A and B fibers last. Clinically, the order of loss of sensation from cocaine is usually cold, warm, pain, and touch.

This furnishes further convincing evidence that pain is carried by the unmyelinated and small myelinated fibers. We

should remember, however, that a single fiber may not be of the same diameter throughout its course and that the peripheral branches may be small, the main peripheral fiber larger, and the central process to the posterior roots again smaller. As Lissauer's tract is composed of unmyelinated and small myelinated fibers, and part of this tract is of posterior root origin, the evidence again strongly suggests that Lissauer's Tract is at least partly concerned in the conduction of pain within the spinal cord.

Hyndman (1942) and Hyndman and Wokin (1943) have recently stimulated new interest in the Lissauer zone. Hyndman reported section of Lissauer's tract in the human for relief of intractable pain. He performed unilateral and bilateral sections of Lissauer's tract and unilateral section combined with anterolateral chordotomy. He summarized his results as follows: "Section of the tract (Lissauer's) in nine cases has shown that this tract accounts for the discrepancy between the level at which the section of the anterior cord is made and the upper level to which the analgesia reaches. A section of the tract in the thoracic region results in analgesia and thermoanesthesia in a band three to five segments wide on the same side. When anterior chordotomy is done at the first dorsal segment on the opposite side, analgesia reaches the axilla (first dorsal segment) on the side of section of Lissauer's tract. Hence, this additional procedure serves to obtain a high level of analgesia up to and including the first dorsal dermatome.

Section of Lissauer's tract in the cervical portion of the cord in two patients has not resulted in analgesia of the upper extremity".

Unfortunately, Hyndman's lesions were not confirmed by autopsy material and the lesions may have been larger than clinically estimated in some of the cases. Also the follow-up times were relatively short in his cases, but this was probably unavoidable.

Nevertheless, these results are very interesting and indicate that the fibers conveying pain, which enter the cord from the dorsal roots, may ascend for three to five segments before synapsing with cells which send processes to the opposite side. If so, we should be able to find such fibers intact in Lissauer's tract following section. This was made the basis for some of the experiments of this study.

On the other hand, the same results would be possible if the fibers of dorsal root origin synapsed within one or two segments after entering the cord, as usually agreed, but the processes of the secondary neurone (or heurones) ascended three to five segments elsewhere before crossing to join the opposite spinothalamic tract.

Thus, the following problems may be stated: (1) Are there long fibers in Lissauer's tract, either endogenous or exogenous? (2) Where do the fibers conveying pain make there first synapse within the cord? (3) What are the cells of origin of the lateral spinothalamic tract and what is the course of these fibers in crossing to the opposite side?

This study was designed to answer the first question and perhaps throw some light on the second. The third question could easily form the basis for an independent study in the future.

Ranson suggested the gelatinosa cells as the secondary neurones from the fact that the fibers of Lissauer's tract could not be followed beyond these cells. Against this conclusion is the fact that cells as small as the gelatinosa cells do not usually have axons that run for such long distances as those of the lateral spinothalamic tract would have to do. Also, Golgi and pyridine silver preparations show the gelatinosa cells as having relatively short processes (Figs. 4 and 9).

Foerster (1936) and Edinger (1891) would have the lateral spinothalamic tract take origin from cells in the dorsal gray columns, based largely on the findings in lower vertebrates and comparison with human material.

Most anatomists and textbooks including Edinger (1891) and Ranson and Clark (1949) show the fibers conveying pain as crossing to the opposite side in the anterior white commissure of the spinal cord, but Dejerine (1914) and others consistently show them crossing in the posterior commissure. Recently Wertheimer (1949) and Accassat (1944) in France have relieved pain by incising the posterior commissure and call the procedure "posterior commissural myelotomy". It is

pointed out, however, that their incisions were shown subsequently to include usually the anterior commissure in the few cases in which autopsy material had been studied (Girard et al, 1945).

From this review, then, it is clear that the entrance zone of the dorsal roots, the tract of Lissauer, and the origin of the lateral spinothalamic tract are far from being completely understood, either anatomically or in their relation to pain.

III. EXPERIMENTAL STUDY AND TECHNICAL COMMENTS.

The cat was chosen as the experimental animal so that results could be compared with those of Ranson (as described in the historical review).

The spinal cords of six adult cats were first studied by various methods of staining to determine the best method for Lissauer's tract. The pyridine silver methods of Cajal and Ranson proved to be the most satisfactory. Glees method was less consistent, and being done on frozen sections, was less suitable for serial sections.

The problem of concurrently doing the Swank-Davenport method as a partial control (that is, to check the general extent of the lesion and the degeneration of the myelinated fibers alone) presented difficulties because the silver methods, as originally outlined, require pyridine, alcohol, or chloral hydrate fixation, whereas Swank's method requires formalin fixation. This problem was quickly solved, however, when it was found that cords fixed initially in formalin could be de-formalinized with chloral hydrate as recommended by Lhotka and Ferriera (1949) and gave equal or superior results to those fixed initially in pyridine, alcohol or chloral hydrate alone.

It also became apparent that the course of the fibers from the dorsal roots into Lissauer's tract could best be

followed by complete serial sections and that longitudinal and parasagittal planes, in addition to the usual horizontal plane, were very helpful.

Experimental lesions were then made in nine cats as outlined in Figure 10.

The following procedure was employed:

Operation: LAMINECTOMY

Anesthetic: Nembutal (Abbott) 0.5 cc. of a sterile 5% solution per kilogram body weight, given intravenously.

Operative procedure: The lower half of the back was shaved and the cat placed in prone position with a pad under the pelvis to straighten the lumbar spine. The skin was prepared with soap, water, ether, and merthiolate and sterile drapes applied. A skin incision was made in the midline from the spinous process of the third lumbar vertebra to the spinous process of the first sacral vertebra. Laminectomy was performed, removing one spinous process completely, amd small portions of the laminae above and below. The exposure was made as small as possible to prevent postoperative herniation or injury to the spinal cord.

In the first seven experiments the dura was incised longitudinally and the dorsal roots and posterolateral sulcus visualized. A lesion was made by inserting the point of a sharp scalpel or needle cautery into the region of Lissauer's tract, i.e., the region beneath the postero-lateral sulcus, to a depth of about one millimeter. The lesions are diagrammed

in Figure 10 on the basis of clinical estimation and sections stained by Marchi and pyridine silver methods. The lesions were often found to be larger than had been estimated clinically, due to regional vascular damage. In all cases, the tract of Lissauer was completely destroyed on one side only with varying degrees of damage to the adjacent gray and white matter. The opposite tract of Lissauer was intact. Three additional experiments were excluded from this series because, at autopsy and on sections, the lesions were found to be partially bilateral (due to vascular damage).

These lesions were made to determine the oral and caudal extent of fibers within Lissauer's tract and whether or not long fibers exist within the tract. The lesions were made unilaterally so that the tract of Lissauer on the normal side could be compared with the side of the lesion.

In the last two experiments (P50-210 and P50-211), in which only nerve roots were severed, the procedure differed in that only the roots involved were exposed unilaterally and cut extradurally to avoid damage to the cord. Both dorsal and ventral roots were cut central to the spinal ganglia. This was done in order to determine what portion of Lissauer's tract was made up of incoming dorsal root fibers, and conversely, what portion was of exogenous origin. In P50-210 the entire sacral supply and sixth and seventh lumbar roots were severed bilaterally and the fifth and fourth lumbar roots on the right

side only to determine the contribution of a single root to Lissauer's tract.

After five to nine days the cats were killed with nembutal given intraperitoneally and the spinal cord removed immediately. The dura was incised longitudinally and the cord suspended in a vertical cylinder of 10% formalin by threads secured to the dura. After 48 hours the cord was removed and sectioned into two groups of blocks as follows:

1. The Swank-Davenport technique for degenerating myelin.

Small blocks about 3 to 4 millimeters thick were taken from each lumbar segment and from the seventh thoracic and seventh cervical levels. These blocks were kept in order and the right side marked by passing a needle and fine cotton thread through the right anterolateral quadrant of each block. These blocks were then stained for degenerating myelin by the Swank-Davenport modification of the Marchi method (Swank-Davenport, 1935; Swank, 1950). Swank has shown that the chlorate-osmic acid method stains degenerating myelin in the spinal cord of the cat in less than five days. Good staining was obtained in all of these experiments in which at least five days were allowed for degeneration. Short degeneration periods of five to nine days were used so that degenerations of the fine unmyelinated fibers and "boutons terminaux" could be concurrently investigated by silver methods.

The technique as used in this experiment was outlined for me by Dr. Roy L. Swank (1950) and performed as follows:

1) Blocks were fixed in 10% neutral formalin for 48 hours. (Intravascular perfusion is contra-indicated, particularly with saline.)

2) The blocks were then placed without washing in 1% potassium chlorate for a few moments.

3) Stained in the dark in the following solution for 7 to 14 days or 3 to 7 days on a rotor, changing the solution twice. (A 50 cc. wide mouth glass bottle with a ground glass stopper was found to excellent for use on the rotor.)

Formula: 1% aqueous solution of potassium chlorate..... 60 cc.
1% aqueous solution of osmic acid ..... 20 cc.
Glacial acetic acid ..... 1 cc.
Formaldehyde, U.S.P. (40% solution) ..... 12 cc.

(We used clear glassware, but covered the bottles with pieces of surplus black paper in which X-ray films are routinely wrapped.)

4) Washed in running tap water for 24 hours.

5) Dehydrated and embedded in paraffin.

6) Sections cut at 25 micra and mounted on slides.

7) Sections cleared in toluol and mounted in permount.

2. The pyridine silver technique for non-medullated fibers and "boutons terminaux".

A second set of blocks about 4 millimeters thick were taken from each lumbar segment, seventh thoracic and seventh cervical levels. As before, these blocks were kept in order and the right side marked by passing a needle and fine thread through the right anterolateral quadrant.

Formalin was removed prior to silver staining by placing these blocks in two 24 hour changes of 20% chloral hydrate in distilled water. This method of removing formalin was recommended by Lhotha and Ferriera (1949). Blocks were then washed briefly in distilled water and stained by a modified pyridine silver method (Cajal) as follows:

1) Blocks placed in a solution of equal parts pyridine and water for 24 hours.

2) Washed in several changes of distilled water until the strong pyridine odor is eliminated.

3) Immersed in 96% alcohol for 24 hours.

4) Excess alcohol removed by blotting with filter paper. Blocks wrapped carefully in filter paper and placed in the following solution for 4 days at 37 degrees in the dark:

Silver nitrate..... 1.5 grams

Distilled water ..... 100 cc.

The use of filter paper in wrapping the blocks was recommended by Gibson (1937) to reduce surface precipitation.It appears

that this also allows more even impregnation with the silver by keeping the blocks from touching the bottom of the staining dish and thereby allowing equal penetration from all sides. Gauze or cotton will serve the same purpose.

5) Blocks washed for a few seconds in distilled water to remove any excess silver nitrate on the surface.

6) Reduced in the following solutions for 24 hours at room temperature:

Pyrogallic acid..... 1 gram
Distilled water ..... 100 cc.
Formaldehyde, U.S.P. (40%)..... 5 cc.

7) Blocks washed for a few seconds in distilled water, dehydrated in graded alcohols, cleared in toluol and embedded in paraffin.

8) Serial cross sections were cut at 10 micra for a distance of at least 1 millimeter. The blocks were then melted and re-embedded and serial longitudinal, parasagittal, or oblique longitudinal sections cut at 10 micra through the extent of Lissauer's tract.

9) Ribbons mounted serially on numbered slides, cleared in toluol and mounted in permount.

Preliminary fixation of the entire cord with formalin, which is later removed with chloral hydrate after sectioning into blocks, seems to reduce the amount of shrinkage and distortion that frequently occurs when blocks are placed

directly into alcohol, pyridine or chloral hydrate as recommended by most authors for block silver staining. Perfusion was not found to be necessary.

Normal and degenerating fibers and "boutons terminaux" were found to impregnate well by this method and in most experiments the results were superior to previous methods used. This was especially true in regard to the fine fibers and boutons terminaux. As with all block silver methods, the blocks must be relatively small if impregnation is to be uniform.

The importance of avoiding trauma to the blocks and distortion of the cut sections cannot be over emphasized if one is to follow the course of the degenerating fibers. The interpretation is very difficult if the sections are wrinkled or damaged in handling.

IV. OBSERVATIONS AND DISCUSSION

1. General observations regarding Lissauer's tract, the substantia gelatinosa and the course of the unmyelinated fibers of the dorsal roots.

The tracing of fibers, both normal and degenerating, by horizontal sections alone is difficult and often misleading, especially if the fibers take an oblique course. The appearance of the tracts of the spinal cord as seen in the longitudinal, parasaggital, or oblique planes is strikingly different from the cross sectional view. This is true also of a large number of the cells, especially the marginal cells and substantia gelatinosa cells.

In cross sections the marginal cells are inconspicuous, but when viewed in the longitudinal or parasagittal planes they appear as large, widely branched neurones as shown in Figure 11. These cells are rather flat, but quite broad and as large as anterior horn cells and appear to lie upon the substantia gelatinosa cells and send out long processes which intermingle with the fibers of Lissauer's tract and the processes of the gelatinosa cells.

The substantia gelatinosa cells generally stain poorly with silver, even in the best preparations. The nuclei impregnate rather well, but the boundary of the sparse cyto-

plasm is indistinct. Occasionally, however, a gelatinosa cell and its processes are impregnated by the silver and these cells appear to be oriented with their long axis primarily in the longitudinal plane and to send off short, multiple branches from two major processes. This can best be seen in longitudinal, parasagittal and oblique sections (Figs. 9, 11 and 12).

Boutons terminaux were never definitely seen in any of our preparations in or around the cells of the substantia gelatinosa. Szentagothai and Kiss (1949) have also failed to find any "real" boutons in this region and I am unable to find any reports of their existence in the literature. However, in longitudinal and parasagittal sections, a fine network of fibers can be seen interwoven around the gelatinosa and marginal cells (Figs. 11 and 12). Haggar and Barr (1950) have reported variations in size of the end bulbs on different cell groups in the cat's spinal cord, but they also do not mention any observations of end bulbs on gelatinosa cells.

Some of the fibers that are interlaced in this network appear to have small knob-like endings, but the absence of the ring shaped boutons in this region was apparent even in preparations which showed large numbers of boutons on the anterior horn cells (as shown in Fig. 13). This, of course, makes it impossible to draw any conclusions about degeneration

of boutons in this region according to the criteria outlined by Gibson in 1937. We could only look for swelling, distortion and fragmentation of the fibers as evidence of degeneration in this area.

The unmyelinated fibers are distributed equally throughout the dorsal roots until they approach the zone of entrance into the spinal cord (Fig. 5). Near the point of entrance, these fibers begin to separate out in bundles which proceed toward the periphery of the root (Fig. 6). These bundles vary in size at different levels of the cord, but are proportional to the size of the entering rootlet.

These bundles of unmyelinated fibers take different routes at the entrance zone, depending largely upon the angle of entrance of the dorsal rootlet. In the lower lumbar regions, the rootlets enter almost parallel to the cord due to the normal down growth of the spinal column after the cord has ceased to lengthen. In this region the bundles of unmyelinated fibers take a direct downward and lateral, or obliquely lateral course, join Lissauer's tract and ascend or descend within it (Fig. 7a). In the cervical region, however, where the rootlets enter the cord at almost right nagles, those few bundles of unmyelinated fibers which are in a lateral position, proceed directly into Lissauer's tract, but the others take a medial position between the uppermost border of Lissauer's tract and the fasciculus cuneatus. Here they run in a longitudinal direction, over the large myelinated

fibers destined for the posterior white columns, but for a short distance only and then turn obliquely anterior and lateral to join Lissauer's tract (Fig. 7b).

Immediately after the unmyelinated fibers enter the cord numerous bifurcations and collateral branches can be seen. These branches sometimes take an oblique or longitudinal direction for a short distance, but the majority seem to go directly toward the substantia gelatinosa. Cajal's conception of these bifurcating fibers is shown in Figure 3.

The arrangement of the entering fibers as seen in longitudinal and parasagittal sections is shown in Figures 20 and 22.

The variations in size and shape of Lissauer's tract at different levels of the cat's cord is shown in Figure 14. These variations are essentially the same in man.

2. <u>The extent of degeneration following section of Lissauer's tract</u>.

The tract of Lissauer was sectioned in the lumbar region of seven adult cats. The extent of the lesions are shown in Figure 10. In all of these experiments transection of Lissauer's tract was found to be complete by Marchi and silver preparations. One segment oral to the lesion, Lissauer's tract showed slight degeneration of the non-medullated and medullated fibers along the medial border, but the majority of the tract appeared normal (at least 75%). Two segments oral to the lesion, the tract appeared normal in all cases except two where very slight degeneration was found. No evidence was found of degeneration for more than two segments

oral to the lesion. No degeneration was found for more than one segment caudal to the lesion. Figures 15 and 16 illustrate these findings.

In determining the extent of degeneration the following criteria were rigidly followed and it is my belief that these criteria are essential if errors are to be avoided. Changes in the boutons terminaux alone are not sufficient as the boutons vary considerably in different regions (Barr, 1950) and were never found in the substantia gelatinosa.

(1) The lesions were made unilaterally so that the normal side of the cord could be compared with the abnormal side in the same section.

(2) All of the blocks in any one experiment were stained at the same time, by the same method, and in the same dish.

(3) Swelling, vacuolization and fragmentation of fibers was considered as evidence of degeneration. Swelling or fragmentation of boutons was considered reliable only if degenerating fibers could also be traced to the area from the area of the lesion.

(4) The general extent of the lesion was checked by another method, in this case the Swank-Davenport method.

3. The extent of degeneration following section of a single dorsal root.

In this experiment only the fourth lumbar root was sectioned unilaterally as shown in Figure 10. Degeneration was traced by horizontal and longitudinal serial sections stained by pyridine silver.

At the level of section, degeneration of the fibers in the rootlets was complete as shown in Figures 17, 18, 19 and 20. Degenerating fibers could easily be traced (1) into the posteri or funiculus, (2) compact bundles which penetrated the substantia gelatinosa and appeared to end around cells near the base of the posterior gray columns (Fig. 21), (3) scattered throughout the medial division of Lissauer's tract, mostly along the medial border. Some of these degenerating fibers could be traced only as far as the substantia gelatinosa, others seemed to penetrate the substantia gelatinosa and end in the nearby dorsal gray columns. Sections taken one segment oral or caudal to the lesion showed no evidence of degeneration within Lissauer's tract.

4. The extent of degeneration following section of all roots caudal to the fifth lumbar segment bilaterally and of the fourth and fifth lumbar roots only on one side.

When all of the incoming fibers from the sacral and lower lumbar are severed in this manner, all of the fibers of

Lissauer's tract which remain intact must be of endogenous origin as it was shown in the first experiments that fibers descend in this tract for not more than one segment.

At the sixth lumbar level and below, which was completely denervated, Lissauer's tract showed degeneration in the medial division of the tract, but at least 75% of the tract remained intact. In the sacral and lower lumbar regions, Lissauer's tract is not so definitely divided into medial and lateral divisions, but certainly the degeneration was on the medial side of the tract.

At the fourth and fifth lumbar levels on the left, one and two segments respectively above the denervated cord below, Lissauer's tract showed no evidence of degeneration. On the right side, which was denervated below the sixth lumbar level and the fourth and fifth lumbar roots cut above, the same essential degeneration of about half of the medial division of Lissauer's tract was present. At the third lumbar level on this side and above there was no evidence of degeneration in Lissauer's tract.

V. CONCLUSIONS

From these observations, the following conclusions seem justified concerning Lissauer's tract:

(1) Lissauer's tract consists entirely of numerous, short fibers of not more than one or two segments in vertical extent.

(2) The dorsal roots contribute fibers only to the medial division of the tract and these exogenous fibers constitute less than 25% of the total fibers in the tract.

(3) The remainder of the fibers (at least 75%) must, therefore, be of endogenous origin.

The methods of study used in these experiments have their recognized limits, but seem to be more time saving and as accurate as the older methods if the criteria, as outlined, are followed. Special fixation is not necessary for good block silver staining. Indeed, the results obtained from tissue which was fixed primarily in formalin seemed superior, provided the formalin was removed by chloral hydrate as described.

If the fine fibers which enter Lissauer's tract from the posterior roots are "pain fibers", then we must conclude that they terminate as numerous collateral or terminal branches within one or two segments after entering the cord. There is, therefore, no evidence of any long fibers, either endogenous or exogenous, in Lissauer's tract to support the idea of a direct, uninterrupted, pain pathway within this tract. It

should also be emphasized that those fibers of exogenous origin which enter this tract pursue an oblique course and occupy only a small part of the medial division of this tract. The remainder of Lissauer's tract (at least 75%) consists of short, intersegmental connections. These connections appear to be made up of processes of the marginal cells, gelatinosa cells and cells of the dorsal gray columns. Thus, the lateral part of Lissauer's tract seems to correspond to the numerous intersegmental fibers which surround the gray matter of the spinal cord elsewhere.

Based upon all of the evidence previously cited we may state the relation of the fine fibers of the dorsal roots to pain as follows:

The fine fibers of the dorsal roots, which probably carry the sensation of pain, are mixed with other fibers until they reach the root entrance zone. At this point, the fine fibers bifurcate into ascending and descending branches, separate out in bundles, and proceed toward the medial surface of Lissauer's tract, either directly or by passing over the incoming large fibers. Their route depends upon the angle at which the root enters the cord. The main branches run obliquely in the medial division of Lissauer's tract, give off numerous collateral branches at right angles and end within one or two segments around marginal cells, substantia gelatinosa cells or cells of the dorsal gray columns. This conception is summarized

in Figure 22.

The use of the terms "medial" and "lateral" divisions of the dorsal roots should be avoided as they are misleading.

From all available evidence, the secondary neurones which send fibers to the opposite lateral spinothalamic tract are probably the marginal cells or cells in the dorsal gray columns rather than substantia gelatinosa cells. It is still uncertain whether these secondary fibers cross in the anterior or the posterior commissure.

VI. SUMMARY

The history of Lissauer's tract and its relation to the spinal pathway for pain is critically reviewed.

A method for obtaining good silver preparations from formalin fixed material is described and criteria for degeneration in silver are outlined.

Section of Lissauer's tract in seven adult cats and of multiple and single dorsal roots in two cats revealed that (1) Lissauer's tract consists entirely of numerous short fibers of not more than one or two segments in vertical extent. (2) The dorsal roots contribute fibers only to the medial division of the tract and these exogenous fibers constitute only 25% or less of the total fibers in the tract, (3) the remainder of the fibers (about 75%) must be of endogenous origin.

Several general observations are made regarding boutons terminaux, marginal and gelatinosa cells and the course of fibers in the dorsal roots and tract of Lissauer.

VII. ACKNOWLEDGEMENTS

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2. Beitrag zur pathologischen Anatomie der Tabes dorsalis und zum Faserverlauf im menschlichen Rückenmark.

Vorläufige Mittheilung von **H. Lissauer.**

(Aus dem pathologischen Institut zu Leipzig.)

An Präparaten des menschlichen Rückenmarks, welche nach der WEIGERT'schen Hämatoxylin-Blutlaugensalz-Methode gefärbt sind, lässt sich folgendes Verhalten eines Theiles der in den hintern Wurzeln enthaltenen feinen Nervenfasern constatiren: Die betreffenden Fasern sammeln sich jedesmal an der Aussenseite der einzelnen Wurzelstämme, während sich dieselben zum Eintritt an das Rückenmark anschicken; die so entstehenden, aus lediglich ganz feinen Fasern zusammengesetzten Bündel wenden sich gleich nach dem Durchtritt durch die Pia von dem Hauptwurzelstamme nach aussen ab, indem sie gegen den Seitenstrang hinzustreben scheinen. Sie werden jedoch, vertical umbiegend, in einer eigenen Schicht — an der Spitze des Hinterhorns, zwischen Hinter- und Seitenstrang — abgelagert. Diese Schicht (in topographischer Beziehung theilweise identisch mit dem Apex cornu posterioris einzelner Autoren) wird von den compacten hinteren Wurzelstämmen sehr nahe ihrer innern Grenze durchsetzt; auf Querschnitten zeichnet sie sich durch ihre gleichmässige Zusammensetzung aus feinen, longitudinalen Nervenfasern vor der umgrenzenden Substanz der weissen Stränge deutlich aus. Nach einer längeren oder kürzeren Periode verticalen Aufsteigens innerhalb jener Schicht dringen die feinen Fasern dann vorwärts in die gelatinöse Substanz und in die tieferen Regionen des Hinterhorns hinein. Ihre Bahnen sind jedoch, sobald sie den rein longitudinalen Verlauf aufgegeben haben, ausserordentlich complicirt und untereinander verschlungen, sodass die Verfolgung einzelner Fasern in Schnittpräparaten nur selten auf grössern Strecken möglich wird.

Bei Tabes dorsalis fand sich, unter einem Beobachtungsmaterial von 12 Fällen, mit Ausnahme eines initialen Falles, stets eine Betheiligung der im Obigen kurz geschilderten feinen Fasern vor; dieselbe kennzeichnete sich am besten durch das Verhalten des oben erwähnten kleinen Feldes zwischen Seiten- und Hinterstrang. Hier — also auch ein Stück weit ausserhalb des hinteren Wurzeleintritts — liess sich in den besagten Fällen eine mehr oder minder hochgradige Degeneration erkennen, welche erst bei Beginn des eigentlichen Seitenstranges abschnitt, und zwar gewöhnlich mit einer derartig präcisen Grenze, dass an der systematischen Natur des Processes nicht weiter gezweifelt werden konnte. Auch in früheren Stadien der Tabes kann es zu einer Betheiligung des bezeichneten Feldes kommen: es wurden 2 Fälle aus frühzeitigen Epochen der Krankheit untersucht (darunter einer mit leichter Seitenstrangsclerose), woselbst sich, im mittleren und oberen Lumbalmark, an der Spitze des Hinterhorns ein kleines Degenerationsfeld abzeichnete, dessen Ausdehnung mit dem Verbreitungsbezirk jener, aus den hintern Wurzeln herstammenden feinen Fasern auffallend übereinstimmte. Gleichzeitig bestand bei diesen Fällen

im Centrum des Hinterstranges ein zweiter, von dem ersteren räumlich getrennter und offenbar selbstständiger Degenerationsbezirk.

Es scheint somit, dass jenen, für das Hinterhorn bestimmten, zwischen Hinter- und Seitenstrang abgelagerten feinen Fasern eine systematische Sonderstellung gebührt, und dass die letztere in gewissen Stadien der Tabes durch den Degenerationsprocess respectirt wird.

Die feinen Fasern in den vorderen Schichten des Hinterhorns bleiben keineswegs im Laufe der Erkrankung ganz verschont; nur bleibt die Degeneration derselben im Allgemeinen hinter der des geschilderten peripherischen Feldes mehr oder minder deutlich zurück, sodass ein Fortschreiten des Processes im Hinterhorn von der Peripherie nach der Basis wahrscheinlich wird.

Fig. 1

Original article by H. Lissauer from Neurologisches Centralblatt, Bd. 4, pp. 245-246.

103, *j*), au voisinage de la commissure blanche; c'est le noyau commissural des auteurs; un autre, antéro-externe (fig. 103, *h*, *i*), placé en face des racines antérieures et peuplé par les cellules motrices; c'est le noyau moteur, parfois dédoublé; enfin, le troisième, postérieur ou postéro-externe

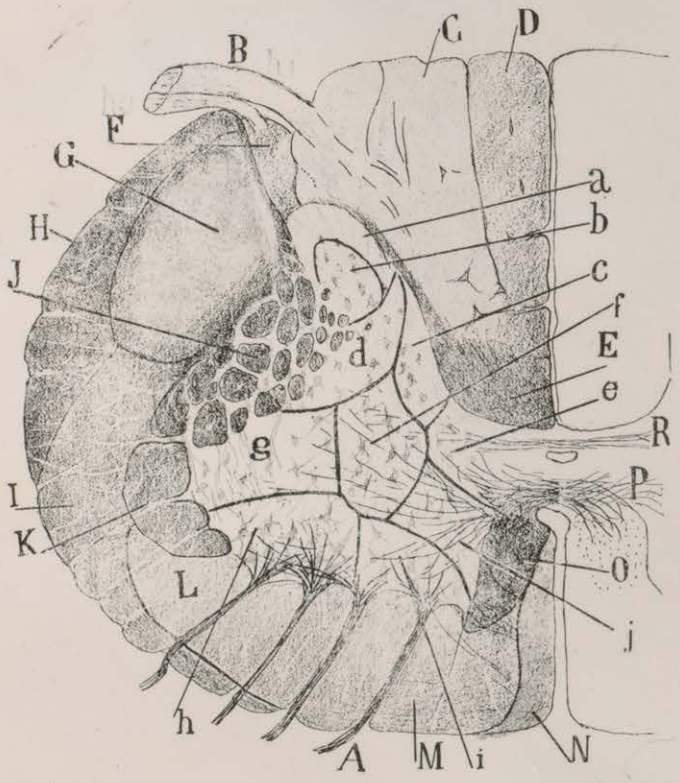
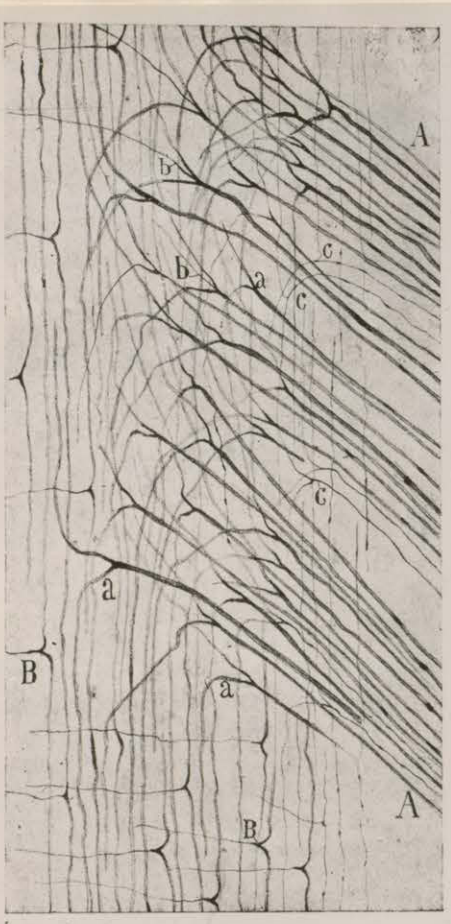


FIG. 103. — Schéma de la moelle cervicale de l'homme, montrant les divers territoires de substance grise et les systèmes de substance blanche.

A, racines antérieures; — B, racine postérieure; — C, cordon de Burdach; — D, cordon de Goll; — E, partie antérieure du cordon postérieur; — F, zone marginale de Lissauer; — G, faisceau pyramidal croisé; — H, faisceau cérébelleux de Flechsig; — I, faisceau de Gowers; — J, système ou faisceau de la corne postérieure; — K, système du noyau gris intermédiaire; — L, cordon intermédiaire; — M, voies courtes du cordon antérieur; — N, faisceau pyramidal direct ou cordon de Türck; — O, faisceau commissural; — P, commissure blanche ou antérieure; — R, commissure grise ou postérieure; — *a*, substance de Rolando; — *b*, tête de la corne postérieure; — *c*, noyau basilaire interne; — *d*, noyau basilaire externe; — *e*, substance grise ou gélatineuse centrale; — *f*, noyau gris intermédiaire; — *g*, noyau du cordon antéro-latéral; — *h*, noyau moteur externe; — *i*, noyau moteur interne; — *j*, noyau gris commissural. — La voie pyramidale est teintée en rouge, les voies sensitives le sont en bleu et les autres voies en bistre.

Fig. 2

The spinal cord from Cajal's "Histologie du Systeme Nerveux".



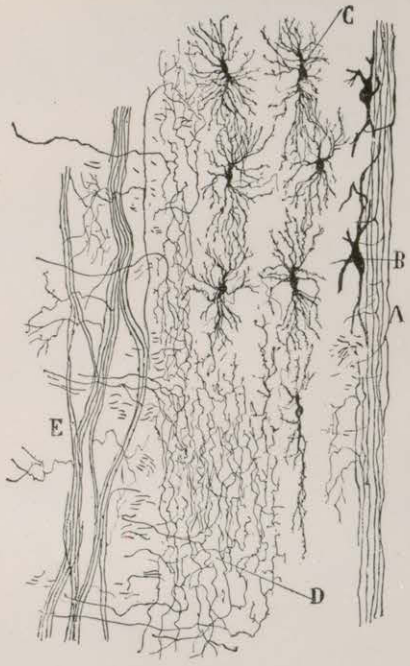
Radiculaires sans myéline.

FIG. 203. — Coupe longitudinale et tangentielle du cordon postérieur aux environs de l'entrée des racines postérieures; chat de 15 jours. Méthode d'Ehrlich.

A, racine postérieure; — B, cordon postérieur avec ses collatérales; — *a, b*, bifurcation et trifurcation des racines sensitives; — *c*, fibres fines bifurquées dans la zone de Lissauer.

Fig. 3

Longitudinal section of the posterior roots from Cajal's "Histologie du Systeme Nerveux". Methylene blue stain of Ehrlich.



Cylindre-axe très fin, et très sinueux

FIG. 150. — Coupe verticale antéro-postérieure et un peu oblique en dehors de la substance de Rolando et de la tête de la corne postérieure ; chien nouveau-né. Méthode de Golgi.

A, fibres du cordon postérieur ; — B, cellules limitrophes de la substance de Rolando ; — C, cellules centrales de la substance de Rolando ; — D, plexus longitudinal formé par les collatérales de la tête de la corne postérieure ; — E, fibres longitudinales, qui sont probablement des collatérales sensitives du sommet de la corne postérieure.

Fig. 4

Vertical section through posterior horn region stained by Golgi method. From Cajal's "Histologie du Systeme Nerveux."

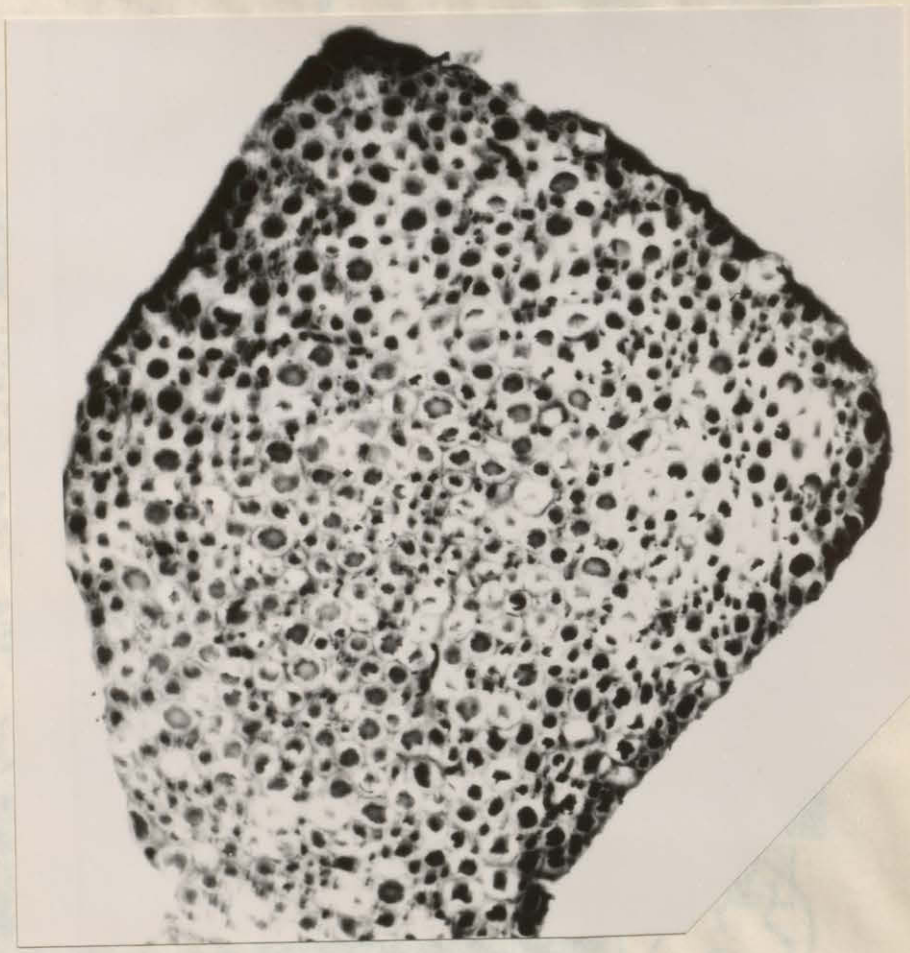


Fig. 5

Cross section of L5 dorsal root in cat about one millimeter from zone of entrance into the cord showing even distribution of unmyelinated fibers throughout the root. X200.

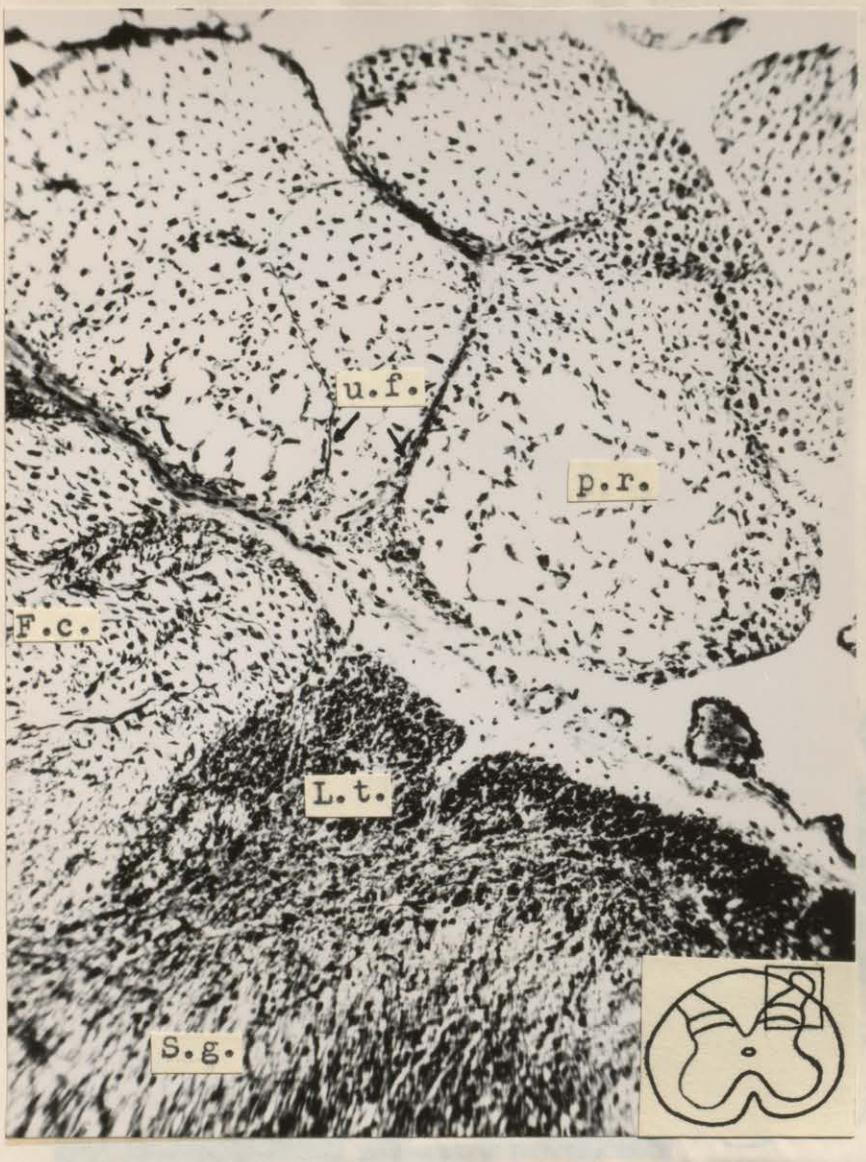


Fig. 6

Cross section of dorsal root near zone of entrance into the cord showing unmyelinated fibers separating out in bundles.
p.r. = posterior root
u.f. = unmyelinated fibers
F.C. = Fasciculus Cuneatus
L.t. = Lissauer's tract.
S.g. = Substantia gelatinosa

Section at L5 level of cat's cord.
Pyridine silver X100.

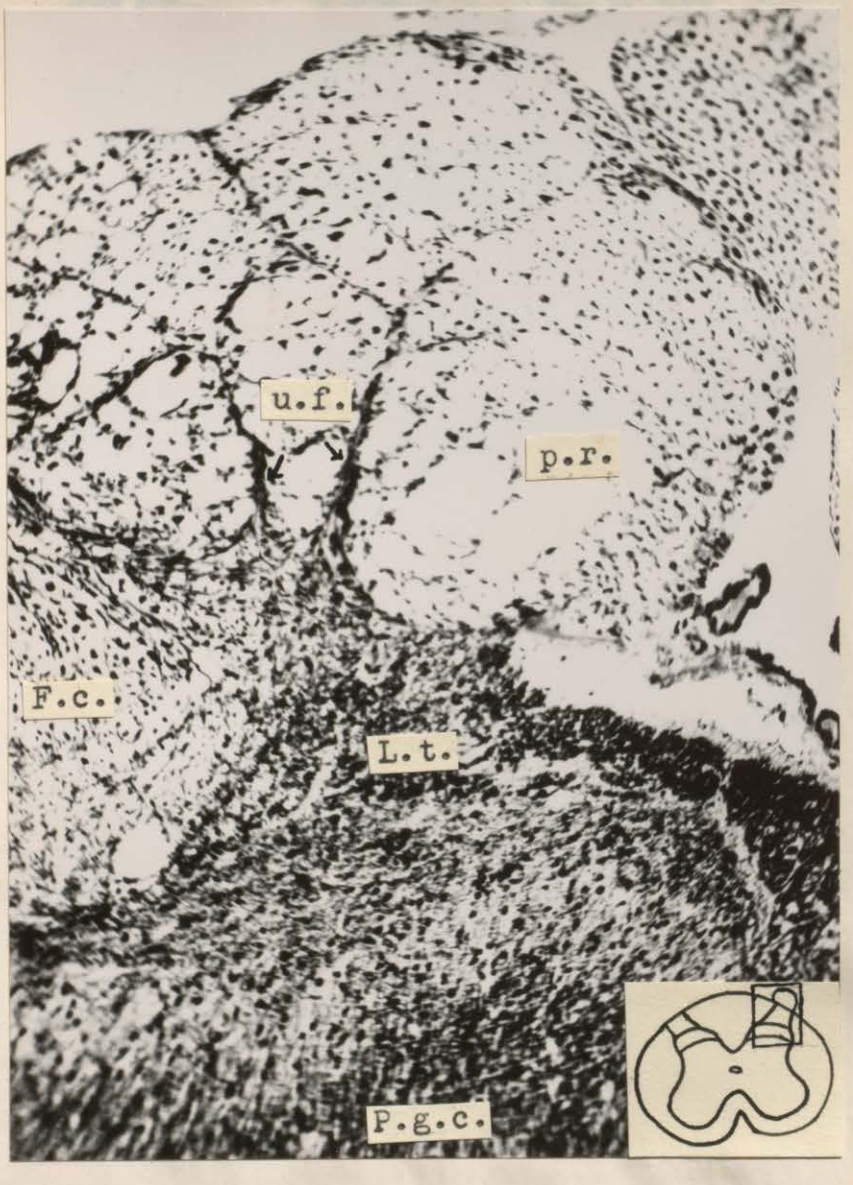


Fig. 7a

Cross section of dorsal root at zone of entrance. L5 level of cat's cord. X100. Pyridine silver. Compare Figs. 5 and 6.
p.r. = posterior root
u.f. = unmyelinated fibers
F.C. = Fasciculus Cuneatus
L.t. = Lissauer's tract
P.g.c. = Posterior gray columns

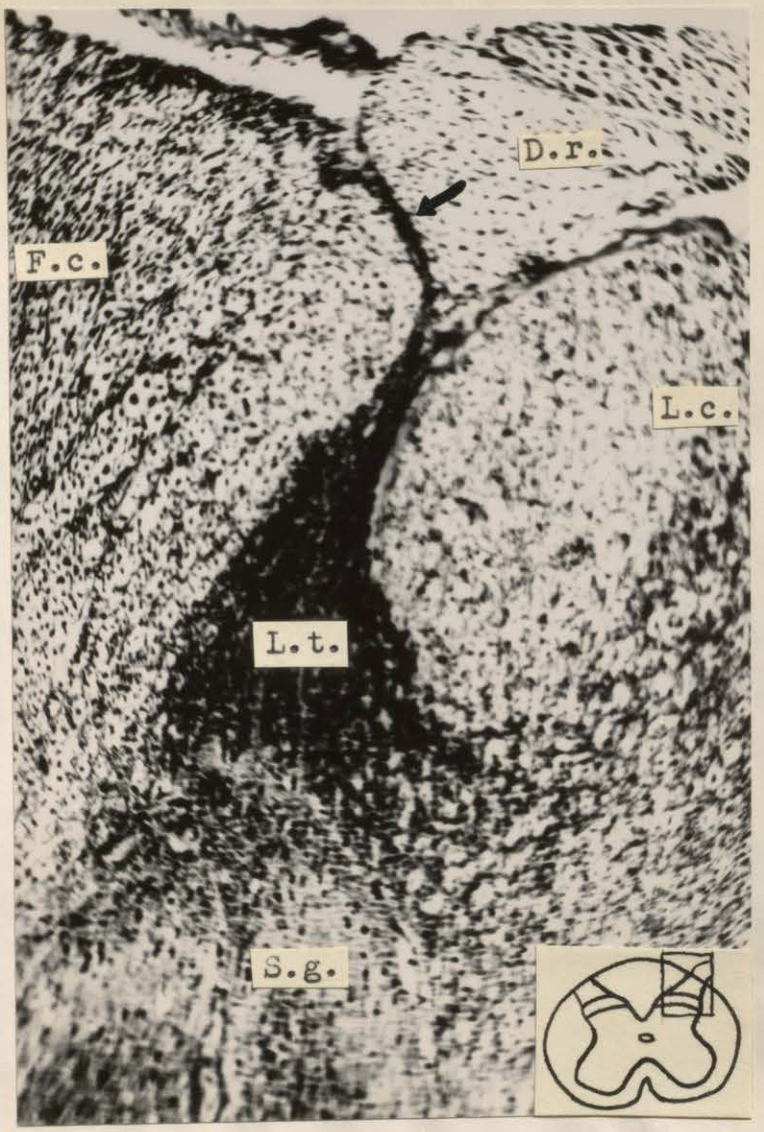


Fig. 7b

Lissauer's tract at C7 in cat's cord showing fibers entering from a medial direction. Pyridine silver. X100.
D.r. = dorsal root
F.c. = fasciculus cuneatus
L.c. = lateral columns
L.t. = Lissauer's tract
S.g. = substantia gelatinosa.

Arrow indicates unmyelinated fibers from dorsal root.

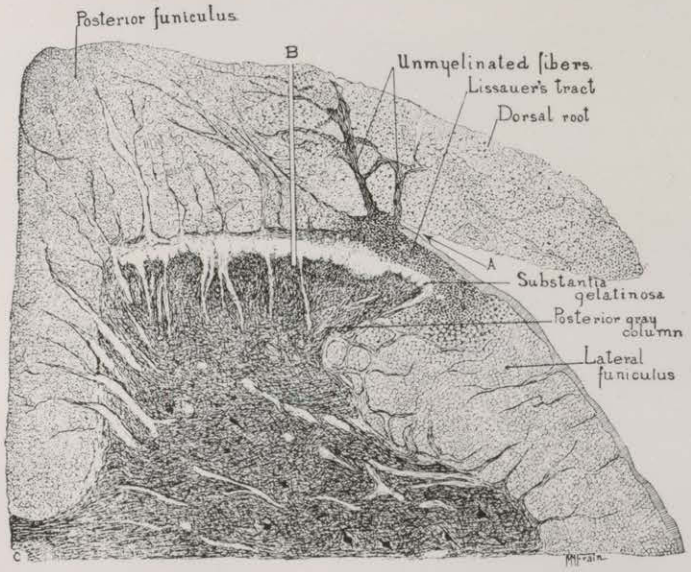


Fig. 129.—From a section of the seventh lumbar segment of the spinal cord of the cat, showing the unmyelinated fibers of the dorsal root entering the tract of Lissauer.

Fig. 8

Ranson's illustration of his experiment to prove that pain is carried by the unmyelinated fibers of the dorsal root. Incision at A resulted in loss of "pain reflexes" such as struggling, rise of blood pressure and respiratory changes. Incision at B resulted in no loss of these reflexes.

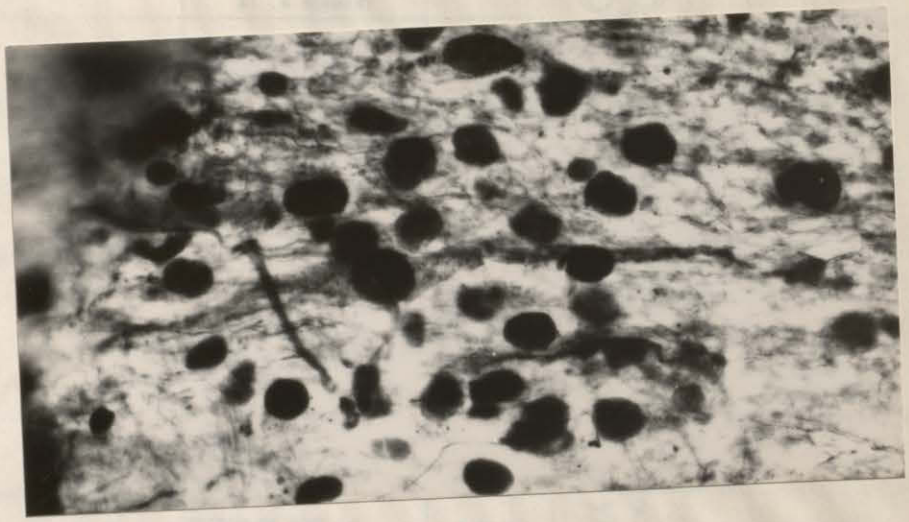


Fig. 9

Parasagittal view of substantia gelatinosa cells stained by pyridine silver. X 440

EXPERIMENT NUMBER	ANIMAL	WEIGHT	OPERATION	DEGENERATION PERIOD	EXTENT OF THE LESION	ORAL EXTENT OF DEGENERATION IN LISSAUER'S TRACT
P50 - 46	♀ CAT	2.6 Kg	RIGHT LISSAUER TRACTOTOMY AT L6 SEGMENT	5 DAYS		TWO SEGMENTS
P50 - 47	♀ CAT	2.3 Kg	RIGHT LISSAUER TRACTOTOMY AT L6 SEGMENT	5 DAYS		ONE SEGMENT
P50 - 61	♀ CAT	2.6 Kg	RIGHT LISSAUER TRACTOTOMY AT L6 SEGMENT	7 DAYS		ONE SEGMENT
P50 - 62	♀ CAT	2.0 Kg	RIGHT LISSAUER TRACTOTOMY AT L5 SEGMENT	7 DAYS		TWO SEGMENTS
P50 - 75	♀ CAT	2.1 Kg	LEFT LISSAUER TRACTOTOMY AT L5 SEGMENT	5 DAYS		ONE SEGMENT
P50 - 76	♂ CAT	3.0 Kg	LEFT LISSAUER TRACTOTOMY AT L5 SEGMENT	5 DAYS		ONE SEGMENT
P50 - 93	♀ CAT	2.7 Kg	RIGHT LISSAUER TRACTOTOMY AT L4 SEGMENT	5 DAYS		ONE SEGMENT
P50 - 211	♀ CAT	4.9 Kg	SECTION OF ROOT L4 ON RIGHT	9 DAYS		ONE SEGMENT
P50 - 210	♀ CAT	5.2 Kg	SECTION OF ALL ROOTS BELOW L5 BILATERALLY, L4 AND L5 ON THE RIGHT	9 DAYS		See Discussion

Fig. 10

Experimental chart

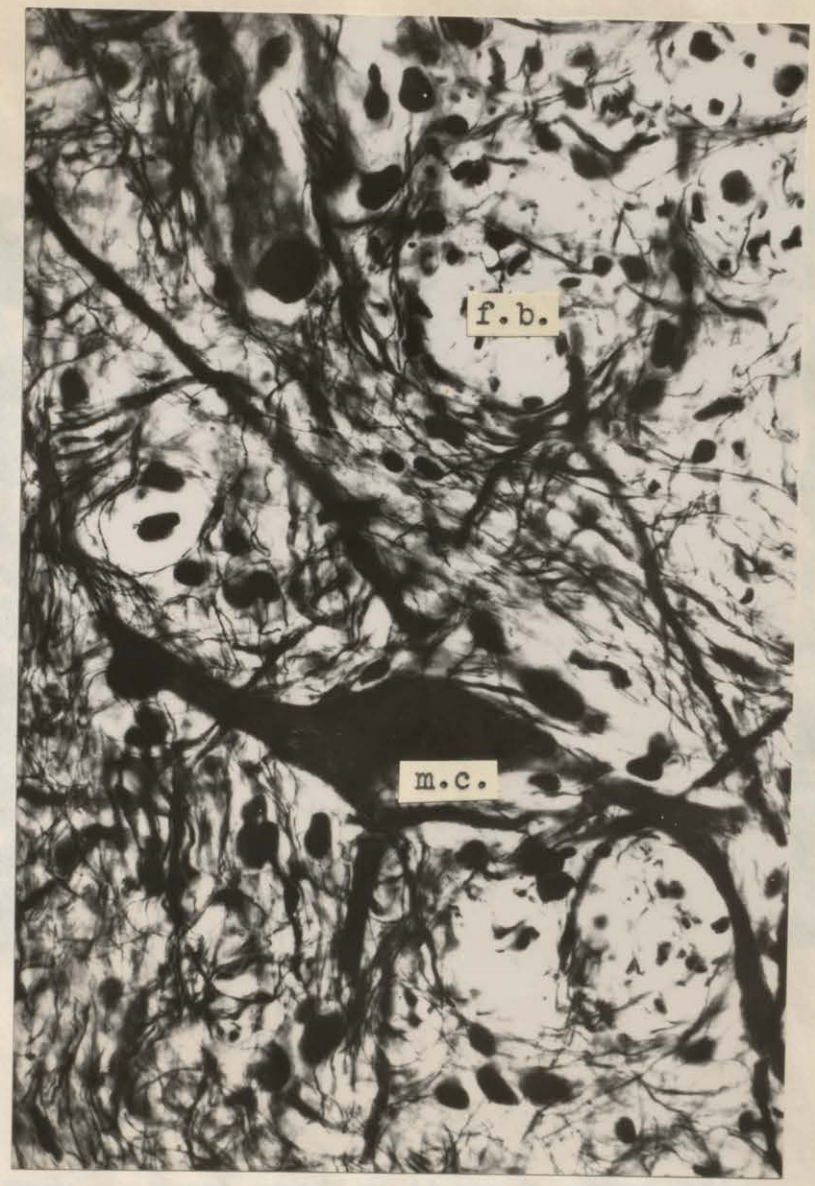


Fig. 11

Longitudinal section through marginal area between Lissauer's tract and the substantia gelatinosa.

m.c. = marginal cell
f.b. = bundles of fibers penetrating substantia gelatinosa. The smaller cells are glia and gelatinosa cells. The network of fibers is part of the Lissauer zone.

Pyridine silver. X440.

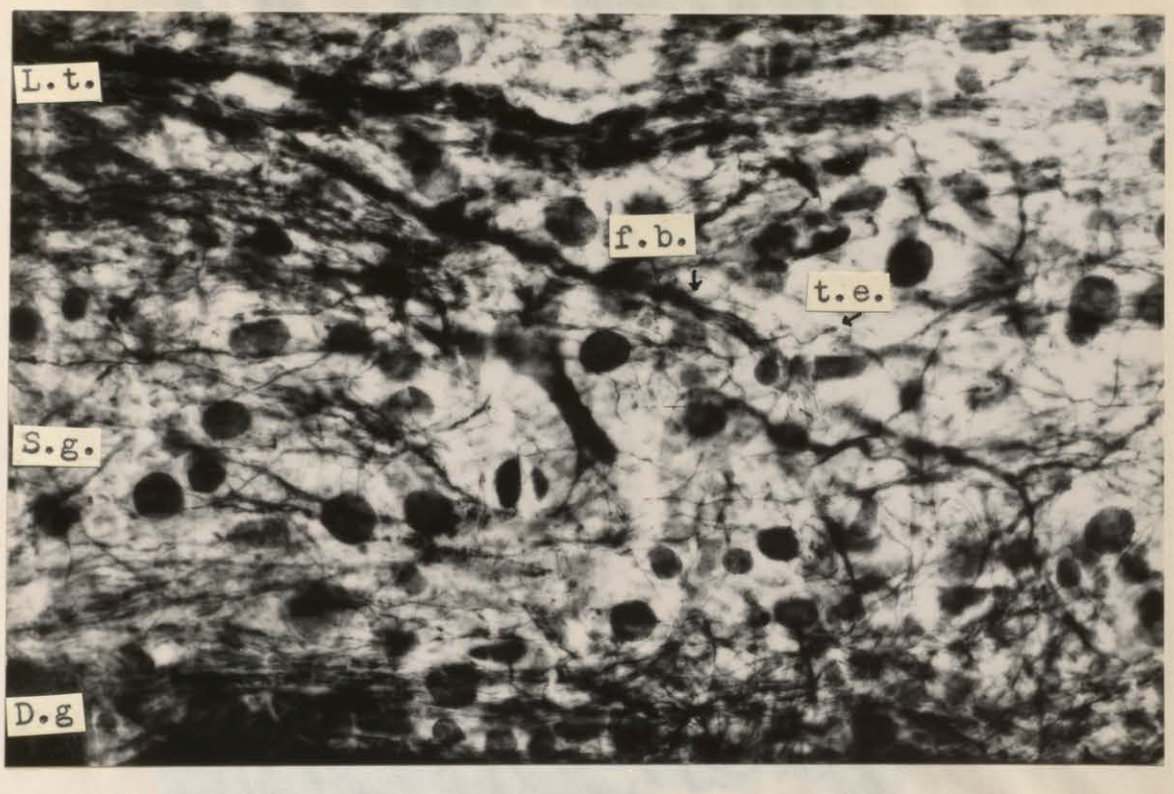


Fig. 12

Parasaggital section through substantia gelatinosa. X440. Pyridine silver.

L.t. = Lissauer's tract
S.g. = substantia gealtinosa
D.g. = dorsal gray columns
f.b. = bundle of unmyelinated fibers
t.e. = knob-like terminal ending.

No ring-shaped boutons terminaux were found in the substantia gelatinosa. Note interlacing network of fine fibers

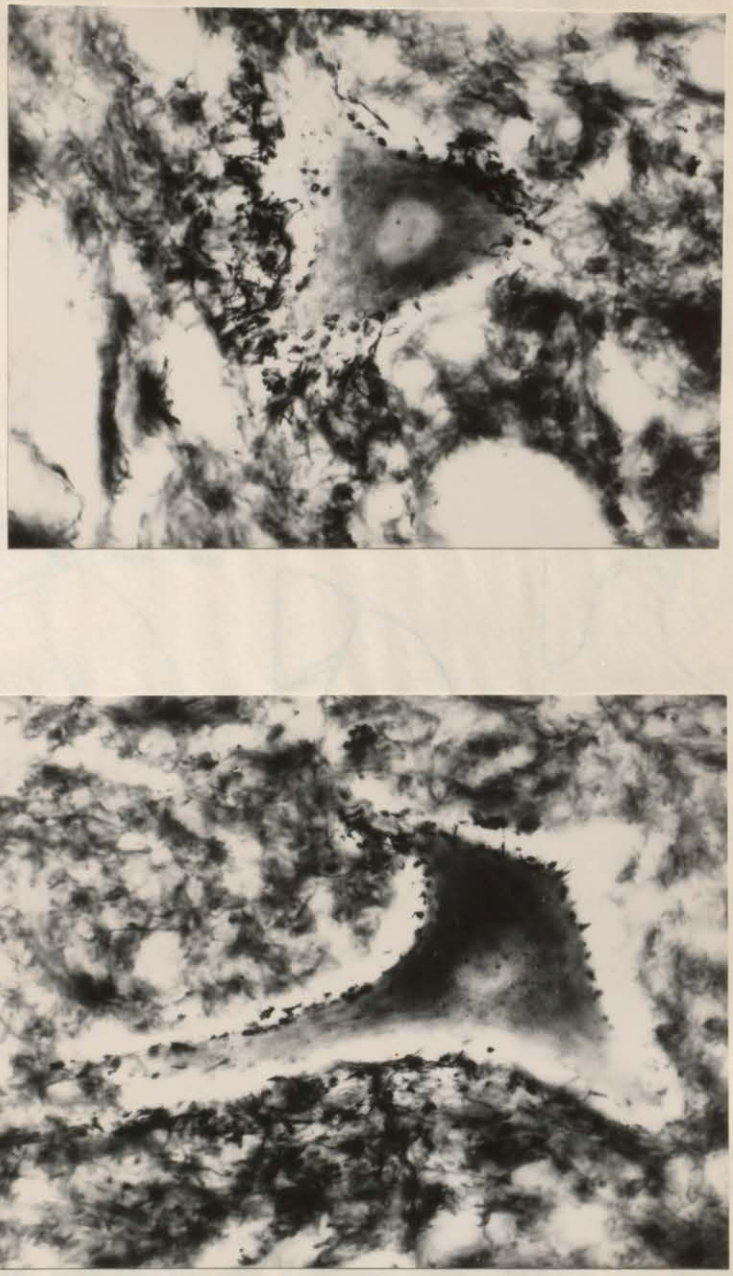


Fig. 13

Boutons terminaux on anterior horn cells stained by pyridine silver method after preliminary in formalin. X440. Although hundreds of boutons could be seen on anterior cells, none were seen in substantia gelatinosa.

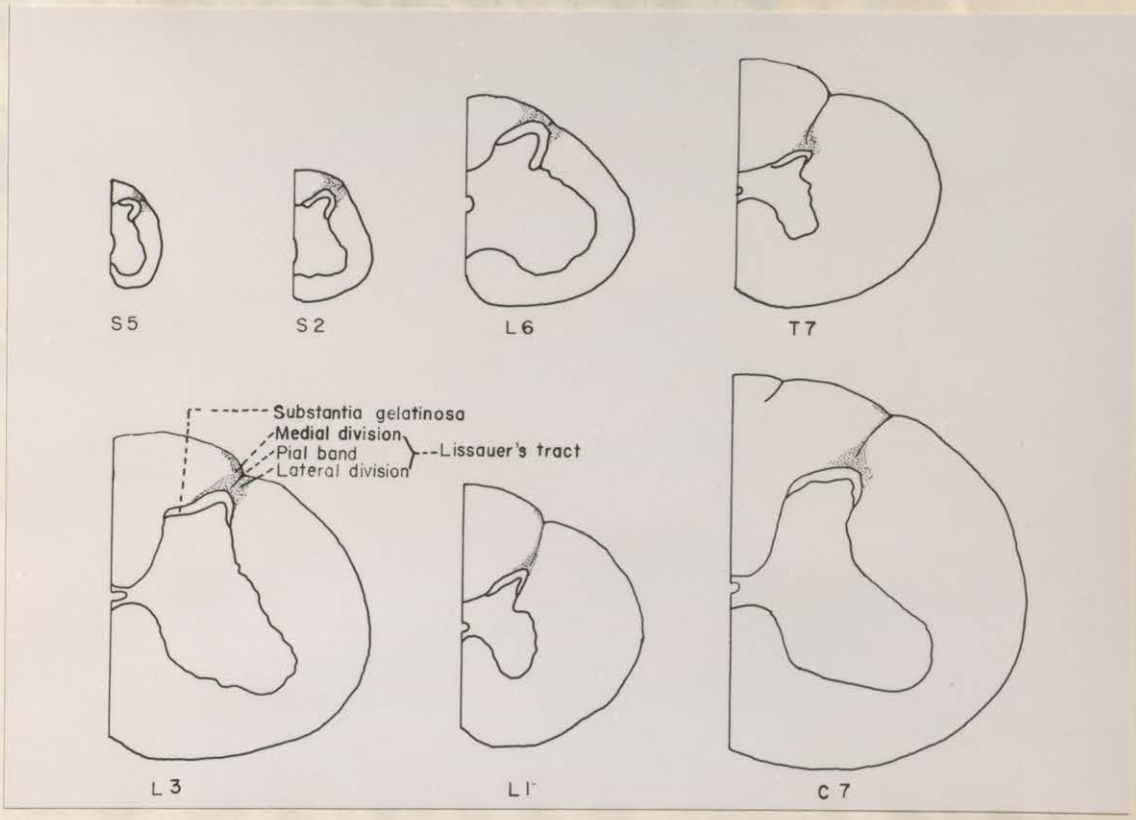
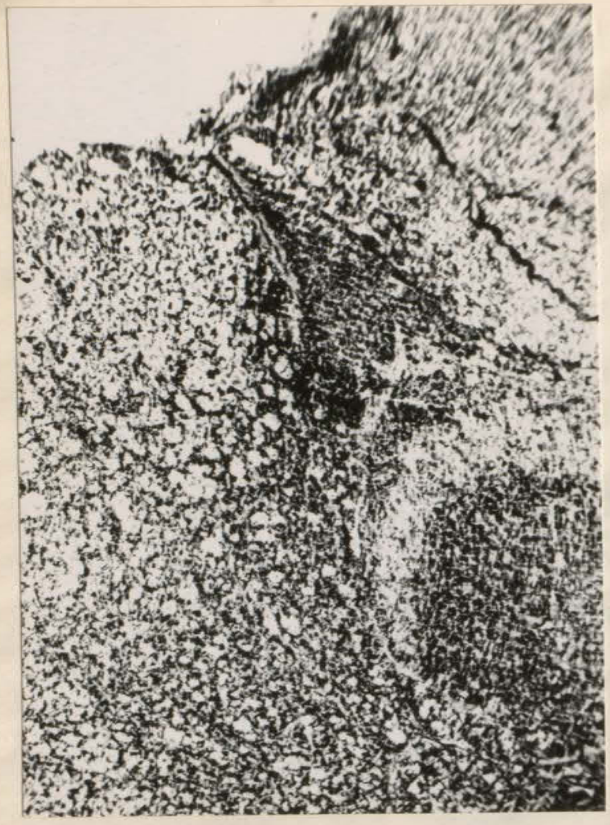
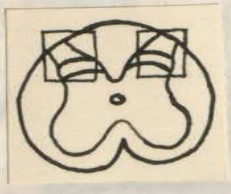


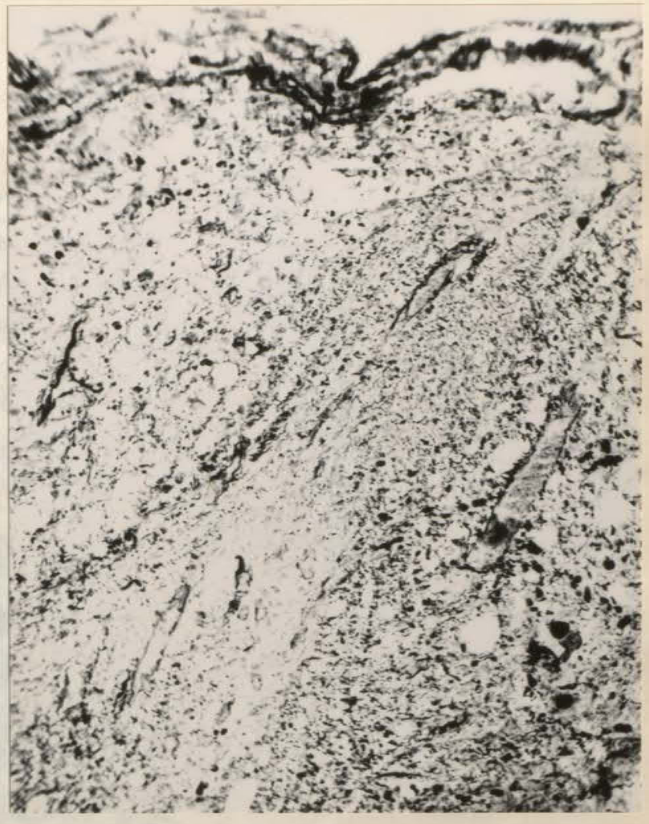
Fig. 14

Drawings to show comparative size and shape of Lissauer's tract at various levels of the spinal cord of the cat. X8.

Notice division of Lissauer's tract by a pial band. This arrangement is essentially the same in man and monkey.







Left side (normal)

Right side (lesion)

Fig. 15

Showing the comparison between normal and degenerating Lissauer's tract in cross section. Pyridine silver stain X100. Cat L4 level.

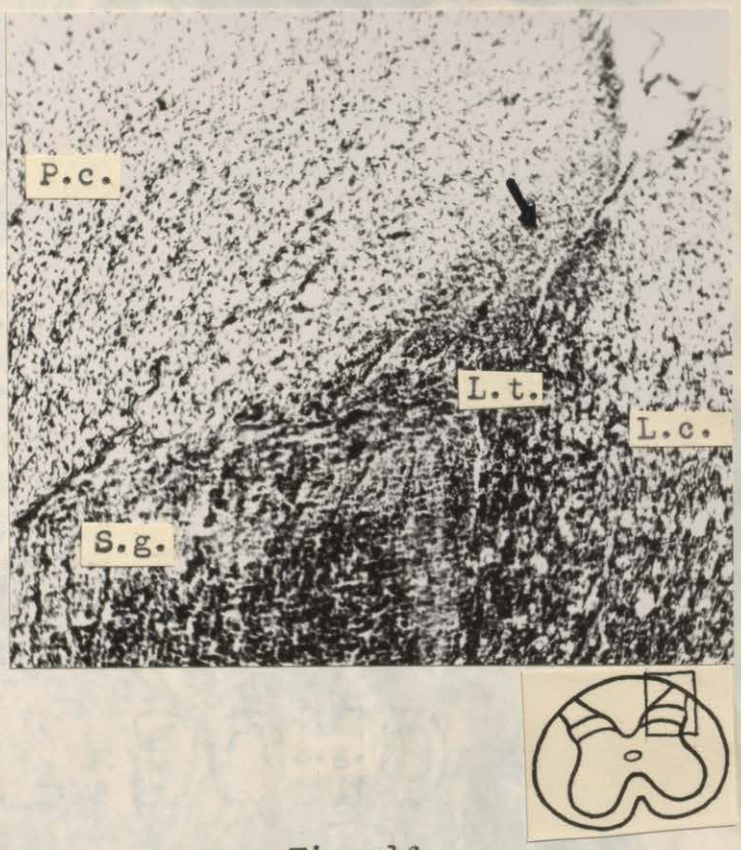


Fig. 16

One segment above transection of Lissauer's tract. Arrow indicates degeneration of part of the medial division of this tract.

P.c. = posterior column
L.t. = Lissauer's tract
L.c. = lateral column
S.g. = substantia gelatinosa.

Pyridine silver stain. X100. Cat. L3 level.

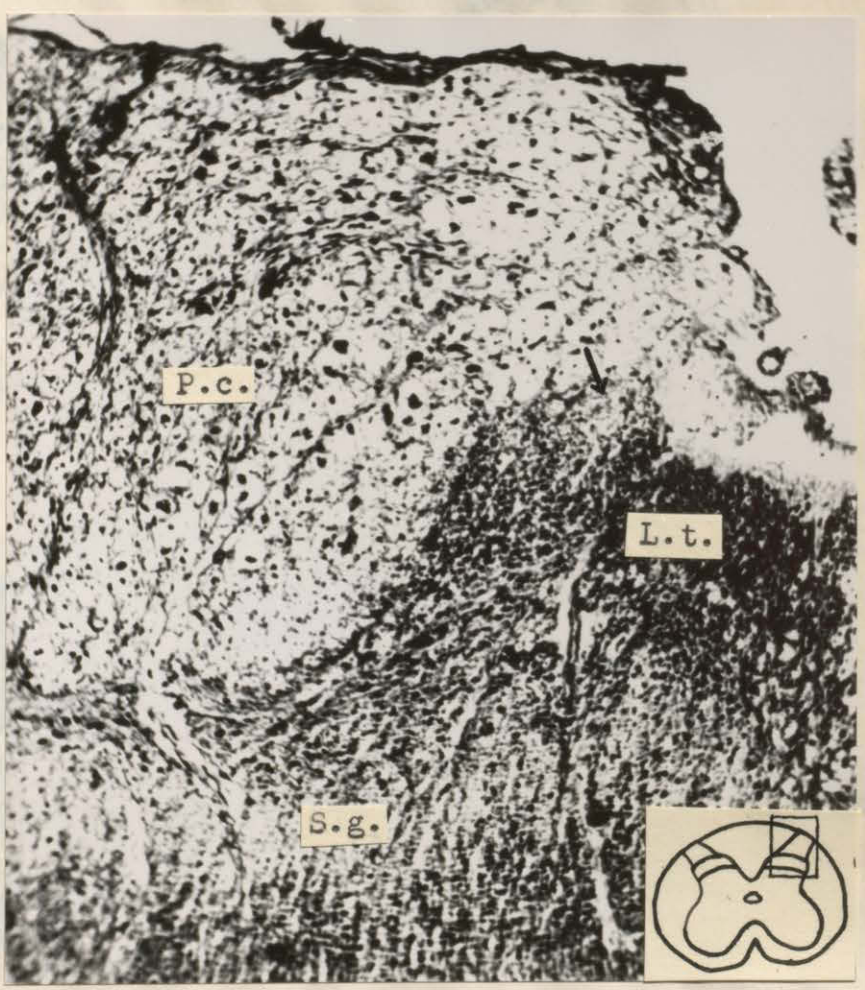


Fig. 17

Showing slight degeneration in Lissauer's tract (arrow) after dorsal root section at this level.

L.t. = Lissauer's tract
S.g. = substantia gelatinosa
P.c. = posterior columns

Compare Fig. 18.
Pyridine silver X100.
L4 level. Cat.

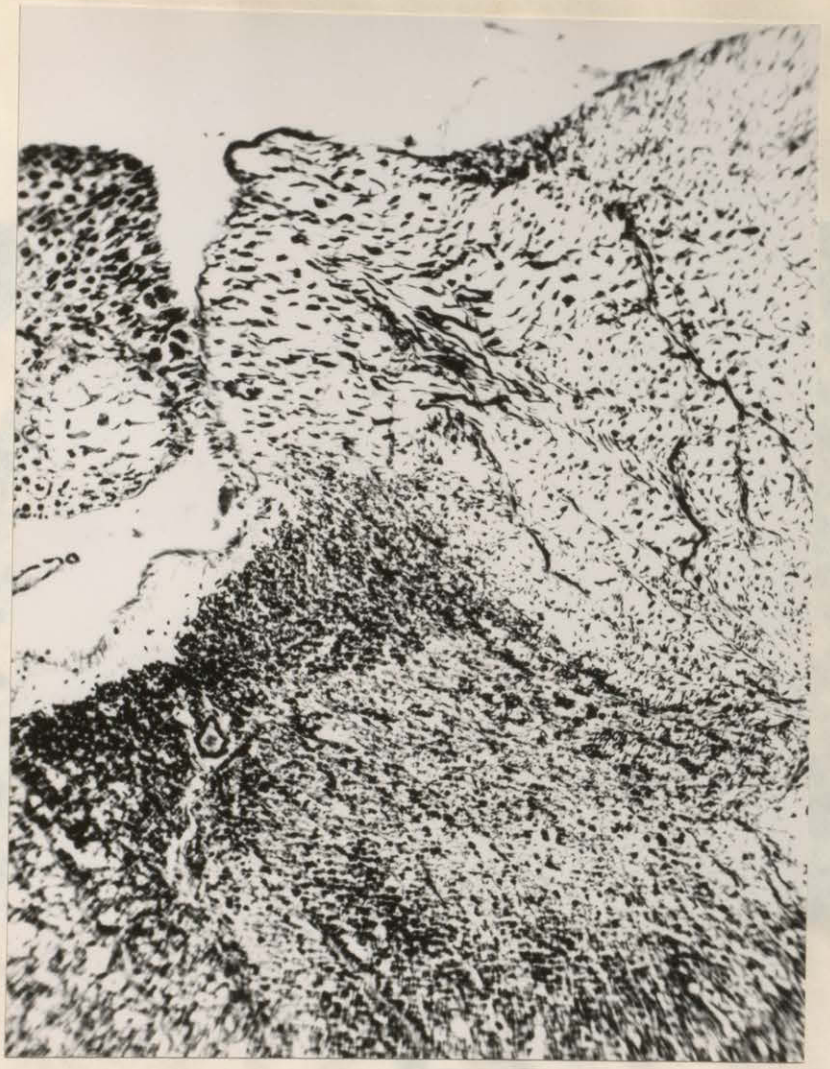


Fig. 18

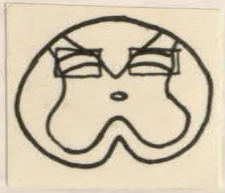
Opposite side of same section as Fig. 17 showing normal dorsal root entrance zone. Pyridine silver X100. L4 level, cat.

Fig. 19

Longitudinal section of degenerating rootlets entering cord at L4 level. Compare Fig.20. X100. Pyridine silver.

Fig. 20

Longitudinal section of dorsal rootlets entering cord (normal). Compare opposite side in Figure 19. Pyridine silver. X100. L4 level of cat's cord.



Left side (normal)

Right side (dorsal root severed at this level)

Fig. 21

Showing degeneration in posterior columns and of fiber bundles following dorsal root section. Pyridine silver. X100.
S.g. = substantia gelatinosa. P.c. = posterior columns
D.g. = dorsal gray columns.

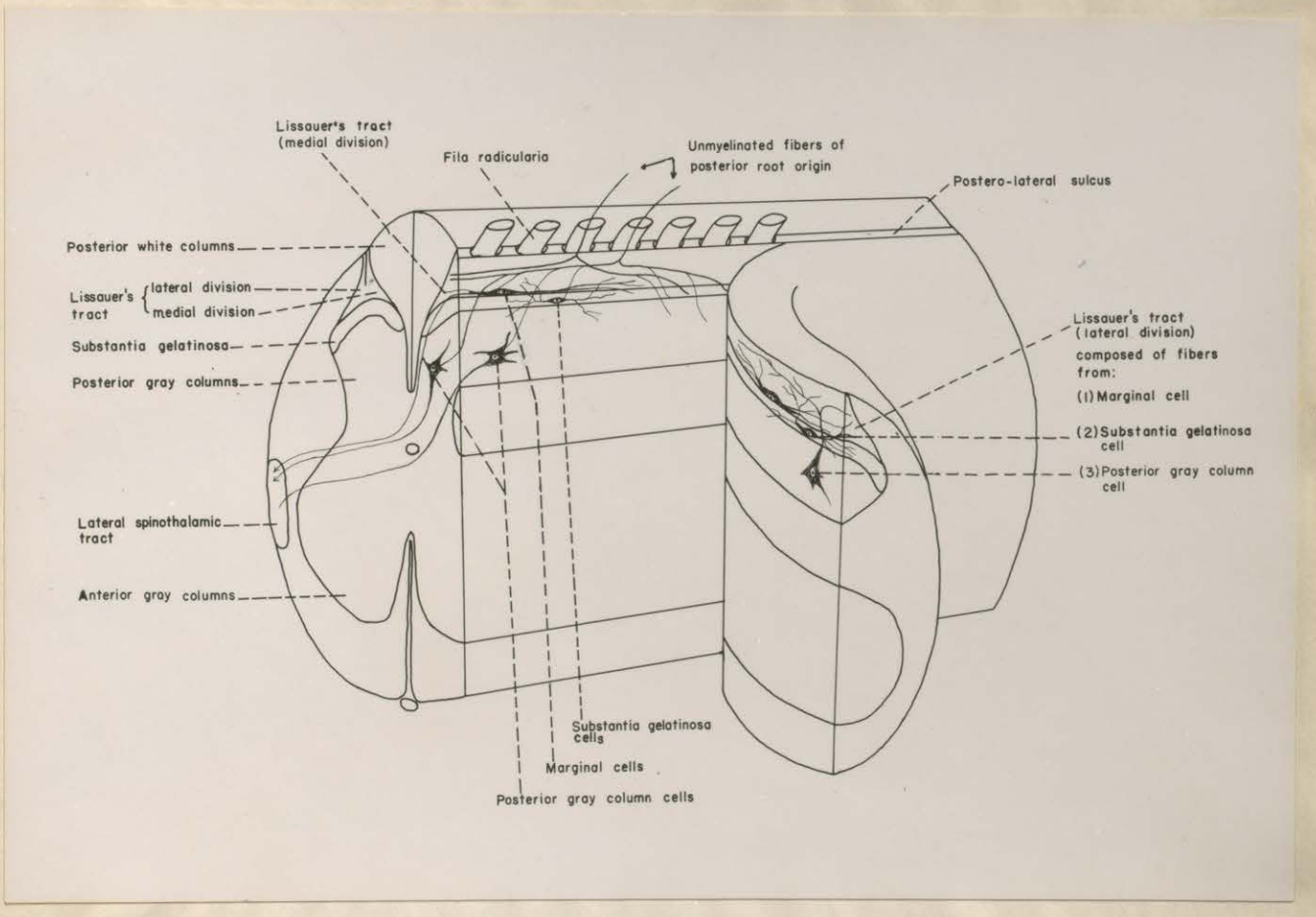


Fig. 22

Diagram to show (1) the composition of Lissauer's tract, (2) the course and probable connections of the unmyelinated fibers of the posterior roots, and (3) the possible origin of the lateral spinothalamic tract.