DOCTORAL DISSERTATION SERIES

PUBLICATION: 5722

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University of Michigan

TITLE: THE AUDITORY PATHWAY OF THE EPILEPTIC WALTZING MOUSE

University Microfilms, Ann Arbor, Michigan, 1953

THE AUDITORY PATHWAY

OF THE EPILEPTIC WALTZING MOUSE

by
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A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy in the
University of Michigan
1953

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THE AUDITORY PATHWAY OF THE EPILEPTIC WALTZING MOUSE

by Muriel D. Karp Ross

Young mice of the particular strain of Peromyscus maniculatus artemisiae described in this study exhibit both epilepsy and waltzing in response to audiogenic stimuli. Jingling keys provide an especially effective stimulus. As these mice become older they gradually lose their hearing. Finally, they become totally deaf and no longer are subject to either the epilepsy or the waltzing. The purposes of this study are twofold: 1) to determine the cause of the deafness, and 2) to attempt to relate any lesions found in the auditory pathway to tonal losses exhibited by the animals in life, using as a basis previous work of many authors on the pattern of projection in this pathway in higher forms.

Brains of partially deaf and totally deaf epileptic waltzers were compared with those of normal mice of a stock of Peromyscus maniculatus blandus. This report is based upon microscopic examination of eight brains: two from normal controls, four from partially deaf and two from totally deaf epileptic waltzers. Three of the partially deaf animals were tested for range of hearing and showed extreme high and low tonal losses. The brains were prepared for study according to the usual technical methods. Two brains, one from a normal control and one from a totally deaf epileptic waltzer were stained with cresyl-echt-violet, two from partially deaf epileptic waltzers were stained with toluidine blue, and the remaining four brains were prepared by Weil's method for medullated fibers.

Microscopic examination of the brains showed that there is a selective and progressive demyelinization of the fibers in the auditory pathways of the abnormal mice. This demyelinization is incomplete in

the case of the young partially deaf epileptic waltzers, but is almost complete in the brains of older totally deaf animals of the same strain. The location of the degeneration in the auditory pathways of partially deaf animals, when compared with these tonal losses, indicates a pattern of projection in the auditory paths. This pattern appears to agree to some extent with the organization of the auditory pathways in higher forms. The special points of agreement are as follows: high tones appear to project to the dorsal part and low tones to the ventral part of the primary acoustic nuclei, and a rostrocaudal relationship appears to exist between pars principalis of the medial geniculate nucleus and the auditory koniocortex.

Aside from the conclusions that the cause of the deafness of the epileptic waltzers is anatomical in nature and that a pattern of projection appears to exist within the auditory pathway of the rodent, this study also indicates that the epilepsy is of "grand mal" type, with the locus of this phase of the disease in the auditory cortex.

PREFACE

Waltzing and epilepsy are two hereditary traits which appear independently or together in various stocks of mice of the genus Peromyscus. The particular stock of Peromyscus maniculatus artemisiae to be described in this paper was bred in the Laboratory of Vertebrate Biology at the University of Michigan. The members of this stock exhibit both waltzing and epilepsy and are further peculiar in that various kinds of sounds provide the necessary stimulus. Moreover, only young or fairly young mice are affected by sound; old animals ultimately become deaf and no longer exhibit convulsions or circling movements.

It was with no little interest that we first saw the epileptic waltzing mice respond to the stimulus of jingling keys. A young mouse was placed in an enclosure three feet square. The sides of the enclosure were made of galvanized iron, although the lower few inches were padded with cotton; the top was not closed in. Nearby, but out of sight of the animal, a bunch of keys was connected to a sewing-machine motor so that they could be set in motion at the mere flip of a switch.

The little animal crouched as the keys were jingled. After a few moments it began to whirl madly in circles, and then to dash wildly about the enclosure, apparently attempting to scale the vertical walls. The reason for the cotton padding now became evident. The "dashing" phase did not last more than a few seconds whereupon the animal fell upon its back in an epileptic seizure. It's body became rigid; its forelegs were flexed and its hind legs extended. After a short time, the animal recovered from the seizure only to resume its circus movements. It whirled to the right or to the left in a graceful manner, but not madly as before.

The violent reaction of such a young mouse was very different from that of an older animal of the same strain. The latter neither waltzed nor had a convulsion when exposed to the sound of jingling keys, although records showed that it was positive for both traits when tested at a younger age. Now it gave no visible sign that it even heard the stimulus, for its ears did not twitch and it showed no uneasiness.

The question arose as to whether such an animal was deaf because of degenerative changes within its peripheral or its central nervous system, or whether it simply did not wish to hear the sounds which subjected it to a convulsion and circus movements. The present study was begun in an attempt to answer this question. At first, sections of the brains of normal mice and of old epileptic waltzers were studied and compared; the results encouraged the undertaking of a more thorough study of the strain of abnormal mice at various ages.

The author is deeply indebted to Dr. Elizabeth C. Crosby for her helpful criticism of this paper, and to Dr. Edward Lauer for his assistance in matters of technique. I also wish to thank Dr. Lee R. Dice and the Laboratory of Vertebrate Biology for making the mice and the testing equipment available to us for this study, and Miss Elizabeth Barto, who tested the mice for range of hearing. George J. Smith gave much valuable assistance in preparing the photographs of the anatomical material, for which the author is grateful. The Alfonso Morton Clover Scholarship and Research Fund for laboratory materials was in use at the time the mouse brains were prepared for microscopic examination. Aid in testing the responses of the experimental animals used in this study was supplied through a grant (MH-375) to Dr. Lee R. Dice from the National Institute of Mental Health, of the National Institutes of Health, Public Health Service.

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INTRODUCTION

Of recent years there has been considerable interest with regard to the causes of the partial deafness of the younger or total deafness of the older so-called 'waltzing' mice. These are mice of a certain strain which, under stress, develop a peculiar type of epileptic attack during which they show a form of circling movements. It was felt that a comparison of the acoustic pathways in the brain of the normal mouse with the corresponding pathways in the nervous system of the partially deaf or totally deaf animals might indicate definite anatomical reasons for the loss of hearing exhibited by the epileptic waltzing mice. The brains of these animals should also provide experimental material on the auditory connections and centers which might be of considerable value for an understanding of the normal mammalian auditory system.

MATERIALS AND METHODS

A total of 26 animals were obtained from the Institute of Human Biology for use in this study. Of this number 8 animals were normal, controls taken from a stock of Peromyscus maniculatus blandus from Tularosa, New Mexico; they showed neither waltzing nor convulsive behavior when exposed to the stimulus of jingling keys for 90". The rest of the animals were epileptic waltzers, hybrids between several subspecies of mice. The convulsive and waltzing behavior is found in a stock of Peromyscus maniculatus artemisiae and is inherited in general as a mendelian recessive (Dice, '35; Watson, '39). Nine of the epileptic waltzers were considered deaf because they did not twitch their ears in response to a tap on glass, to a squeak, nor to key jingling, and the last procedure did not cause waltzing nor a seizure. Six animals were young, possessed acute hearing, and both waltzed and had a convulsive

seizure when exposed to the sound of the jingling keys. Three animals had less acute hearing than the young mice; they suffered less violent reactions to key jingling, as evidenced by a weak dash or ear twitching. One deaf and one young mouse died of natural causes, leaving 24 animals which were actually prepared for study.

All of the animals were sacrificed by the use of ether and were perfused. In 17 cases a 10% solution of formalin in distilled water was used in the perfusion; the brains only were prepared for examination in 6 cases, temporal bones in 5, and both the brains and the temporal bones in 7. A perfusing fluid described by Guild ('19) was used on the remaining 7 specimens, in which both the cochleae and the brains were saved in 4 cases, and the temporal bones, in 3. The Guild stock solution consists of the following:

Mercuric bichloride	50 gm.
Potassium dichromate	25 gm.
Sodium sulfate	10 gm.
Distilled water	1000 cc.

This mixture was kept in an oven at 39° C. until time of use. Before using, 10% (by volume) of 10% formalin (also kept at 39° C.) was added to the stock solution.

In all of the mice prepared for study, the perfusion fluid was injected into the blood stream through the heart. A 10 cc. luer fitted with a small needle was used for this purpose, and usually 10 or 15 cc. of fluid were sufficient to obtain a good perfusion of the animal. Pressure was applied gently by hand. Following the perfusion, small scissors were used to remove the skull cap, lower jaw, and muscle.

At first attempts were made to remove the brains immediately, but it was found just as practical to immerse the brain together with the remaining portions of the skull in 10% formalin for several days to allow the tissues to harden. Subsequently, the brain was easily

removed from the skull. Whenever the Guild method was followed the brain was removed at once and transferred to a 10% formalin solution; the temporal bones were placed in well marked containers filled with 50 cc. of the warm fixing fluid. In all but one case the entire procedure as given by Guild was followed in decalcification, fixing, clearing, and embedding the tissue in celloidin; the tissue was not double embedded, however. In the single exception noted, ordinary procedures for decalcification, fixing, clearing, and embedding in paraffin were followed. The tissue shattered when sectioned, and after this experience the technique given by Guild was used. Some of the celloidin blocks have been sectioned on a sliding microtome, using the "water-on-the-knife" method mentioned by Huber ('04), but none of the cochleae have been intact. Since it is especially desirable that well preserved cochleae be obtained from these animals, it is to be hoped that improved technique will bring better results.

Of the 16 brains which were reserved, 3 were fixed, cleared, and embedded according to the Huber-Guild pyridine-silver method. The tissue became very hard and shattered when cut at a thickness of 20μ. The 13 remaining brains were fixed, cleared, and embedded in paraffin according to usual methods. Seven paraffin blocks were cut on a rotary microtome in section 25μ thick, mounted serially, and stained after Weil's method for fibers. Two brains were cut at 15μ, mounted in serial sections, and stained with cresyl-echt-violet. The remaining 4 brains were cut at 25μ, mounted serially, and stained with Toluidin blue. All of the brains were cut transversely.

This report is based upon 8 series of the brains: 1 normal and 3 abnormal brains, (one of the latter was taken from a deaf animal and 2 were obtained from partially deaf mice), which were stained

by Weil's method; 1 normal and 1 abnormal brain, (the latter from a deafened animal), were stained with cresyl-echt-violet; and two brains from partially deaf specimens were prepared with toluidine blue. Three of the partially deaf mice had been tested for range of hearing with electrical equipment generously made available for this purpose by the Laboratory of Vertebrate Biology.

This testing equipment was located in a room closed off from the rest of the laboratory, thus eliminating a great deal of noise. The animals were placed singly in a small box which had inner dimensions of 6 3/4" on all sides. This box was made of wood 3/4" thick, and three sides as well as the floor were padded with velvet. There was a small opening 3 1/6" x 3" in the fourth side, (which was also unlined); this opening was covered by a wire screen. The animal was free to move about in the box during the tests. The sound producing instrument was a special crystal transducer from the Brush Development Company which produced pure tones from 10 to 100,000 cycles/sec. The sound source was fixed on a stand at one side of the box and was directed downward toward the box at about a 90° angle. It was about 10" from the mouse's head. The intensity varied at different frequencies in these tests, although the intensity of any given frequency was always the same at the sound source. Any difference in the intensity of the sound received by the animal was probably due to a shift in his position in the box. Some sound waves were probably also reflected from the unpadded surface, and the orientation of the animal in respect to this surface possibly affected the intensity of the sound received.

In order to produce the sound a key had to be pressed and released; the depression of the key made a faint click, but attempts were always

made to close the circuit in such a way that no click was audible to human ears. Also, the apparatus was constructed so that the sound was emitted when the circuit was opened rather than when it was closed; thus, the click and the pure tone would not coincide. An ear movement immediately following presentation of the tone was considered evidence that the mouse heard the tone. Dr. Dice states that the "click alone never elicited a strong ear twitch and only rarely a slight twitch", (private communication). The responses of the animal varied from a weak ear twitch to a definite jerk of the whole mouse; frequently slight responses were observed at the ends of the hearing range, and sometimes they occurred when the animal was drowsy or had changed positions in the box.

In the beginning the animals were exposed to frequencies of 100,000 cycles/sec., and then to lesser frequencies until the entire scale had been covered. Frequencies were then increased until the scale had been recovered. Jumps of 10,000 cycles/sec. were used until a response was obtained, whereupon the frequencies were altered by 5,000 cycles/sec. in the range between 65,000 and 20,000 cycles/sec., and by 1,000 cycles/sec. from 20,000 to 1,000 cycles/sec. For ranges from 1,000 to 100 cycles/sec. the rate was diminished or increased by 100 cycles/sec. The mice were tested as many as 7 times (never consecutively) for a tone if response (as indicated by an ear twitch) was not observed at first.

NORMAL MATERIAL

The following description is based upon a study of 2 mice, #87932 (female) and #87120 (male). The brain of the former mouse was stained according to Weil's method for fibers, and that of Mouse #87120

according to Nissl's method for cells. The mice were not tested with the electrical equipment for range of hearing. Dice and Barto ('52) found that mice of the blandus strain from New Mexico were not so responsive to pure tones in general as were the epileptic waltzers, nor did they usually give ear movements to sounds of as high a frequency as did the waltzers.

DORSAL COCHLEAR NUCLEUS: The acoustic tubercle of the mouse is a paired structure comparable with the dorsal cochlear nucleus of higher forms. It is located dorsolaterally in the medulla oblongata in relation to the restiform body (area ovalis) which lies ventromedial to it. The posterior end of the acoustic tubercle lies at the level of the lateral recesses of the fourth ventricle. The dorsal cochlear nucleus increases in size ventrolaterally and to a lesser degree in height, reaching its greatest development in its middle third. In these sections it lies dorsolateral to the ventral cochlear nucleus and to area ovalis. Rostral to the plane of the caudal part of the genu of VII, the dorsal cochlear nucleus shortens and gradually flattens to a narrow band of granular cells. These granular cells cover the dorsolateral surface of the ventral cochlear nucleus and extend to the oral termination of the latter in the plane of the motor nucleus of the trigeminal nerve. Consult pls. 1 to 5.

The internal organization of the acoustic tubercle differs at various levels. Caudally it is composed of a few delicate fibers and numerous cells; the latter are either small in size, fusiform or round, and dark staining, or they are of medium-size, rounded and pale staining. No pattern of distribution of the cells or of the fibers is observed. As the acoustic tubercle broadens, the fibers within it become thicker and more numerous while the cells increase in number. A distinct

lamination of the acoustic tubercle, involving both the cells and the fibers, begins at the level of the facial nucleus and ends rostrally in sections through the genu and roots of VII. The distance between the caudal pole of the acoustic tubercle and the onset of lamination within it is very short.

Among the observers who have described the lamination of the acoustic tubercle in mammals are Ramón y Cajal ('09), Winkler and Potter ('11, '14), and, more recently, Lorente de Nó ('33). Each of these workers recognized four fundamental layers, although the laminae described by each include different elements and the nomenclature varies. Lorente de No, working with Golgi preparations of mouse and cat brains, subdivided the acoustic tubercle still further. In addition to the four laminae he found several other distinct areas. In the primary acoustic nuclei as a group, he defined at least thirteen different regions and forty or fifty types of neurons.

The following description is based upon a study of the lamination as it is found in the Nissl and the Weil preparations of the normal mouse brain. Reference will be made to terminology which has been used previously in the literature and which applies to the conditions observed here.

In the acoustic tubercle of the mouse four layers are distinguished lying in a lateromedial direction; these will be described from the surface toward the inferior peduncle. The most superficial lamina, Layer I, is poor in fibers and cells. Beneath the pia there are small, round or fusiform, dark staining cells intermingled with others medium in size, round or ovoid, and pale staining. This lamina corresponds to both the surface ("epithelial") and the "superficial plexiform"

layers of Ramón y Cajal, and to "stratum griseum superficiale" of Winkler and Potter. The latter observers gave the name "lamina cellularis" to the second layer, which is rich in cells as the terminology suggests. This lamina is also Ramón y Cajal's "zone of granule and large fusiform cells". Layer II is characterized by the presence of spindle-shaped cells which generally lie with their long axes at right angles to the surface of the acoustic tubercle. These cells are of small or of medium size in the mouse and vary in their staining quality; interspersed among them are many small, dark, round cells. In the third layer, polymorphous cells are arranged between numerous diagonally cut fibers. The fibers are, for the most part, of two derivations: some of them are cochlear nerve fibers on their way to the cells of the dorsal cochlear nucleus where they terminate; others have their origin within the latter nucleus and are axial processes of secondary neurons which ascend to higher levels. This layer corresponds to Winkler and Potter's ('14) "stratum medullare superficiale", and to Ramón y Cajal's "deep plexiform layer" or "zone of large nerve cells". The deepest layer of the acoustic tubercle, the "stratum medullare profundum" of Winkler and Potter, is composed of cochlear nerve fibers entering it ventrally, and of the axial processes of the previously mentioned secondary neurons which are gathering into a heavy bundle medially. This bundle of fibers emerges from Layer IV dorsomedially, and then swings dorsalward over the restiform body and toward the midline as secondary dorsal cochlear fibers. Their course will be fully described in the discussion of the acoustic pathway.

Aside from this lamination some authors have recognized further organization within the acoustic tubercle. Thus, a group of cells

called nucleus proprius by Winkler and Potter is present. In Mouse brain #87120, stained for cells, nucleus proprius begins in sections at the level of the facial nucleus, just caudal to the beginning of lamination, and some of its cells are traced rostrally to sections through the posterior end of the genu of VII. At this level there is an increase of cells similar to those of nucleus proprius within the rest of the acoustic tubercle and the former nucleus can be distinguished no longer.

Nucleus proprius varies considerably in size within the acoustic tubercle, but its small, round, dark staining cells are found at all its levels. They were called "grains" by Winkler and Potter ('11, '14), and are closely grouped together. Most caudally these "grains" spread in a thin layer across the ventromedial two thirds of the acoustic tubercle. Initially the cells do not attain the most ventral portion of the dorsal cochlear nucleus, but do come to this area shortly. Nucleus proprius reaches its greatest size, occupying most of the ventral fourth of the acoustic tubercle, in sections in the plane of the nucleus of VII and of the caudal pole of the ventral cochlear nucleus. As the cells of the ventral cochlear nucleus increase in number ventralward, they divide nucleus proprius into a lateral and a medial portion. The medial portion is smaller and ends within 60μ. The dorsal portion becomes reduced in size but can be traced to the oral limit of the nucleus.

The fiber content within nucleus proprius in Mouse brain #87932 is never great; delicate fibrils ramify between the closely arranged cells.

VENTRAL COCHLEAR NUCLEUS: The ventral cochlear nucleus does not extend so far caudalward as does the acoustic tubercle, but begins at the level of the facial nucleus and ends rostralward at the level of the motor nucleus of the trigeminal nerve. Plates 1,2, and 5 should be consulted.

Ramón y Cajal ('09) and Lorente de Nó ('33) have described various zones in the ventral cochlear nucleus. According to Ramón y Cajal this nucleus has two parts, an anterior or rostral portion and a posterior or caudal portion. This division is based upon the presence of a "tail" or dorsal extension of the ventral cochlear nucleus which lies internal to the posterior part of the acoustic tubercle. Four zones were described by Ramón y Cajal for the ventral part of the ventral cochlear nucleus, but were not present in the dorsal extension nor in the anterior levels of the nucleus. These zones were named in lateromedial order: 1) an "epithelial" layer, 2) a superficial plexiform zone, 3) a zone of small cells, 4) a zone of large cells and of fiber bundles. This description of the lamination appears to have been based upon his preparations of the cat, the rabbit, and the guinea pig. Lorente de Nó ('33), working with mouse and cat brains, divided the ventral cochlear nucleus in dorsoventral direction into regions I, II, and III.

In the mouse brains reported here a division into anterior and posterior portions has been made. The posterior subdivision begins as a few cells lying ventromedial to the tubercle. From this modest beginning the ventral cochlear nucleus increases rapidly in size to form a rounded hillock; the dorsal slope of the hillock is extended dorsally so that it lies medial to the acoustic tubercle and lateral to the restiform body. This dorsal portion is lengthened in such a

fashion in both mice and corresponds to the dorsal extension or "tail" described by Ramón y Cajal. In the plane of the caudal part of the genu of VII the dorsal slope of the ventral cochlear nucleus rounds considerably and such a tail is no longer observed. With the disappearance of the dorsal extension, the posterior division ends and the anterior portion begins. The anterior subdivision extends rostralward to the level of the motor nucleus of the trigeminal; posteriorly it is rounded, but at the level of the vestibular nerve the hillock shortens and the lateral surface of the nucleus soon flattens. The entire body diminishes in size very gradually in such a way that rostrally it is narrower dorsally than ventrally. Its lateral surface is rather straight and its ventral border slopes gently.

The high degree of organization of cells and fibers into a definite pattern as was described for the acoustic tubercle is not evident in the ventral cochlear nucleus of these mice. A layer of flattened pial cells covers the nucleus except in the tail. Internal to this lamina a thin layer of dark, closely arranged, granular cells is observed. These cells are directly continuous with the granules observed in nucleus proprius and in the anterior end of the acoustic tubercle; they are not present along the dorsolateral border of the ventral cochlear nucleus caudal to the level of the superior olive. Medial to the layer of granular cells and in the so-called tail of the nucleus are the cells and fibers which make up the bulk of the ventral cochlear nucleus. The most prominent cells are large, triangular or oval in shape, and have large, oval nuclei; their cytoplasm takes on a very characteristic violet color in Nissl's stain. Smaller, round and fusiform cells are intermingled with the large ones. In the anterior portion, as the nucleus becomes flat, the cells located dorsally are chiefly oval in

shape and are closely grouped, while those found ventrally are mostly triangular or spindle-shaped. These cells are, on the whole, smaller than those found caudally and are also more numerous and closely grouped.

In the posterior portion of the ventral cochlear nucleus, the cells are divided into several rows by layers of longitudinally running fibers. The layers of fibers approximate each other more and more toward the middle of the nucleus, as the level of the cochlear nerve is approached. Here, the ventral cochlear nucleus is divided into a lateral and a medial zone by the thick bundle of cochlear nerve fibers, and a small group of cells is situated dorsomedially between the fascicles. (See pl. 1) In these zones the fibers form a network among the cells. The cochlear nerve enters the ventral cochlear nucleus ventromedially at the level of the roots of VII, occupying almost all of the ventral and medial parts of the nucleus. Here, only the dorsolateral area exhibits numerous cells and ramifying fibers. Rostral to this level, the nucleus is again divided for a few sections by a layer of fibers and lateral and medial zones can be distinguished. In most of the anterior portion of the ventral cochlear nucleus the fibers are evenly distributed and no such subdivisions are found.

(pl. 1)

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: The superior olive is a folded gray mass extending between the level of the facial nucleus caudally and that of the motor trigeminal nucleus rostrally. Its cells are of medium-size and of polygonal or fusiform shape; their long axes generally follow the curves of the nucleus. Internal to the superior olive and closely associated with it lies the accessory superior olive. This nucleus is somewhat semi-lunar in shape, although it is much less definite in contour in the mouse than in other forms. Its cells are

also of medium size and of fusiform or polygonal shape.

Associated with the superior olive and with the trapezoid body are two small nuclear masses, the internal and external parolivary nuclei. They lie between the fibers of the trapezoid body ventral and ventrolateral to the superior olive, respectively. The cells of these nuclei are spindle-shaped and are slightly smaller in the external than in the internal parolivary nucleus. In both cases the cells are smaller than those in the superior olive.

Medial to the accessory superior olive and lateral to the medial lemniscus lies as aggregation of cells called the nucleus of the trapezoid body. Its ovoid or polygonal cells are more closely arranged and smaller than those in the accessory superior olive. (See pl. 1).

NUCLEI OF THE LATERAL LEMNISCUS: Two nuclear masses are intercalated in the course of the lateral lemniscus, the superior and the inferior nuclei of the lateral lemniscus. The inferior nucleus extends from the level of the upper pons caudally to the level of the posterior part of the inferior colliculus rostrally. Posteriorly, it lies internal to the brachium pontis and anteriorly, it is continuous with the more ventral portion of the superior nucleus of the lateral lemniscus. The cells are large, polygonal, and closely arranged. (See pls. 6 and 7).

In sections through the posterior part of the inferior colliculus and extending to the anterior end of that body there is a loosely organized and elongated cellular aggregation, the superior nucleus of the lateral lemniscus. It is dorsolateral to the inferior nucleus of the lateral lemniscus, to which it is joined caudally by a few strands of cells. The main mass of the nucleus lies in a dorsolateral position, ventral to the nucleus of the inferior colliculus. The cells are

large and fusiform or ovoid in shape; many of them lie with their long axes in a horizontal plane. (See pls. 6 and 7).

Within these nuclei are numerous fibrils, while heavy bundles of fibers connect the inferior nucleus and the dorsal main mass of the superior nucleus. The fibers separate the ventral cells of the latter nucleus into strand-like formations; these strands caudally provide a continuity between the two nuclei of the lateral lemniscus. These heavy fascicles may be regarded as internuclear components of the lateral lemniscus.

INFERIOR COLLICULUS: In the mouse, as in other mammals, the inferior colliculus consists of two portions, a central nuclear mass and a peripheral capsular portion. The cells of the nucleus are rather large and polygonal in shape. At the periphery of the central nucleus lies the capsular portion which consists of fibers leaving the inferior colliculus. Among the fibers are scattered small or medium-sized cells which are fusiform or polygonal in shape. (See pls. 6 and 7).

The fibers of the lateral lemniscus ascending to the inferior colliculus enter the central nuclear mass at its periphery. According to Held ('93), Ramón y Cajal ('11), and others, most of the axons of the large cells of the central nucleus enter the peduncle of the inferior colliculus through the capsular portion. Ramón y Cajal also believed that some of the smaller cells of the capsule send their axons to the medial geniculate nucleus. In this material, the peduncle of the inferior colliculus forms ventrolateralward at the periphery of the inferior colliculus.

MEDIAL GENICULATE NUCLEUS: The medial geniculate nucleus appears caudally as a small, oval-shaped mass on each lateral surface of the

midbrain at the level of the superior colliculus. In its caudal two thirds it lies posterior to the lateral geniculate body. The medial geniculate nucleus attains its greatest size in its middle third. Its rostral third lies medial and slightly ventral to the lateral geniculate body. The rostral tip of the medial geniculate nucleus tapers off to a small group of cells lying in relation to the external medullary lamina ventrally, the ventral nucleus of the thalamus medially, the posterior portion of the lateral nucleus of the thalamus dorsally, and the lateral geniculate body laterally and dorsolaterally. These cells merge with those of the ventral nucleus of the thalamus at levels through the anterior half of the posterior commissure.

Many investigators have described this nucleus in a number of animals: Ramón y Cajal ('09) in the cat, guinea pig, and mouse; Winkler and Potter ('11, '14) in the rabbit and cat; Gurdjian ('27) in the rat; Rioch ('29) in the carnivores; Le Gros Clark ('30, '33) in Tarsius and insectivores; and Malone ('10), Walker ('37, '38), and many others in primates. Subdivisions have been described by several of these workers, although there is disagreement as to the functional (or even anatomical) significance of these divisions.

In the mouse several regions are present in the medial geniculate body. The major subdivisions are a <u>pars principalis</u> and <u>pars magnocellularis</u>, as the two areas have been named by Rioch ('29). Pars principalis is the larger division and extends the entire caudorostral extent of the nucleus. It is the more laterally located of the two parts, and in its middle third it is bean-shaped. Pars principalis can be subdivided further into a series of groups of cells or zones. Of these, the two major groups are a dorsal and a ventral portion. (See pl. 8).

The dorsal group of cells is a distinct subdivision of the medial geniculate nucleus in the mice studied. It is characterized by cells which, on the whole, are of medium size, although they tend to be somewhat smaller rostrally than caudally. Their cell bodies are triangular or spindle-shaped. These cells stain more darkly and are more loosely arranged than are those of the ventral portion. The dorsal group begins in the posterior fifth of the medial geniculate nucleus as a cap of cells over the ventral portion of pars principalis. In more rostral sections, it assumes a dorsolateral position in relation to the ventral group, and along its medial border cells of different types appear. Some of these cells are large, polygonal, and have a reddish tinge to their cytoplasm; others are small, round or spindle-shaped, and dark staining. These cells are continued into the dorsal part of the lateral geniculate nucleus and, more rostrally, occupy the position formerly taken by the dorsal portion of pars principalis. In sections through the anterior part of the Edingher-Westphal nucleus, the cells typical of the dorsal group of pars principalis disappear, the last few being located in a dorsolateral position within the medial geniculate nucleus. The dorsal group of cells corresponds to Ramón y Cajal's superior lobe, and to the caudal part of Winkler and Potter's area "b".

The ventral part of pars principalis corresponds to Ramón y Cajal's inferior lobe of the medial geniculate nucleus. It extends the entire caudorostral length of this nucleus and may be subdivided into at least three portions: the chief mass, the lateral part, and the ventral group. The chief or central mass of pars principalis consists of cells of medium-size, and of oval, triangular, or fusiform shape;

they possess large, oval, pale staining nuclei, and a cytoplasm which takes a pale violet stain with cresyl violet. In the central mass the cells are arranged in small groups but are generally close to one another. This part corresponds to area "a" of Winkler and Potter, and to noyau interne of Ramón y Cajal. It extends from the posterior to the anterior pole of the medial geniculate nucleus. In sections through the caudal part of the mammillary bodies, the more dorsal cells of this portion of pars principalis grade over into the cells of the posterior part of the lateral nucleus of the thalamus. In the region of continuity of these nuclei the cells are small and spindle-shaped or round, or are of medium-size and triangular or polygonal in shape. More rostrally, the cells ventrally located within the main mass of pars principalis are not sharply delimited from those within the ventral nucleus of the dorsal thalamus.

Along the lateral border of pars principalis the cells which constitute the pars lateralis are more flattened and more closely arranged than they are in the chief or central mass. The lateral portion is very thin in the mouse and is not observed in the most caudal sections nor in the rostral fourth of the medial geniculate nucleus. This part is the portion superficielle of Ramón y Cajal.

The third or ventral portion of pars principalis consists of spindle-shaped cells which are smaller than those of the other two portions of pars principalis, and more ventrally located. The cells are arranged in a crescentic mass which is joined to the chief or central part of pars principalis caudally. This ventral portion corresponds to area "c" of Winkler and Potter, and to noyau sus-pédunculare of Ramón y Cajal. It extends from sections 75 μ anterior to the posterior pole of the medial geniculate nucleus to

the rostral termination of the latter nucleus in Mouse brain #87120. It lies dorsal to the cerebral peduncle for most of its extent, and ventral to the main mass of pars principalis. Rostrally it is lateral to zona incerta at first, but then becomes continuous with the latter medially and with the reticular nucleus anteriorly. Le Gros Clark ('30) has described a similar termination for this group of cells in insectivores.

Pars magnocellularis begins in the most caudal fifth of the medial geniculate nucleus in the mouse; it ends rostrally, along with pars principalis, by merging with the cells of the ventral nucleus of the dorsal thalamus in sections through the anterior half of the posterior commissure. Pars magnocellularis is composed of large, polygonal cells among which are found small, spindle-shaped or round cells. It has no subdivisions. Caudally it lies medial to pars principalis, but rostrally it is located dorsomedial to the latter portion of the medial geniculate nucleus.

AUDITORY CORTEX: The three primitive fissures found in all mammalian brains are present in the mouse; these are the hippocampal, the rhinal, and the endorhinal fissures. The endorhinal fissure is not prominent macroscopically, but under the microscope the infolding of the cortical laminae and the presence of the lateral olfactory tract within the shallow groove thus created are evident. The mouse brain possesses no fissures in the neopallium, and because of their absence the cortical areas are distinguished from one another chiefly on a cytoarchitectural basis. Both Droogleever Fortuyn ('14) and Maxmillan Rose ('29) have given excellent descriptions of the cytoarchitecture of the mouse brain; the works of both authors were used as references in the study

of the animals reported here.

The area ascribed to audition is subdivided into two parts, the primary and the secondary auditory areas, or T_1 and T_2 (Rose). At the present time this subdivision in the mouse does not depend upon functional, but rests wholly upon histological, differences. T_1 is bounded by the postcentral area anteriorly, the secondary auditory area inferiorly, the occipital area posteriorly, and the parietal region superiorly. It extends farther caudalward than does the secondary auditory area. T_2 lies in relation to the postcentral area anteriorly, the posterior insular area and the ectorhinal area inferiorly, the occipital area posteriorly, and the primary auditory area superiorly. It extends farther rostralward than does T_1.

A six-layered plan of organization, with modifications, exists in the mouse auditory areas, as it does in all other neocortex. According to the nomenclature used by Brodmann('09), these layers are, in lateromedial order: Layer I, lamina zonalis; Layer II, lamina granularis externa; Layer III, lamina pyramidalis; Layer IV, lamina granularis interna; Layer V, lamina ganglionaris; Layer VI, lamina mutiformis.

In the primary auditory area, lamina zonalis is narrow and contains very few cells. Those cells present appear fusiform in cross section. The second layer is not distinct, but is masked by the medium-sized pyramidal cells of the third layer. Rose, for example, speaks of Layer II+III. The fourth layer is rather broad and contains numerous granular cells grouped together into clusters or knobs. These clusters are a characteristic feature of the primary auditory area and serve to distinguish it from surrounding areas in which such

an arrangement of the granular cells of Layer IV is never found. Its highly developed lamina granularis interna suggests further that this area corresponds to the auditory koniocortex of higher forms. Layer V is of medium breadth and is divided into lateral, middle, and medial strata. The lateral and medial strata possess small pyramidal cells that are widely scattered, but rather closely arranged large pyramidal cells are found in the middle stratum. The sixth layer consists of polymorphous cells which are more dense directly beneath the fifth layer than they are medially.

The primary auditory area differs from surrounding areas chiefly in the characteristic arrangement of the internal granular layer. It may be distinguished also from the parietal area by the larger size of the pyramidal cells found in Layer V of that area; from the postcentral area in which broader Layers III and V are present; from the occipital area in which a broader Layer I, narrower Layer IV, and lack of stratification in Layer V is observed; and from the secondary auditory area in which both Layers I and V are broader.

The secondary auditory area possesses a Layer I of about medium breadth. Layer II is again masked by the medium-sized pyramidal cells of Layer III. The fourth layer exhibits no clustering of its granular cells. Layer V is very broad in the secondary auditory area and is divided into lateral, middle, and medial strata. The middle stratum is broad and is composed of large pyramidal cells; the lateral and middle strata possess small pyramidal cells. The sixth layer is narrower than in the primary auditory area; its polymorphous cells are more densely grouped laterally than medially.

The secondary auditory area is distinguished from the postcentral, the occipital, and the primary auditory areas by its rather broader Layer I and its very wide Layer V. It differs from the postcentral area also in possessing a narrower Layer IV than does the latter. The secondary auditory area is easily distinguished from the areas located ventral (or inferior) to it. Inferior to it, anteriorly, lies the posterior insular area in which a very wide Layer I and narrow Layers II and III are found, and in which Layer IV is not evident. Inferior to the secondary auditory area, posteriorly, lies the ectorhinal area which possesses a broad Layer I and in which Layers II, III, and IV are indistinctly separated from each other.

THE ACOUSTIC PATHWAY: The first neurons in the acoustic pathway are bipolar cells, the cell bodies of which are located in the spiral ganglia within the cochlea. The dendrites of these cells extend peripheralward to terminate on the hair cells of the organ of Corti; their neuraxes accumulate on leaving the spiral ganglia, to form the cochlear division of the eighth cranial nerve. The cochlear division comes into relation with the vestibular part of VIII in its course centralward, but enters the medulla oblongata posterior to the latter and ventromedial to the ventral cochlear nucleus. Each fiber of the cochlear nerve divides immediately into an ascending and a descending branch, (Held '93, Ramón y Cajal '09, and others). The destination of the ascending branch is the ventral cochlear nucleus, and the descending branch terminates in the acoustic tubercle and in the dorsal extension of the ventral cochlear nucleus.

The secondary acoustic neurons leaving the dorsal and the ventral cochlear nuclei ascend by way of several routes to higher centers. A

bundle of fibers emerges dorsomedially from the fourth layer of the acoustic tubercle as the secondary dorsal cochlear fibers. They swing dorsalward over the restiform body, then medialward through the region of the vestibular nuclei, becoming more separated from one another in their course. Many of the fibers cross the midline in the region ventral to the medial longitudinal fasciculus, forming the dorsal acoustic decussation, before turning downward to reach the region dorsolateral to the superior olive. Here they join secondary acoustic fibers from the ventral cochlear nucleus to form the lateral lemniscus. The number of secondary dorsal cochlear fibers remaining on the same side could not be determined in these mice.

From the ventral cochlear nucleus, secondary acoustic fibers course ventromedialward as the fibers of the trapezoid body. These fibers pass below or around the superior olive, through the region of the medial lemniscus, cross the midline in the ventral acoustic or trapezoid decussation, and enter the contralateral lateral lemniscus. The trapezoid decussation is much heavier than the dorsal decussation in the mouse. The more dorsal fibers of the trapezoid body are spread apart lateral to the medial lemnisci by the nuclei of the corpus trapezoideus. Numerous fibers ramify within these nuclei. In higher forms it is generally conceded that some of the secondary neurons from the ventral cochlear nucleus synapse in the trapezoid nuclei, and that contributions from the latter join the lateral lemnisci to ascend to higher auditory centers. (See pls. 1 and 2).

Between the dorsal and the ventral acoustic decussations is the decussation of Held. The fibers crossing the midline here appear, in the available material, to originate in the dorsal portion of the

ventral cochlear nucleus as was described by Ramón y Cajal ('09) and Yoshida ('24). These fibers run dorsalward over the restiform body and then dip ventralward immediately to gain a position between the dorsal secondary acoustic fibers and the trapezoid body. The fibers of Held are not numerous in the mouse.

The lateral lemniscus is composed, then, of secondary cochlear fibers from the ventral cochlear nucleus of the opposite side and from the acoustic tubercle of the same and of the opposite sides. It also carries fibers from the trapezoid nuclei. In this manner, both ears are represented in each lateral lemniscus.

At lower midbrain levels the lateral lemniscus swings dorsolateralward. Both superior and inferior nuclei of the lateral lemniscus are present and probably receive collaterals from and add fibers to the lateral lemniscus. In the mouse, many of the fibers of the lateral lemniscus enter the inferior colliculus. Fibers leave the inferior colliculus laterally, turning ventralward in the capsular region. They join the portion of the lateral lemniscus which does not enter the collicular gray; together these fascicles constitute the peduncle of the inferior colliculus which enters the medial geniculate nucleus caudomedially. Thus, fibers project to the medial geniculate nucleus directly through the lateral lemniscus, or indirectly, after synapsing in the nucleus of the inferior colliculus.

The geniculo-cortical fibers gather medial to the anterior part of the medial geniculate nucleus. They assume a more lateral position as all of the cells of pars principalis except those situated most ventromedially disappear near the rostral tip of the nucleus. These fibers form the auditory radiations which run to the cerebral cortex

along with the dorsal thalamic radiation. The course of the auditory radiations in themouse corresponds to that previously described in the rat by Gurdjian ('27). There are thought to be efferent as well as afferent fibers with respect to the auditory cortex in the auditory radiations.

DEAF MICE

The two mice described here were thought to be completely deaf, as they did not respond to a squeak, a tap on glass, or key jingling. They were not tested with the electrical equipment. After sacrificing the animals, the brain of Mouse #85836 (male) was stained according to Nissl's method for cells, and that of Mouse #85842 (female), according to Weil's method for fibers.

DORSAL COCHLEAR NUCLEUS: The acoustic tubercle begins caudally at the level of the lateral recesses of the fourth ventricle. It diminishes to a narrow band of cells over the dorsal surface of the ventral cochlear nucleus in the plane of the facial roots; these cells are present to the rostral termination of the ventral cochlear nucleus. The caudorostral extent of the acoustic tubercle in the deaf animals corresponds, then, to that of the normal mice. The dorsal cochlear nucleus is not diminished in length nor in breadth in the deaf mice, but is considerably flattened at all levels. Along with the flattening of the nucleus is a loss of internal organization which is more complete on the right side of both specimens, but which is more extensive in Mouse #85836 than in Mouse #85842.

In Mouse #85836, caudal to the level of lamination in the nucleus, the medium-sized ovoid cells and the smaller spindle-shaped cells

prominent in the posterior part of the acoustic tubercle in the normal mouse brain are not present. Microglia, however, are more numerous than usual. In sections at the level of the facial nucleus there is an indication of lamination of the tubercle. The superficial layer is composed of few cells, as is the case normally. The typical fusiform cells of the second layer, lamina cellularis, are not observed here nor at any other level in the nucleus; instead, the cells are large, ovoid, and pale-staining. This layer is differentiated from the other laminae because its numerous microglia give it a very dark appearance. Layers III and IV consist of large, pale-staining cells, also, and there is a proliferation of glia especially medially. Thus, these layers cannot be distinguished from one another. The region of nucleus proprius is filled with supporting elements.

There are no fibers in the caudal fourth of the acoustic tubercle nor at any level in nucleus proprius in Mouse brain #85842. Delicate fibers appear in the ventromedial part of the acoustic tubercle in the second fourth of its extent, and gradually become more numerous. The fiber supply is best in the anterior half of the nucleus, and here, also, lamination becomes evident. The layers are thin and the fibrils in the second and third laminae are few in number and very close to one another. Layer IV is composed of small fascicles which are entering the acoustic tubercle ventrally, and of others which are leaving the nucleus dorsally.

VENTRAL COCHLEAR NUCLEUS: The ventral cochlear nucleus extends from the level of the facial nucleus caudally to that of the motor trigeminal nucleus rostrally. It is divisible into anterior and posterior parts as in the normal animal.

The cells of the ventral cochlear nucleus are closely grouped and usually pale-staining in cell material, although occasionally they assume a characteristic violet color in Nissl's preparation. In general, they are more ovoid or round than triangular in shape; the central parts of the cell processes usually appear ghost-like, indicating degeneration. At the level of the vestibular division of the acoustic nerve, some of the cells in the medial portion of the ventral cochlear nucleus are triangular-shaped and have well-stained Nissl granules, but are more closely arranged than in normal material. An unusually large number of microglia are scattered between these cells. This group of better preserved cells was traced for only 30μ.

The ventral cochlear nucleus never assumes the shape nor attains the size typical of the normal mouse brain. The most caudal part of the nucleus is much more nearly flat and narrower than in the normal preparation. It is extremely difficult to locate the cochlear nerve fibers in Mouse brain #85836. At the level of the entrance of the vestibular nerve the ventral cochlear nucleus increases in size and assumes a triangular shape; the base of the triangle is medialward and its apex points lateralward. The dorsal side of the triangle is concave; the ventral side is straight at first, but within 100μ also shows a concave curvature and becomes very short. The rostral one-half of the ventral cochlear nucleus is a flat layer of closely arranged cells; its dorsolateral surface is long and concave. The nucleus diminishes in size very gradually to its rostral termination. Far anteriorly glia increase ventrally and along the dorsal surface of the nucleus. (Consult pl. 3).

In Mouse brain #85842 the ventral cochlear nucleus also exhibits its greatest size in sections immediately anterior to the level of the

cochlear nerve. It differs from this nucleus in Mouse #85836 in that it is more rounded and not so triangular in shape at these levels. Caudally, there are no fibers in the ventral part of the nucleus. Cochlear nerve fibers, very few in number, enter the medulla oblongata lateral to the descending root of the trigeminal nerve and divide into ascending and descending branches. Some of the descending branches cross the ventral cochlear nucleus, dividing it into several laminae, to enter the dorsal extension of the nucleus. The ascending branches are most numerous in the ventrorostral part of the nucleus. The ventral cochlear nucleus, except in sections at and immediately in front of the entrance of the cochlear nerve, is extremely flat.

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: The cells of the superior olive in Mouse brain #85836 are of medium-size and are polygonal or fusiform in shape. They are very close to one another and neuroglia are numerous among them. The cells are arranged in various directions as though following those of the curves or foldings of the nucleus, but aside from this arrangement no folding, such as characterizes the normal superior olive, could be demonstrated. The superior olivary nucleus is atrophied at all levels in Mouse brain #85836; in Mouse #85842 it is smaller than normal but appears as a folded mass of gray which contains fibers throughout its entire extent.

The accessory superior olive also consists of medium-sized fusiform or polygonal cells which are closely grouped together. There is an increase in the number of microglia in this nucleus in Mouse #85836. In both specimens the accessory superior olive is more typical in size anteriorly than posteriorly. Caudally the nucleus is small and rather

round in outline.

The parolivary nuclei are difficult to demonstrate in these preparations. There is a little gray between the fibers of the trapezoid body ventral and ventrolateral to the superior olive in Mouse brain #85842; in Mouse #85836 a few polygonal cells and numerous neuroglia are found in these locations.

The nuclei of the trapezoid body are well developed in both mice. The cells of the trapezoid gray are of medium-size and polygonal or ovoid shape. They are closely arranged in Mouse #85836, and there is a proliferation of glia in the nucleus. In Mouse #85842, although there are fewer fascicles separating the gray of the nucleus, many fibers leave it medially, and there is a heavy trapezoid decussation in the region between the gray of the two sides.

NUCLEI OF THE LATERAL LEMNISCUS: The inferior nucleus of the lateral lemniscus is composed of closely arranged, polygonal or fusiform cells of medium-size. Here, again, microglia are more numerous than in the normal material. Anteriorly, the inferior nucleus is connected to the superior nucleus of the lateral lemniscus by strands of cells which are part of the latter nucleus. These strands are widely separated in Mouse brain #85836, indicating the passage of many fibers, and in Mouse #85842 there are marked fiber connections between these nuclei.

The dorsal main portion of the superior nucleus of the lateral lemniscus consists of fusiform cells which are arranged with their long axes in a horizontal plane. The cells are closer to one another than they are in normal material, and a few microglia are present. In Mouse #85842, very few fibers enter the nucleus of the inferior colliculus from the superior nucleus of the lateral lemniscus.

INFERIOR COLLICULUS: The inferior colliculus is divided into a central nucleus and a peripheral capsular portion, as is the case in the normal animal. The central nucleus is a dense, cellular area; the large polygonal cells characteristic of this nucleus are present, but between them and in the capsular portion are numerous neuroglia. The dark, round nuclei of the microglia give a granular appearance to the inferior colliculi. In Mouse #85842 there are many fibrils in the central nucleus, but few fibers enter the peduncle of the inferior colliculus.

MEDIAL GENICULATE NUCLEUS: The medial geniculate nucleus begins caudally at the level of the superior colliculus, and terminates rostrally in sections through the middle third of the posterior commissure. Anteriorly, the cells of this nucleus are confluent with the cells of the ventral nucleus of the dorsal thalamus. In these respects, then, the deaf mice do not differ from the normal animals. They do differ from them in that the medial geniculate nucleus is atrophied, especially lateromedially and dorsally, and that it shows an absence of internal organization.

Most caudally the medial geniculate nucleus in Mouse brain #85836 appears as a small mass of compactly arranged cells. These cells are of two kinds: some of them are ovoid, medium-sized neurons; others are neuroglia, particularly microglia. As the nucleus increases gradually in size pars principalis and pars magnocellularis are distinguishable, mainly on the basis of their locations.

Pars principalis is laterally situated and is composed of pale, ovoid cells of medium-size and of many microglia. The nuclear membranes of the ovoid cells are well-stained and clearly visible, but neither the cytoplasm nor the karyoplasm stain well. Frequently the cell processes are pale or do not stain at all. The dark, triangular or

spindle-shaped cells of the dorsal group are not present; there are microglia and ovoid cells in this part of pars principalis. Laterally, the cells are ovoid, also, and are much more closely arranged than in the normal animal. The central mass of pars principalis is atrophied in its entire caudorostral extent. The ventral part of this nuclear mass, which is less atrophied than the more dorsal portion, contains some scattered triangular or fusiform cells. The most ventral cell group of pars principalis is filled with neuroglia, although a few pale, ovoid cells can be distinguished.

Pars magnocellularis of the medial geniculate nucleus is poorly defined caudally; its cells are close to one another and numerous glia are present here as well as in the area between this nucleus and pars principalis. In the rostral third of its extent the large, polygonal cells typical of this area in the normal mouse brain are occasionally evident.

The degeneration in the medial geniculate nucleus is very similar in both Mouse #85842 and Mouse #85836, although some differences also exist in the two brains. There are no fibers in the caudal fourth of pars principalis of the medial geniculate nucleus except in the most ventral group in the former mouse. Fibers are present in the anterior three-fourths of the extent of pars principalis. Caudally in this better-preserved portion, they are in the central mass of pars principalis, but not in its dorsal or lateral areas. At the level of the caudal pole of the dorsal part of the lateral geniculate nucleus, a few fibers ramify laterally and dorsally in pars principalis. Rostral to this level in Mouse #85842, pars principalis is an oval-shaped gray mass in which there are few fibers.

Pars magnocellularis is not rich in fibers in Mouse #85842; it is a small mass of gray.

The auditory radiations are not numerous. A small bundle of fibers from the medial geniculate nucleus joins the dorsal thalamic radiation to ascend to cortical levels. Cortico-geniculate fibers also may be present in the auditory radiations.

AUDITORY CORTEX: The histological structure of the auditory cortex is not well differentiated in Mouse brain #85836 except in a few areas. The most prominent feature of the degeneration in the auditory cortex of this animal is the similarity of the cells in Layers II, III, and IV; these cells are rather ovoid in shape and possess pale-staining nuclei and cytoplasm. The outlines of the large pyramidal cells of the middle stratum of the fifth lamina are usually typical, but the cytoplasm and nuclei of these cells stain very lightly. The proportion of neuroglia is increased in the auditory areas of the deaf mice, but these supporting elements are not nearly so plentiful here as they are in the primary acoustic nuclei.

The first layer of the primary auditory area in Mouse brain #85836 is relatively unaffected. Layers II and III are confluent and consist of the inflated, ovoid cells described above. There are a very few dark, small pyramidal cells in the medial part of Layer II+III on the right side. These are located in the most superior and rostral portion of the primary auditory area, and are not observed elsewhere. There is a clustering of the granular cells in Layer IV superiorly in the auditory koniocortex bilaterally throughout the rostral third of its extent. Immediately ventral to these clusters Layer IV has thinned out and the cells are not arranged in knobs, as in typical

auditory cortex. Most ventrally in this area, Layers II, III, and IV, all of which consist of ovoid cells, are not distinguishable from one another. There is confluence of these layers in the entire caudal two-thirds of the primary auditory area. Layer V is also best differentiated rostrally. Its three strata are distinct, as the cells are more scattered laterally and medially than in the middle zone. The large pyramidal cells of the middle stratum are slightly enlarged and take a pale stain. Caudally, the stratification of Layer V is not evident. Layer VI is composed of polymorphous cells which do not appear to differ in arrangement in lateromedial direction.

Layer I of the secondary auditory area is not affected in this mouse. Layers II, III, and IV are indistinct, all of them being composed of pale, ovoid cells. Layer V is very broad, and its pyramidal cells are large and ghost-like. Layer VI is not differentiated into lateral and medial strata. On the left side Layers II, III, IV, and V are confluent, indicating that degeneration is more complete, (and perhaps earlier), on this side.

Unfortunately, some of the sections of the auditory cortex are missing from the left side in Mouse #85842; these were lost in preparation of the material. In the rest of the sections fibers reach the auditory areas and, in some cases, radiate into Layer IV. The primary auditory area exhibits the knob-like arrangement of Layer IV rostrally on both sides. This is best seen superiorly on the right and inferiorly on the left. There are clusters of neurons in the fourth layer throughout approximately the caudal third of the auditory koniocortex. Delicate fibers can be traced through Layer IV in this region.

The secondary auditory area is better supplied with fibers on the right side than on the left; these enter Layer II+III toward the

middle of the area. On the left side fibers are found only in Layer VI and in the medial part of Layer V.

THE ACOUSTIC PATHWAY: None of the parts of the acoustic pathway are completely degenerated in these deaf mice, except the roots of the cochlear nerve on both sides in Mouse #85836. It is doubtful whether any of the fibers of this nerve are structurally present. The fibers in other portions of the auditory pathway are diminished in number.

The cochlear nerve is much reduced in size even in Mouse #85842. It appears to be about one-third the size of the nerve in the normal mouse. Upon entering the medulla oblongata each fiber bifurcates into two branches: the descending branch runs in a dorsal direction through or medial to the ventral cochlear nucleus to end in the dorsal extension of this nucleus or in the acoustic tubercle; the ascending branch terminates in the ventral cochlear nucleus. This bifurcation is well defined in sections cut at an angle. Within the primary acoustic nuclei the regions containing most fibers are those close to the entrance of the cochlear nerve. The acoustic tubercles are almost completely degenerated in Mouse #85836, but only the caudal fourth of these nuclei in Mouse #85842 entirely lacked fibers. Nucleus proprius of the latter mouse brain is atypical throughout its extent. The ventral cochlear nucleus is largest and is best supplied with fibers at the level of, and just anterior to, the entrance of the cochlear nerve in Mouse #85842; it is in this same area that the nucleus is of large, triangular shape in Mouse #85836.

A few fascicles swing dorsalward from the acoustic tubercles of Mouse brain #85842; they turn ventromedialward to cross the midline in the dorsal acoustic decussation. There are also a few fibers of Held which arise in the dorsal extension of the ventral cochlear nucleus

in this material, run dorsalward over the restiform body, then dip ventralward. It is impossible to determine what percentage of these fibers remain on the same side; these secondary acoustic neurons from the acoustic tubercle and the dorsal extension of the ventral cochlear nucleus enter the lateral lemniscus, situated lateral to the superior olive, where they are joined by other fibers from the contralateral ventral cochlear nucleus. The fascicles from the ventral cochlear nucleus are not so numerous as in the normal brain. They leave the nucleus ventromedially and may send collaterals into the nuclear complex of the superior olive and into the trapezoid gray. The cells of these nuclei are more closely spaced than in the normal material. In spite of the fact that fewer fibers of secondary neurons leave the ventral cochlear nuclei in both abnormal brains, there is a well developed trapezoid body medial to the trapezoid gray, and a heavy ventral acoustic decussation.

There are many spaces between the fibers of the lateral lemniscus in Mouse #85842, but the fiber pathway is still present. The lateral lemniscus begins to swing dorsalward at upper pons levels and some of its fibers enter the inferior colliculus. Collaterals are probably also added to the lateral lemniscus from the inferior and superior nuclei of the lateral lemniscus, as these nuclei are well represented in the totally deaf mice and there is a thick bundle of fibers interconnecting them. Some of the more medial fibers of the lateral lemniscus appear to pass directly to the medial geniculate nucleus after joining fascicles from the nucleus of the inferior colliculus in through its peduncle. The fibers are most numerous in the medial part of pars principalis in the caudal two-thirds of its extent, but

are evenly distributed rostrally. Some fibers leave the medial geniculate nucleus as auditory radiations and, in their course to the cerebral cortex, join the dorsal thalamic radiation. The auditory fibers are traced into Layer IV rostrally in the auditory koniocortex, and are most numerous inferiorly in this area on the left and superiorly on the right side of Mouse brain #85842. The right secondary auditory area of this same brain is better preserved than the left; toward the middle of the right area delicate fibers enter Layer II+III.

In general, degeneration is more extensive in the primary acoustic nuclei than at higher levels, and is more complete on the left side in both specimens. The ventral cochlear nuclei, however, are about equally atrophied on both sides.

PARTIALLY DEAF MICE

Three of the partially deaf mice described below were tested with the electrical equipment for range of hearing. With vibrissae clipped to the length of the surrounding fur, Mouse #96835 (male) heard frequencies ranging between 300 and 65,000 cycles/sec.; under similar conditions Mouse #96362 (female) heard frequencies between 4,000 and 60,000 cycles/sec., and Mouse #96836 (female) recognized tones of frequencies between 500 and 55,000 cycles/sec. All of the animals except Mouse #96835 gave ear twitch responses to a slightly wider range of frequencies with the vibrissae intact; this may be due to changes in the position of the animal in the box at the time of the second testing, or may indicate that the vibrissae reinforce sound vibrations. All of these mice waltzed when exposed to the stimulus of jingling keys, and in two cases a similar response was evoked by

certain pure tones of low frequencies. Effective pure tones in the case of Mouse #96836 were 8,000, 10,000, and 20,000 cycles/sec. Time of exposure in each case was 240 sec., 140 sec., and 60 sec., respectively. Exposure to a frequency of 18,000 cycles/sec. for 40 sec. resulted in convulsion, and dashing and stupor followed the waltzing at 10,000 cycles/sec. after exposure to the stimulus for 175 sec. In the case of Mouse #96835 effective frequencies were 6,000 and 8,000 cycles/sec. Both waltzing and dashing ensued after 65 and 55 sec., respectively. Mouse #96362 was tested with a frequency of 16,000 cycles/sec. for a period of 180 sec., but showed no abnormal behavior.

After these tests were made, the click was eliminated from the apparatus and the equipment underwent further improvement, so that the intensity of the sound delivered through the system could be measured. Under these conditions Dice and Barto ('52) found that epileptic waltzers of the artemisiae type "showed ear movements in response to sound frequencies between 500 and 95,000 cycles/sec. when tested at ages between 25 and 70 days".

A fourth mouse, #96050 (female), was not tested with the electrical equipment for range of hearing, but was considered partially deaf because she did not twitch her ears in response to a squeak nor did she waltz when stimulated with the jingling keys. This animal had been considered a high grade waltzer previously. The sounds of jingling keys and of metal striking glass did cause a positive ear twitch, however.

Two brains, Mouse #96836 and Mouse #96050, were prepared and stained for cells with toluidine blue; the brain of Mouse #96835 and that of Mouse #96362 were made ready for study according to Weil's method for fibers.

DORSAL COCHLEAR NUCLEUS: The acoustic tubercles of the abnormal brains extend from the level of the lateral recesses of the fourth ventricle caudally to the level of the roots of the facial nerve rostrally. At the latter level the acoustic tubercles diminish in size and are continuous with a narrow band of cells over the ventral cochlear nucleus, as is the case in the normal brains. There is, however, a partial loss of fibers or of internal organization in the dorsal cochlear nuclei of the abnormal mouse brains.

In Mouse #96836, the most caudal cells of the acoustic tubercles are ovoid or spindle-shaped. Microglia are numerous in the region of nucleus proprius and are scattered elsewhere in the caudal third of the dorsal cochlear nucleus. Large, ovoid, and very pale-staining cells are gathered without organization into the medial half of the tubercle at levels which are laminated in the normal material. Under high power of the microscope, some of these cells have a fusiform appearance, large nuclei, and very little cytoplasm. The central ends of the processes of these cells do not stain well, and for this same reason many of the other cells appear ovoid. On the right side, neuroglia increase in number ventrally in the middle third of the nucleus and spread dorsalward in the anterior third. On the left side, the ventral portion of the acoustic tubercle is atrophied at all levels and is filled with glia. There are numerous neuroglia ventrally and far dorsally in the anterior third of this left nucleus.

VENTRAL COCHLEAR NUCLEUS: The ventral cochlear nucleus extends from the level of the facial motor nucleus caudally to the level of the motor nucleus of the trigeminal rostrally in these abnormal brains,

as it does in the normal material. There are posterior and anterior subdivisions of the ventral cochlear nucleus in the brains of the four partially deaf epileptic waltzers.

The cells of the posterior subdivision of the ventral cochlear nucleus of Mouse brain #96836 are extremely closely arranged, in contrast to the scattered cells of the normal nucleus. Most caudally there are a number of large cells in the middle part of the nucleus, but they are completely surrounded by neuroglia. Very few of these large cells are of typical polygonal shape; fusiform and ovoid cells are numerous. The so-called "tail" is completely filled with glia. There are a few large cells in this dorsal extension within 100μ, but they are more nearly flat and smaller than typical cells and are closely arranged. More rostrally in the posterior subdivision of the nucleus, the glia become less numerous and disappear. The ventral cochlear nucleus broadens lateromedially and becomes rounded caudal to and at the level of the cochlear nerve; it is not, however, the size of a normal ventral cochlear nucleus at a similar level. The cells are separated into several laminae by the dichotomizing cochlear nerve fibers at these levels. In the caudal part of the anterior subdivision of the ventral cochlear nucleus, at the level of the vestibular nerve, the cells are closer to one another than in normal preparations. The cells are ovoid or spindle-shaped dorsally, and round, fusiform, or triangular ventrally. The triangular cells are not numerous. The ventral cochlear nucleus is moderately flattened throughout its anterior two-thirds. The right and left sides are similar in respect to the locations of the degeneration, although the left side is less extensively affected than the right. The cells are more scattered ventrally in the posterior subdivision

and in all parts of the anterior portion of the left ventral cochlear nucleus.

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: In Mouse #96836 the superior olive is slightly atrophied and the folded arrangement of this gray mass is not so apparent as it is in the normal material. Many of the cells are round or ovoid in shape, possess very pale nuclei and pale-staining cytoplasm; some are fusiform in shape and have dark-staining cytoplasm. All of the cells are more closely arranged than those of the normal superior olive. The accessory superior olive is rounded in outline in this specimen. The closely grouped, pale cells of this nucleus are smaller than normal and are mostly of triangular or spindle-shape.

The medial nucleus of the trapezoid body is quite typical throughout its extent, although the cells are slightly closer to one another than in this nucleus in the normal brain. The parolivary nuclei are small, typical masses of gray. All of the nuclei of this complex have a similar appearance on both sides of the brain.

INFERIOR COLLICULUS: The nucleus of the inferior colliculus is distinct in all of the specimens. The cells of this nucleus are closely grouped, particularly in Mouse brain #96836, and are frequently pale-staining due to a loss of Nissl's granules. Neuroglia are numerous in both the nucleus and in the capsular portion, and the cells of the capsule are very closely arranged dorsally in this mouse brain.

MEDIAL GENICULATE NUCLEUS: The medial geniculate nuclei of most of the abnormal specimens exhibit more degeneration caudally than rostrally.

Glia are more numerous and pars principalis is usually atrophied in a lateromedial direction.

The main mass of pars principalis of the right medial geniculate nucleus is flattened lateromedially in Mouse #96836. The pale, ovoid cells have very little cytoplasm and are close to one another; neuroglia have increased numerically, giving a crowded, granular appearance to the nucleus. One hundredμ from the caudal end of pars principalis, the ventral half of the main mass is rounded and some typical polygonal cells are located in this portion, especially ventromedially. The dorsal part of pars principalis is densely cellular except for the dorsal border where, for a short distance, there are dark-staining, spindle-shaped cells typical of the dorsal group. Rostral to this level supporting elements increase dorsally and the spindle-shaped cells disappear. Toward the end of the caudal third of pars principalis, the cells are closely arranged and there are many neuroglia in the dorsal one-half and along the lateral border of the main mass of cells; the "c" group is not differentiated in this third. Pars principalis is typically bean-shaped for 75μ near the anterior end of its middle third, but at other levels in this portion only the ventral half of the nucleus is plump and consists of scattered cells. These cells are pale-staining and round or ovoid. The "c" group is differentiated only caudally in the middle third and there are many neuroglia between the flattened, spindle-shaped cells of this nucleus. Pars principalis is rather atypical in its rostral third; the cells are pale and crowded appearing and numerous glia are found among them. Far rostrally the nucleus is difficult to trace as it is filled with glia and cannot be distinguished from the nuclei which lie in relation to it.

The magnocellular portion of the medial geniculate nucleus is not a definite nuclear mass on the right side except for a few sections in the middle third of its extent. The cells are closely grouped and consist largely of glial forms; few large, multipolar cells are present.

Pars principalis is more atrophied lateromedially caudally on the left side than on the right in Mouse #96836. The most dorsal cells of the dorsal group of pars principalis are distinct through most of the caudal third of the nucleus. Anteriorly in the caudal third and posteriorly in the middle third, the dorsal half of pars principalis, including the dorsal group, exhibits closely arranged cells and numerous neuroglia. The nucleus is flattened lateromedially in the posterior part of its middle third. Rostral to this level the nucleus broadens somewhat; dorsally the cells are still close to one another. The cells of pars principalis are pale-staining and glia are numerous rostrally, so that it is very difficult to trace the nucleus through its rostral third to its oral tip.

Glia are also numerous in pars magnocellularis of the left medial geniculate nucleus. The large cells of this portion of the nucleus are evident in the middle third of its extent; these cells are ghost-like, due to a loss of Nissl substance, and are almost masked by neuroglia.

AUDITORY AREAS: The right auditory koniocortex is less affected than the left in Mouse #96836. There are a few scattered pyramidal cells denoting a Layer II+III through most of the caudal third, but the other laminae are not differentiated except at the anterior end of this third. There are no knobs to distinguish Layer IV, Layer V is not divided

into bands (or strata), and Layer VI is very compact. The cells are rather large, ovoid, pale, and possess little cytoplasm; because of their similarity the six-layered plan of organization of the koniocortex is not observed. This delamination and the presence of the enlarged cells are characteristic of the degeneration of the auditory area as observed in the abnormal brains stained for cells. Near the transition from caudal to middle thirds of the right primary auditory region, however, the small pyramidal cells of Layer II+III become numerous dorsally and all of the other laminae assume a typical appearance. Throughout the middle third of the auditory area, approximately the dorsal fourth is laminated; there are small, typical, dark-staining pyramidal cells in Layer II+III, the cells of the fourth lamina are arranged in clusters, and Layers V and VI are distinct although they appear somewhat compressed and confluent. The ventral portion is laminated for only 100μ posteriorly in the middle third of the area. There is some typical koniocortex in the rostral third of the primary auditory area; for about 50μ posteriorly there is delamination and a lack of differentiation of cells, and far anteriorly, as well as along most of the ventral border, only Layers V and VI are distinct. Throughout the rest of this third the dorsal portion is best represented; there are typical pyramidal cells in Layer II+III, the cells of Layer IV are grouped in clusters, three bands are present in the fifth lamina, and Layer VI is broad.

The caudal half of the right secondary auditory area is typical except along its dorsal border, at the junction of the secondary with the primary auditory area. At this border, the cells are pale-staining and ovoid. The anterior and posterior ends of the rostral half of the

area are laminated ventrally, but the rest of this portion is delaminated, consisting of ovoid cells similar to those described previously.

Most of the caudal third of the primary auditory area is degenerated on the left side. The ventral half of auditory koniocortex, excluding its ventral border, is laminated for 100μ at the anterior end of this third. Immediately rostral to the midpoint of the area, in the dorsal half of the field, there are some typical pyramidal cells in Layer II+III, Layer V is broad and divided into three strata, the polymorphous cells of the sixth lamina are scattered, and the fourth layer is dense but lacks true knobs. This region is 150μ long. From this level to the rostral end of the area, where Layers V and VI are typical and distinct, the pale-staining, ovoid cells occupy much of the cortex, involving even the sixth lamina.

Throughout most of the secondary auditory area on the left side, there are ovoid cells which, in their similarity to each other, make the differentiation of the cortical layers difficult. The cells and laminae are typical ventrally anteriorly in the middle third of the area and at its rostral end.

MOUSE #96050

DORSAL COCHLEAR NUCLEUS: The acoustic tubercles in the brain of Mouse #96050 differ from those in Mouse #96836 in exhibiting more distinct lamination of the nucleus and more typical cells. The four layers characteristic of the normal dorsal cochlear nucleus are present at the proper levels in this abnormal brain; the cells are enlarged, however, and pale-staining. Neuroglia are more numerous than normal in the caudal two-thirds of the acoustic tubercle; they are found ventrally in Layer II, III, and IV, and in nucleus proprius. In the

rostral third of the nucleus, neuroglia are numerous dorsally and ventrally but are few in number in the middle portion. This is true of both the right and the left acoustic tubercles.

VENTRAL COCHLEAR NUCLEUS: The cells are more closely grouped and there are more glia in the ventral cochlear nuclei of Mouse #96050 than in these nuclei in Mouse #96836. The left side is less affected than the right in both specimens, however. Mouse #96050 exhibits many glia laterally and medially in the posterior subdivision of the ventral cochlear nucleus, and there is a broad strip of typical cells through the middle. The cells are most crowded superficially in the caudal part of the anterior subdivision of the nucleus; they are more closely arranged than the cells of the ventral cochlear nucleus of Mouse #96836 at similar levels. Rostrally, however, the left ventral cochlear nucleus has a broader and more typical ventral tip in Mouse #96050 than in Mouse #96836. This tip is severely affected on the right.

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: Atrophy of the various divisions of the nuclear complex is marked in Mouse #96050. The cells of the superior olive are very closely arranged and both the cytoplasm and the nucleus of the cells stain lightly in most cases. Some of the cells are dark-staining and rounded or spindle-shaped. There are many neuroglia in the superior olive, and this mass of gray is not folded as in the normal. The accessory superior olive is distinguished by its large cells rather than by its shape in this brain, for it is not separated from the superior olive. The cellular outline of these large cells is rounded; the central parts of the cell processes do not stain well. Spindle-shaped cells are infrequent. The parolivary nuclei

are small, ill-defined gray masses; some of the cells in the internal nucleus are very pale.

The medial nucleus of the trapezoid body is composed of pale, round, closely grouped cells. Except for a few sections in the plane of the middle third of the superior olivary nucleus, the nuclear complex is more affected on the left side than on the right. In the exception noted the superior olive is folded; elsewhere its surfaces are smooth and do not exhibit lamination. The cells are especially crowded on the left side and the large cells, because of the absence of Nissl's granules, are ghost-like. Neuroglia are more numerous on the left side than on the right.

INFERIOR COLLICULUS: The inferior colliculus is slightly less affected in both its nuclear and in its capsular portion in this mouse than in Mouse #96836. The nucleus of the inferior colliculus is a well defined mass; neuroglia are scattered here and in the capsular portion, but are more numerous than in the normal mouse brain.

MEDIAL GENICULATE NUCLEUS: There are fewer glia caudally in the right medial geniculate nucleus of Mouse #96050 than in the comparable nucleus of Mouse brain #96836. The main mass of pars principalis is flattened to a slight degree in the caudal third of its extent; in the dorsal portion and along the lateral border the pale, ovoid cells are very closely arranged, as is the case in Mouse #96836. The dorsal group of dark-staining cells is distinct far dorsally, but the cells are not scattered. In the middle third of the extent of the nucleus, a wide strip of closely grouped cells extends along the dorsal and lateral borders of pars principalis, but the cells are scattered

ventrally and ventromedially. Pars principalis is round and its cells are well-spaced in its rostral third, although the cells are pale-staining. There are numerous glia at all levels of the "c" group of pars principalis. The cells of this group are ovoid rather than flat and fusiform, as in the normal material.

Some large, multiangular cells are found in the right pars magnocellularis of the medial geniculate nucleus in the caudal half of its extent. Neuroglia increase rostrally, however, and the large cells of the nucleus are closely grouped.

Pars principalis of the medial geniculate nucleus is more affected posteriorly on the left side. The main mass of the left pars principalis exhibits numerous glia and a close arrangement of cells in the caudal third of its extent. At the anterior end of this third, the nucleus is atrophied and the dorsal half is most dense and crowded appearing; within the next 40μ only the dorsal fourth is greatly affected. Degeneration extends along the ventrolateral border caudally in the middle third of the nucleus; anteriorly in this third and in the rostral portion the nucleus is typical in shape, the cells are well-spaced, and neuroglia are not numerous. The "c" group of cells is differentiated through only a portion of the middle third of the medial geniculate nucleus, and the dorsal group is never distinct on this side.

The left pars magnocellularis is composed of well-spaced, large, polygonal cells in its caudal two-thirds; rostrally, the cells are very close to one another. Neuroglia are not so numerous on the left side as they are on the right.

AUDITORY CORTEX: The ventral border of the right primary auditory cortex is degenerated throughout its extent, and most caudally its

fifth lamina is not stratified. The nucleus and cytoplasm of the pyramidal cells of this layer are pale-staining and the cellular processes are most indistinct. Some of the small pyramidal cells of Layer II+III are also lightly stained and rounded, this lamina appearing to be continuous with the fourth layer. This degeneration spreads in the ventral portion, involving the ventral half of the primary auditory area, and then regresses in such a way that at the anterior end of the caudal third of the area only its ventral border is affected. The rest of the auditory cortex exhibits normal appearing cells and well defined layers in its caudal third. Posteriorly in the middle third of the area, Layers II+III and IV are not well differentiated ventrally, appearing somewhat confluent; Layers V and VI are typical. The dorsal half of the area is well developed here and, from level to level, clusters appear in the fourth lamina ventrally except along its ventral border. In the far ventral portion, Layers II+III and IV are confluent and there are no strata in Layer V. Midway in the primary auditory area, there is complete degeneration of all but the far dorsal part of the area. Slightly rostralward, the bands in Layer V are evident again and the pyramidal cells become more numerous in Layer II+III. The dorsal half of the area is better developed than the ventral portion. At the anterior end of the middle third of auditory koniocortex, degeneration begins ventrally and spreads dorsalward to envelop the entire region, extending into posterior sections of its rostral third. Shortly this degeneration becomes confined to the ventral border where Layers II through V are confluent. The degeneration begins to spread dorsalward again as the anterior end of the area is approached, and another separate region of delamination appears at the dorsal border.

Ultimately, at the rostral tip of the area, there is a narrow zone near the dorsal border which is typical; the rest of the koniocortex exhibits the ovoid cells and the confluence of laminae which characterizes the degenerated portions of the auditory area in these abnormal mice.

The right secondary auditory cortex is not laminated nor are there normal appearing cells except in 5 isolated places: two small zones in the rostral third of the area, two in the middle third, and one far caudally. These unaffected portions are generally located toward the midportion of the area and are only 25-50% in extent.

The left primary auditory area is more affected caudally than the right; in the posterior half of the caudal third of the area the layers are indistinct and all of the cells are rounded and pale-staining. The anterior half of this third is laminated, although far anteriorly the layers are not differentiated along the dorsal and ventral borders. This degeneration extends rostralward into the middle third of the auditory region, meanwhile spreading medialward from both borders and sparing only the middle zone. Ventrally, Layers II+III, IV, and V are confluent, whereas dorsally only the first two of these layers are involved; the fifth lamina is stratified dorsally. There is a gradual improvement of Layer V, and then of Layers IV and II+III posteriorly in the middle third of the area, so that the entire region assumes a typical appearance. The ventral portion of the auditory koniocortex is degenerated near its midpoint, but more rostralward the bands in Layer V, the knob-like arrangement of the fourth lamina, and typical pyramidal cells in Layer II+III become prominent once again. The extreme dorsal border, however, exhibits a confluence of laminae in the anterior half of the middle third of the area. The rostral third

of the primary auditory cortex, except for the dorsal border which remains confluent, is well developed and typical.

The secondary auditory area is laminated far caudally and along most of the dorsal border on the left side. Only in the caudal third of its extent is the entire area differentiated; throughout the rest of the region the ventral portion of the cortex is composed of large and rounded cells and Layers II+III, IV, and V are confluent.

MOUSE #96835

DORSAL COCHLEAR NUCLEUS: There are no fibers in the caudal third of the acoustic tubercle on either side of the brain in this specimen. On the right side the ventral portion of the nucleus is atrophied and lacks fibers completely. Fibers are found in Layer IV in the dorsal two thirds of the acoustic tubercle, but not ventrally, in the posterior part of the middle third of its extent; within 50μ they are observed in Layer III, also. The cells of lamina cellularis stand out clearly, for ramifying fibers are absent; nucleus proprius is extremely flat.(See pl. 4). At the anterior end of the nucleus, fascicles occupy only its middle portion as both the dorsal and the ventral regions are degenerated. The fibers are diminished at all levels of the left acoustic tubercle. They are located only in the dorsal half of the nucleus in its middle and rostral thirds, and ramify within Layers III and IV. The ventral portion is not atrophied, although its fascicles are degenerated.

VENTRAL COCHLEAR NUCLEUS: The posterior subdivision of the ventral cochlear nucleus in Mouse #96835 is completely degenerated laterally and medially in the more ventral part, but the dorsal extension (see pl. 4) and the middle portion ventrally are well supplied with fibers. Near the

rostral end of this subdivision, the nucleus is divided into several laminae by the bifurcating cochlear nerve fibers and it broadens to assume the shape of a hillock. The ventral cochlear nucleus contains fewer than the normal number of fibers as the anterior subdivision begins. More rostrally the nucleus flattens; some fibers are lacking dorsally, laterally, and medially, but are numerous in a narrow strip through the middle of the nucleus. Gradually the fascicles become more dense lateroventrally but diminish elsewhere in the nucleus. The right and the left ventral cochlear nuclei are about equally affected in the posterior subdivision, but the anterior portion is more typical on the left side than on the right.

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: The accessory superior olive is not distinct from the gray of the superior olive in Mouse #96835; the common mass of gray is atrophied. Folding of the nucleus is observed laterally toward the anterior end of the left superior olive only. The fiber supply in the entire nuclear complex is better on the left side of the brain, and the gray of the trapezoid body and of the parolivary nuclei are more conspicuous on the right than on the left. None of these masses lack fibers completely.

INFERIOR COLLICULUS: The central nucleus and the peripheral capsular portion of the inferior colliculus are rather well developed. Both parts exhibit a general loss of fibers, however; this loss is less pronounced in this mouse, #96835, than in Mouse #96362. See pl. 7.

MEDIAL GENICULATE NUCLEUS: Pars principalis of the right medial geniculate nucleus in this brain is atrophied caudally and has a triangular shape. The dorsal two-thirds of the main mass is severely

degenerated and there are no fibers in this part of the nucleus, although there are some in the more ventral and ventromedial portions. Near the region of transition from caudal to middle thirds of the nucleus (see pl. 8), degeneration involves only the dorsal third and the ventrolateral border of pars principalis. The loss of fibers is less pronounced, except along the dorsal and lateral borders, at the posterior end of the middle third of the nucleus. There are few fibers throughout the rostral third, especially dorsally. The "c" group of cells has a fiber supply at all levels except for the middle third of its extent where its far lateral portion is degenerated.

Pars magnocellularis of the right medial geniculate nucleus is well represented toward the anterior end of the caudal third, and in the posterior part of the middle third, of its extent. Rostrally and caudally there is a general but incomplete loss of fibers. (Consult pl. 8).

The left medial geniculate nucleus differs from the right in the severity of its degeneration in this mouse; the left side is slightly less affected far caudally but more degenerated rostrally than the right side. The dorsal group of pars principalis is without fibers through most of the caudal third of the nucleus; at other levels there are fewer fibers in the dorsal and ventrolateral portions on the left side than on the right. The lateral and dorsal regions are severely degenerated far rostrally. The "c" group is conspicuous and lacks fibers at all levels.

Pars magnocellularis is slightly better preserved caudally on the left than on the right, but rostrally there is little difference between the two sides.

AUDITORY CORTEX: The right primary auditory area in Mouse #96835 has

a poor fiber supply throughout its extent, although there is never a complete absence of stratification of the cortex and in places there is a knob-like arrangement of the fourth lamina. There are few fibers at the caudal end of the area, even in Layer VI. This degeneration extends through the region for only 50μ and then there appears a clustering within the fourth layer, although the fibers are very delicate. The fibers become numerous everywhere except far dorsally, at the border of the area, and far ventrally. In the more affected portions the fibers reach Layer VI and extend part way into the fifth lamina. Shortly, another degenerated zone appears in the midportion of the area. In the more typical parts of the auditory koniocortex the fibers form knobs in the fourth layer and extend into Layer II+III. At the anterior end of the caudal third of the primary auditory area, the ventral portion is still affected, the midportion is typical, and a narrow strip dorsally exhibits a loss of fibers and a lack of clusters in the fourth lamina. The dorsal degeneration disappears and there is a general increase of fibers posteriorly in the middle third of the extent of the auditory area. This improvement persists for 175μ; the middle part of the area then suffers a loss of fibers and an absence of knobs in the fourth layer. Just in front of the midpoint of the area there is a knob-like arrangement in the dorsal part of Layer IV; ventrally the fibers are delicate and few in number in Layers V and VI as well as in Layers II+III and IV. There are clusters in all parts of the fourth lamina in the rostral third of auditory koniocortex, but the fibers are usually thicker and more numerous dorsally than ventrally. The ventral portion exhibits a rich fiber supply in two places--in one small area located near the midpoint, and in another slightly posterior to it.

The fibers of the right secondary auditory area are delicate at all levels; they are most numerous far rostrally and in the dorsal part of the middle and caudal thirds of the region. The ventral portion is not laminated throughout the middle and most of the caudal thirds of the area, but the layers are distinct ventrally near the caudal tip of the region.

The left auditory koniocortex is more affected caudally than rostrally, also. In certain places, which will be described shortly, the fiber supply to the left primary auditory area is rich and unparalledled by any level on the right. The fibers are extremely delicate far caudally and the cells of the 6 laminae are evident. There are no clusters in the fourth layer, but the cellular arrangement of the fifth and sixth laminae is typical. The fibers become numerous 2254 rostral to the caudal tip of the area and have a knob-like arrangement in the fourth lamina ventrally, but then they become sparse throughout for some distance. Gradually the knobs reappear in Layer IV ventrally, and there is a similar arrangement of the fourth lamina dorsally although the fibers are not numerous. At the transition from the caudal to the middle third of the auditory area, fibers increase dorsally and then decrease numerically in dorsal and midportions of the region; the clusters in Layer IV are retained ventrally. Still more rostrally, delicate fibers enter the fourth lamina, forming clusters in the dorsal three-fourths of the area. Here, the fiber supply increases until it becomes relatively rich near the midpoint of the auditory koniocortex. All the area then appears normal except for its uppermost border. This border improves somewhat rostralward and then gradually regresses. As the rostral third of the area is approached the ventral

half of the field exhibits an abundant fiber supply. Dorsally the fibers are delicate and few in number, but they still form clusters in Layer IV. There is a general increase in fibers anteriorly in the area, and far rostrally the entire auditory koniocortex is richly supplied with fibers.

Other than in the three locations to be described immediately, the secondary auditory area on the left side is typical. The affected portions are: 1, in the midportion of the field far caudally; 2, at the junction of the caudal and middle thirds where the dorsal part is atypical; and 3, in the anterior part of the middle third where the fibers are extremely delicate dorsally for quite a distance.

MOUSE #96362

DORSAL COCHLEAR NUCLEUS: The caudal third of the acoustic tubercle is degenerated on both sides of this mouse brain. There are fibers in the dorsal half of the nucleus, including Layer II, III, and IV, in the middle third of its extent. The fibers increase slightly in number, but are located only in this dorsal portion at the rostral end of the acoustic tubercle. Both sides exhibit this distribution of fibers, although the left side is more affected. See pl. 4.

VENTRAL COCHLEAR NUCLEUS: Mouse #96362 differs slightly from Mouse #96835 in respect to the location and extent of the degeneration of the ventral cochlear nuclei. There are no fibers in the lateral or medial parts of the posterior subdivision of the right nucleus (see pl. 4); they are present in a strip through the middle of the nucleus. This strip of fibers is broader in Mouse #96362 than in Mouse #96835, although it contains fewer fibers; the dorsal extension is more affected

in the former animal. The fibers do not separate the ventral cochlear nucleus into several laminae in Mouse brain #96362, and degeneration is most pronounced laterally and medially at the rostral end of the posterior subdivision. The dorsoventral extent of the nucleus is decreased as compared with this measurement in normal material and there are scattered fiber losses ventrally at the level of the cochlear nerve. Caudally in the anterior subdivision of the ventral cochlear nucleus, the lateral and medial borders are affected although there is a good fiber supply to the middle and dorsal portions. No part of the nucleus is degenerated for 50μ at the level of the vestibular roots. Rostral to these sections the fibers are less numerous laterally and ventrally than elsewhere in the nucleus. Far orally the nuclear gray is atrophied ventrally and is more seriously affected than on the left.

The left ventral cochlear nucleus is more degenerated than the right caudally and in the middle part of its extent. Caudally, in the posterior subdivision of the nucleus, the dorsal extension exhibits fiber losses and the ventral portion is atrophied. More rostrally there are few fibers in the whole ventral portion and they are completely absent laterally. The nucleus is never rounded on this side; caudal to, and at the level of, the cochlear nerve it is triangular in shape. The fiber losses are evenly distributed as the ventral cochlear nucleus narrows down rostrally in its anterior subdivision.

NUCLEAR COMPLEX OF THE SUPERIOR OLIVE: The superior olive is less atrophied in Mouse #96362 than in Mouse #96835, and is distinct from the accessory superior olive. The nuclei are not typical in shape, however, being more rounded in outline, and the superior olive is not laminated. The medial nucleus of the trapezoid body and the parolivary

nuclei are well supplied with fibers and are alike on both sides.

INFERIOR COLLICULUS: The gray of the inferior colliculus is rather well developed in this mouse brain as it is in Mouse #96835. Fewer fibers are present in the capsular portion and in the central nucleus than are found in similar locations in Mouse #96835. The fiber losses are generally evenly distributed in these portions of the inferior colliculus in both brains.

MEDIAL GENICULATE NUCLEUS: Mouse #96362 exhibits less degeneration in the right medial geniculate nucleus than does Mouse #96835, but its left nucleus is poorly supplied with fibers. On the right side (see pl. 8), the dorsal and ventrolateral borders of pars principalis are chiefly affected. In the caudal third of the nucleus, fibers are diminished dorsally and in a strip extending ventrolateralward. More anteriorly, in the middle third, the ventral half of the main mass of pars principalis and its dorsomedial portion have a good fiber supply but the dorsolateral part of the nucleus is degenerated. The whole nucleus is more affected near the middle of its extent. The dorsolateral and lateral regions, as well as a narrow border ventrally, show a loss of fibers in the rostral third of pars principalis. Part "c" of the nucleus is best in the middle third of its extent.

Pars magnocellularis is poorly supplied with fibers far caudally on the right side. In the posterior part of the middle third of the nucleus, the fibers are still delicate and few in number, but anteriorly they become numerous so that the rostral third is less affected.

The medial geniculate nucleus of the left side is severely degenerated. Fibers are few in number and very delicate in the caudal

third of pars principalis; the ventral half of the nucleus and its ventrolateral border are chiefly affected. The whole gray mass is atrophied near the transition from caudal to middle thirds of the nucleus, but more rostralward only the dorsal half and the lateral border of pars principalis exhibit a loss of fibers. The ventral portion of the nucleus is most typical far orally. The "c" group of pars principalis is not distinguishable on this side.

The left pars magnocellularis has an abundant fiber supply in two places: posteriorly in the anterior half of its extent, and at its rostral tip. The rest of the nucleus appears as a gray mass through which delicate fibrils are traced. It is much more degenerated than the magnocellular portion of the right side.

AUDITORY CORTEX: The right primary auditory area of Mouse #96362 is more typical than the left. In the caudal third of the area (pl. 9) on the right, fibers are extremely few in number along the dorsal border. They extend through the fifth lamina ventrally but do not form knobs in Layer IV. The rest of the region is well supplied with fibers throughout this caudal part, the knob-like arrangement of the fourth layer being most clear near the midportion. The dorsal border exhibits a severe loss of fibers and delamination in the middle third of the auditory koniocortex. This degeneration spreads ventralward to involve the entire dorsal half of the area and the fibers largely disappear from this portion for some distance. Ventrally, the fibers are traced into Layer V. Anterior to the midpoint of the area, the dorsal border and a strip in the midportion of the field lack fibers in all but the sixth lamina. Then the ventral border shows a gradual loss of fibers.

At the transition from the middle to the rostral third of the auditory koniocortex, the fibers gradually increase ventrally in the fourth lamina, forming distinct clusters there. The knob-like arrangement of the fourth lamina is less apparent dorsally, the upper two-thirds of the field being most affected. Fibers reach only the fifth layer along the ventral border and the sixth lamina far dorsalward in the anterior part of the area. They become more numerous throughout the rest of auditory cortex at the rostral tip.

The entire caudal half of the right secondary auditory cortex (see pl. 9) is devoid of lamination and the fibers, which are pale and delicate, reach only the deepest part of the cortex. The anterior half of the area is laminated. Here, the fibers are most numerous in the fifth and sixth laminae, although they extend up through Layer II+III.

There are no fibers at the caudal tip of the left primary auditory cortex in Mouse #96362 and it is difficult to distinguish this area from those surrounding it. On the basis of the total length of the primary auditory area on the opposite side, approximately the caudal sixth lacks distinct lamination on the left. Fibers gradually become more numerous rostral to this portion and reach Layer II+III, forming knob-like clusters in the fourth lamina. The fibers then become delicate far dorsally and the knobs gradually disappear from Layer IV. Ventrally there are fibers in the fifth lamina, but in the middle strip they reach the fourth layer without knob formation. Toward the anterior end of the caudal third of the area, the fibers become extremely delicate, extending into the fifth lamina in the middle portion and into Layer VI ventrally and dorsally. A narrow zone dorsally and the entire ventral half of the area are severely degenerated throughout the middle third

of auditory koniocortex. Posteriorly in this third, the fibers extend into Layer V and rarely reach the fourth lamina; anteriorly, they are found in Layer II+III and form clusters in Layer IV. The fibers disappear from these laminae for a few sections but reach them again in the rostral third of the primary auditory region. Here, the dorsal border is degenerated for a short distance, whereupon there are fibers in Layer II+III and knobs in Layer IV. This border shows no further delamination rostrally. In the rest of the dorsal portion of the area, fibers are found in both Layer II+III and Layer IV. The ventral part is degenerated except far rostrally, where fibers are numerous in the sixth and lower part of the fifth laminae.

The layers are confluent in most of the left secondary auditory cortex, but delicate fibrils are present dorsally throughout the area except for a short distance in its middle third, and are also found ventrally in the rostral third. The fibers, where they are present, extend into the fourth lamina and occasionally into Layer II+III, but they are not so numerous as in normal material.

THE ACOUSTIC PATHWAY: All of the various portions of the acoustic pathway in these partially deaf mice exhibit some fiber loss; because of this, and also because of the slant of some of the sections, the course of the fibers is often more evident in these specimens than in normal material. The following description is based largely upon a study of two mice, #96362 and #96835.

The fibers which enter the primary acoustic nuclei over the cochlear nerve are less numerous in these abnormal brains than in normal preparations. Also, the brain of Mouse #96362 is more affected than that of Mouse #96835. The fibers dichotomize as they enter the medulla

ventromedial to the ventral cochlear nucleus. One branch extends caudalward to the acoustic tubercle and to the posterior part of the ventral cochlear nucleus; another branch proceeds rostralward to the anterior part of the latter nucleus. In Mouse #96835 these branches divide the nucleus into several laminae near the level of the cochlear nerve. Some of the fibers cross the ventral cochlear nucleus to reach the dorsal extension of this nucleus and the ventral part of the acoustic tubercle; others appear to run medial to the ventral cochlear nucleus toward the more dorsal part of the tubercle. In this material the axons of secondary neurons in the "tail" region of the ventral cochlear nucleus first course dorsalward over the restiform body. Then some of them dip sharply ventralward, pass through the descending root of the trigeminal nerve, and bend medialward. These fibers are apparently similar to those described by Winkler and Potter ('14) as the fibrae Held. In our material, however, the fibers could not be traced across the midline. The rest of the fibers continue in a dorsal direction to join the axons of secondary neurons of the acoustic tubercle, forming with them the dorsal acoustic striations. The combined fascicles cross to the opposite lateral lemniscus through the dorsal acoustic decussation. In these specimens, the fibers originating in the ventral part of the posterior subdivision and in the entire anterior portion of the ventral cochlear nucleus form a thick bundle which leaves the nucleus ventromedially. This bundle of fibers runs along the ventral surface of the medulla beneath the descending root of the trigeminal nerve. Medial to this root some of the fibers turn sharply dorsalward and then medialward, passing above or through the superior olive. These fibers form several fascicles as they leave the main bundle, but they cannot be traced across the midline of the brain. Perhaps some of them synapse in the superior olive. The rest of the fibers continue medialward, splitting

into many fascicles which pass through the region of the medial lemniscus. These fascicles appear to turn dorsalward and then lateralward, crossing the midline in the trapezoid decussation, to reach the contralateral nucleus of the trapezoid body or the region immediately dorsal to this gray. These fibers cannot be traced laterally in Mouse #96835, but in Mouse #96362 some of the fibers appear to run lateralward from the trapezoid nucleus to enter the lateral lemniscus.

The lateral lemniscus turns dorsalward in upper pons and lower midbrain levels, and lying against this fillet medially at these levels are the inferior and superior nuclei of the lateral lemniscus, where some collaterals from this lemniscus probably end. The internuclear bundle of fibers connecting such superior and inferior nuclei is relatively thick in these abnormal brains. Fibers enter the inferior colliculus from both the lateral lemniscus and from the superior nucleus of this fillet.

The nucleus of the inferior colliculus is well developed in these abnormal specimens. The fibers which leave it ventrolaterally in the peduncle of the inferior colliculus are joined by fibers of the lateral lemniscus which did not enter the collicular gray and, as a single bundle, proceed forward to the medial geniculate body. The fascicles just described and the auditory radiations are less numerous than in the normal brain. Such auditory radiations probably include corticogeniculate fibers. Through these radiations fibers reach the auditory areas where they extend into Layer II+III, or IV, or V, or only VI, depending upon the portion involved.

REVIEW OF THE LITERATURE

1. The anatomical organization of the acoustic pathway.

The acoustic pathway and the various auditory centers of normal specimens have been described for several forms by a number of workers. References to these descriptions in the literature were made in the main body of this report, but will be summarized briefly at this time. A study of the normal mouse brain showed that there is lamination within the dorsal cochlear nucleus (acoustic tubercle), and that it corresponds to the organization of this nucleus in the rabbit, guinea pig, and cat as described by Ramón y Cajal ('09-'11), and also agrees with the lamination as reported by Winkler and Potter ('14) for the cat, although the terminology used was different in each case. The ventral cochlear nucleus is subdivided into anterior and posterior subdivisions upon a structural basis as was mentioned by Ramon y Cajal; however, the lamination of the ventral cochlear nucleus which this same author describes for the cat is not evident in this nucleus in the material reported here.

The nuclear components of the medial geniculate nucleus which are found in the normal mouse brains correspond substantially with those described for the mouse by Ramón y Cajal ('09-'11), for the rat by Gurdjian ('27), and for the rabbit and cat by Winkler and Potter ('11, '14). The superior lobe or dorsal group of the medial geniculate nucleus appears to be a distinct one in this material, just as Ramon y Cajal described it several years ago as present in his mouse specimens; it does not seem to be continuous with the pars posterior of the lateral nucleus of the thalamus, as Le Gros Clark ('33) believed.

Rather, in this material, it comes to lie lateral to the caudal end of the dorsal portion of the lateral geniculate nucleus and then disappears as a distinct cell group. A pars magnocellularis and a pars principalis as recognized by Rioch ('29, '31) in the carnivores are also distinguished in the medial geniculate nucleus of the mouse. The main mass of pars principalis and the pars magnocellularis appear to be continuous rostrally with the ventral nucleus of the thalamus as Gurdjian ('27) found to be the case in the rat, and the "c" group with zona incerta as Le Gros Clark ('30) found in the insectivores. Vogt ('09), Malone ('10), and Walker ('38) have observed subdivisions of the medial geniculate nucleus in primates.

The cytoarchitecture of the auditory areas of the normal mouse brains used in this study is similar to that described for the rodent by Rose ('29) and Fortuyn ('14). Rose mentions the knob-like arrangement of the fourth cortical layer as a characteristic feature of the primary auditory area.

The division of the cochlear nerve fibers into two branches, descending and ascending ones, has been described several times in the literature. Kölliker ('89-'02) was the first to mention such a bifurcation, and Ramon y Cajal ('09-'11), Lorente de No ('33a), and others have confirmed it. This division into branches is observed in the present material, also. Held ('93), and other have described the "fibrae Held", and Ramon y Cajal ('09-'11) and Yoshida ('24) postulated that these fibers arise in the tail of the posterior subdivision of the ventral cochlear nucleus. There are a few fibers of Held in the mouse brains reported here; some of the fibers from the posterior subdivision also appear to enter the lateral lemniscus of the same side.

The manner in which the fibers of the lateral lemniscus enter the nucleus of the inferior colliculus, and the formation of the peduncle of the inferior colliculus have been described by Held ('93), Ramón y Cajal ('09-'11), and many others. Gurdjian ('27) mentions that the geniculo-cortical fibers gather medially in the anterior part of the medial geniculate nucleus in the rodent, then are located laterally as this nucleus disappears, and course toward the auditory cortex as auditory radiations.

2. The functional organization of the auditory pathway.

Ever since the work of Lashley ('21, '22, '26, '31), Maier ('32, 32a, '34) and Wiley ('32) there has been considerable controversy over the functional significance of the cerebral cortex of lower animals. The results of their research on the rodent indicate that there is no extensive localization of function in the cerebral cortex of this form, nor is function related to the structural features of particular portions of the cortex. The whole cerebral mass acts in some manner to take over various functions even when specific portions of the cerebrum are removed. Wiley, in his experiments on the rat, was able to show that removal of the auditory area, area p as defined by Fortuyn ('14), affects a simple auditory habit. He says, however, "the loss of this region after formation of the habit does not preclude the possibility of the reformation of the habit. It is possible that the cerebral cortex outside of area p may assume this function." Later, Lashley ('41) attempted to relate the auditory koniocortex of the rat as outlined by Rose ('29) to the medial geniculate nucleus by removing localized portions of the koniocortex; subsequently, he found diffuse rather

than localized degeneration within the medial geniculate nucleus.

There has been extensive research into the pattern of projection within the auditory system in carnivores and in primates. Among the workers who have contributed to our knowledge of this pattern may be mentioned Poliak ('26, '27, '32), Lorente de No ('33), Lewy and Kobrack ('36), Walker ('37, '38), Waller ('34, '40), Ades and Felder ('42, '45), Ades ('43), Licklider and Kryter ('42), Woolsey and Walzl ('43), and Walzl ('47). Walzl ('47), working with cats, found that fibers originating in the basal coil of the cochlea are concerned with transmitting high tones, fibers from the apical coil with transmitting low tones, and that the middle tones are carried over the remaining fibers which are spread through the midportion of the cochlea. Earlier, Lewy and Kobrack ('36), in some very fine work on rabbits, were able to establish a pattern of projection of high, middle, and low tones from the cochlea to the primary acoustic nuclei. They made small lesions with a dentist's drill at various points in the cochlear spirals in the rabbit, and after two weeks the animals were sacrificed and the brains were prepared according to the Marchi method. They learned that fibers from the superior spiral of the rabbit cochlea terminate in the deep and medial layer of the most ventral part of the acoustic tubercle, and also in the ventral region of the ventral cochlear nucleus. Some of the descending branches of the fibers from the inferior spiral end in the deepest layers of the acoustic tubercle where they tend to be dorsally disposed; others run to the dorsal extension, or "tail", of the ventral cochlear nucleus. The majority of the fibers from the inferior spiral of the cochlea ascended and split up in the ventral cochlear nucleus in their material. In this case, however, the closer

the lesion came to the middle turn of the cochlea, the more the fibers projected to the dorsal part of the ventral cochlear nucleus. The fibers of the middle turn constituted the large part of the cochlear nerve root; these fibers ended in the more middle portion of the acoustic tubercle in relation to lamina cellularis, although occasionally they were found in deep and superficial parts of the nucleus, and in the medial third of the ventral cochlear nucleus. The turns of the cochlea, then, are represented largely in an inverse manner in the primary acoustic nuclei, with the apical coil of the rabbit cochlea projecting to the ventral parts of the nuclei and the basal turn to more dorsal portions.

Woolsey and Walzl ('42), using the cat, and Walzl and his associates ('47), using both the carnivore (cat) and the primate (macaque), found that stimulation of the apical fibers of the cochlea of the cat (transmitting low tones) causes responses in the posterior part of the primary auditory area and also in the anterior part of the secondary area for hearing. Stimulation of fibers of the basal coil (carrying high tones) causes action potentials to arise in the rostral part of the primary area for audition and in the posterior part of the secondary area. They also found that stimulation of each cochlea causes responses on both cerebral hemispheres, so that each ear is represented bilaterally as well as twice on each side. The study of this pattern of projection in the monkey made by Walzl and his associates agreed with the observations of Licklider and Kryter ('42). Many others have described this pattern in the primate, among them, Poliak ('32), and Walker ('38). Because of a phylogenetic rotation of the auditory radiations in the primate, (which is described by Poliak), the low tones are projected to the anterolateral portion of auditory cortex and the high tones

to the posteromedial part of the koniocortex.

Several workers have concluded that pars principalis of the medial geniculate nucleus projects to the primary auditory area and pars magnocellularis to the secondary auditory area. These parts are in caudorostral relationship to one another in lower forms. Moreover, pars principalis appears to be laminated; the outer part of the nucleus sends fibers to the dorsal part of the primary area, the more ventromedial portion to the ventral part of auditory koniocortex, and the middle strip between these portions of the nucleus is related to the midportion of the auditory area. Also, the posteroventral part of the pars magnocellularis projects to the posterior portion of the secondary auditory cortex, and the anterodorsal part sends fibers to the anterior portion of this area. The intermediate portion of the nucleus projects to the more middle part of the secondary auditory area. This description is based largely upon the work of Waller in the cat ('40). Earlier, in his work on the rodent, Waller ('34) mentions some evidence which he found for relating the dorsal cortex to the medial part of the medial geniculate nucleus in this form, although he did not feel it was sufficient evidence on which to base a definite conclusion. He describes the caudorostral relationship existing between the medial geniculate nucleus and the auditory cortex in the rodent in this same report. Walker ('38) found that the lateral part of the medial geniculate nucleus is related to the lateral part of the auditory cortex and the medial portion of the nucleus to the medial part of the auditory area in the primate.

The relationship between the primary acoustic nuclei and the medial geniculate nuclei has not been worked out up to the present time. Such a relationship must certainly exist because of the presence of

specific patterns of projection between cochlea and primary acoustic nuclei, and between medial geniculate nucleus and the auditory areas.

One difficulty in attempting to relate the various nuclei of the acoustic pathway to one another experimentally in the rodent is the comparatively small size of the animals. It is a far from simple matter to gain access to the cochleae or to certain parts of the brain in order to stimulate them or to make experimental lesions for the study of localization within the auditory system. Hence, one advantage derived from the use of material such as these abnormal epileptic waltzing mice lies in the fact that Nature has performed the surgery! The lesions found are due to some inherent weakness, and the peculiarity in behavior or the loss of special senses may be related directly to what is happening in the conduction pathways within the central nervous system, or to degeneration of the peripheral nerves. In making experimental lesions there is always the danger of damaging adjacent tissue to such an extent that the results noted following the degeneration are colored by this additional loss. There isn't the same danger in interpreting the degeneration caused by disease. However, the artificial lesions may result in small but significant retrograde degeneration. In diseased animals, the degeneration may be widespread and hence difficult to interpret accurately.

GENERAL DISCUSSION

1. The apparent cause of the deafness of the abnormal mice.

A comparison of the normal with the abnormal brains demonstrates conclusively that there is degeneration of the acoustic pathway and in the auditory centers. The degeneration is almost complete in the case of the two old, deaf mice, but is partial and varies in intensity in

the young, partially deaf, epileptic waltzers. Thus, the progressive deafness of the abnormal mice is explained upon an anatomical basis and is not psychogenic in nature.

It appears that the degeneration begins as a demyelinization of the fibrous extensions of the cells, following which the cell bodies become atypical in appearance, exhibiting a loss of Nissl substance and a rounded contour. The demyelinization is not confined to one part of the acoustic system but occurs throughout it. Moreover, the degeneration of fibers does not occur in a haphazard manner, for certain portions of the nuclei and auditory areas are affected initially while others are spared, and the animal loses only a small part of the hearing range at first. This might indicate that certain fibers are more vulnerable than others to the demyelinization, or that those fibers affected first were incompletely covered with myelin during development, or that this is an example of transneuronal degeneration. In view of the poor condition of some of the other myelinated fibers in the brains of these specimens, it appears that there is a developmental disturbance in the myelinization process. This disturbance is evidently transmitted through heredity from one generation to the next in a recessive manner (Dice, '35).

The fact that the degeneration is progressive rather than sudden and complete provides an opportunity for study of the localization of the losses within the acoustic system. An attempt will be made to discover whether or not agreement exists between the extent of anatomical losses suffered and that portion of the range of hearing which is defective, and also whether or not a like pattern of projection for the various frequencies exists in the mouse as apparently exists in higher forms.

2. The range of hearing and degeneration of the primary acoustic nuclei and auditory areas.

In this study of the acoustic system young, partially deaf animals were used in the hope of finding the degeneration at an early enough stage so that any existing interrelationship of parts would be evident. All of the mice exhibited degeneration of the auditory centers to some degree. The ventral portions of the acoustic tubercles are degenerated in all of the specimens, and are sometimes atrophic. The dorsal part of the tubercle is affected rostrally on the right side in Mouse #96835 and on both sides in Mouse #96050. The dorsal extension or "tail" of the posterior subdivison of the ventral cochlear nucleus is generally affected in these abnormal brains, as are lateral and ventral portions of the rest of the nucleus. The caudal end of the medial geniculate nucleus is atypical in shape. In most cases, the middle third of the nucleus is best developed, and the rostral portion varies in extent of degeneration. The medial geniculate nucleus is seriously affected rostrally on the left side of Mouse brain #96836. In the primary auditory area, the rostral and caudal ends are usually more degenerated than the middle part, with the caudal end exhibiting the greatest losses as a rule. The condition of the secondary areas for hearing varies in these specimens. In some cases (which will be more fully described later in this discussion), degeneration of the secondary auditory area occurs in locations much the reverse of those of the atypical parts of the primary auditory cortex. For example, the dorsal part of one area and the ventral portion of the other may be similarly affected.

On the basis of the scheme of projection within the auditory pathway as given by Lewy and Kobrack ('36), Woolsey and Walzl ('42),

and others, one would expect these partially deaf animals, because of the location of the degeneration in the primary acoustic nuclei and in higher centers, to lose the high and the low tones of the hearing range first. Such was the case in the animals studied.

The mouse brain exhibiting the most typical primary auditory nuclei and auditory cortex is that of Mouse #96835, and this mouse gave the ear twitch response to a wider range of frequencies than did either of the other two mice tested with the electrical equipment for range of hearing. The caudal third of the acoustic tubercle and its rostroventral portion are degenerated on both sides of this brain. On the left, the fibers are delicate and are located in the dorsal half of the nucleus throughout the anterior two-thirds of its extent, but on the right, the fibers ramify within the dorsal two-thirds first and only in the middle part rostrally. The dorsal extension of the posterior subdivision of the ventral cochlear nucleus is only slightly atypical on both sides of the brain; the more ventral part of this subdivision is somewhat affected laterally, ventrally, and medially. The nucleus is well-shaped near the entrance of the cochlear nerve. More rostralward, it is more nearly flat than in normal material, with the midportion best supplied with fibers. The ventral region of the ventral cochlear nucleus is more typical than the dorsal part far orally. The left acoustic tubercle and the anterior part of the right ventral cochlear nucleus are more affected than on the opposite side. The significant losses are those of the caudal third and the ventrorostral part of the acoustic tubercles. According to Lewy and Kobrack's ('36) description of tonal localization in the rabbit cochlea, only the low tones should be affected by the degeneration ventrally in the acoustic tubercles, and such tones are

doubtless compensated for in the more typical ventral cochlear nucleus.

There is a knob-like arrangement of Layer IV throughout much of the primary auditory area on both sides of this mouse brain. The caudal end of the left auditory koniocortex is severely affected, but there are portions of the middle and rostral thirds which have a very rich supply of fibers. On the right side, the fibers are delicate but there is never a complete lack of stratification. The secondary auditory area is quite typical on the left side and, on the right, the fibers are delicate, especially ventralward. Here again, sufficient cortical tissue remains in good condition to account for the range of hearing to which this animal gave ear twitch responses. This range extended from 300-65,000 cycles/sec.

Mouse #96362 heard frequencies between 4,000 and 60,000 cycles/sec. It's auditory pathway was more degenerated than that of the previously described animal. Fibers were located only in the dorsal half of both acoustic tubercles; they extend through the midportion of the posterior subdivision of the ventral cochlear nucleus, and the dorsal extension of this division is more affected in this mouse brain than in the brain of Mouse #96835. On the right, the lateral and medial borders of the posterior subdivision are affected rostrally; in the anterior subdivision, the fibers are less numerous lateroventrally and ventrally than elsewhere in the nucleus. Far orally, the nucleus is atrophied ventrally. On the left side, (which is more seriously damaged caudally), the ventral portion of the posterior subdivision of the ventral cochlear nucleus is atrophied posteriorly, and then degeneration becomes lateral and ventral. At the level of the entrance of the cochlear nerve, the nucleus is triangular in shape on the left side. The losses tend to

be evenly distributed rostralward, although the nucleus is not so flat far orally on the left as it is on the right. High and low tonal losses would be predicted in this case because of the ventral degeneration of the acoustic tubercles, the lessening of fibers in the dorsal extension of the posterior subdivision of the ventral cochlear nucleus, and the involvement of the ventral parts of this nucleus. The exact nature of the tonal losses due to diminished fibers anteriorly on the left is more obscure.

The caudal end of the primary auditory area is completely degenerated on the left side in this brain. Caudally on the right side, the midportion of the area exhibits knobs in Layer IV although the fibers are not rich. The fibers chiefly extend into the fifth and sixth laminae of auditory koniocortex rostrally on both sides. They are found only in the ventral part of the area in Layer VI on the left, but reach Layer II-III dorsally. The ventral portion, except for a short distance near the rostral end of the area, exhibits clusters in Layer IV on the right. There are delicate fibrils dorsally at the anterior end of the secondary area on both sides; the caudal portions of the areas are delaminated. The location of the degeneration at these higher levels also indicates a loss of some high and low frequencies.

Only one of the mouse brains (#96836) stained for cells was taken from an animal which had been tested with the electrical equipment for its range of hearing. This mouse heard frequencies between 500 and 55,000 cycles/sec. The acoustic tubercles are greatly affected in Mouse #96836. The cells are gathered without organization in the medial part of the tubercles. On the left side, the ventral portion of the dorsal cochlear nucleus is atrophic and filled with neuroglia. Caudally,

the so-called "tail" of the posterior subdivision of the ventral cochlear nucleus is completely filled with glia on both sides, and the more ventrally located cells are few in number on the right but are scattered and more numerous on the left. A short distance from the caudal end of this division, more typical cells appear in the dorsal extension and the neuroglia disappear. Caudal to and at the level of the cochlear nerve, the nucleus is shaped like a hillock, but is not so plump here as in the normal material. The nucleus is more flattened rostralward, and the triangular cells are less numerous ventrally on the right side. The ventral portion of the nucleus is less typical on the right than on the left far orally. A great impairment of high tones should have occurred, on the basis of Lewy and Kobrack's ('36) description of the termination of fibers carrying high frequency vibrations, because of the disorganization of the cells of the acoustic tubercles and the presence of the glia most caudally and dorsally in the posterior subdivision of the ventral cochlear nucleus. It would appear that low tones should have been impaired due to the degeneration of the acoustic tubercles and some involvement ventrally in the ventral cochlear nucleus.

The rostral third of the primary auditory area on the left side and the anterior end as well as the entire rostroventral border on the right are degenerated in Mouse brain #96836. Most of the caudal third of the area is delaminated on the left. On the right side, there are small pyramidal cells in much of Layer II+III, but none of the other laminae appear typical. The fifth and sixth layers are particularly affected caudally on the right. The ventral portion of the rostral tip of the secondary auditory area is laminated on both sides; the caudal half of the area is delaminated on the left but caudally on the right side, all of the area except its dorsal border is typical. It

is not difficult to understand the extensive loss of the higher frequencies from the range of hearing which this animal showed in life, for all of the appropriate portions of the cortex except for part of the secondary auditory area on the right are seriously affected. It is difficult to explain why more low tone impairment was not observed due to the delamination of caudal portions of the auditory koniocortex. The only clue which we have to point to the possibility of such impairment lies in the fact that exposure of the animal to single pure tones of low frequencies caused dashing and waltzing.

The cells of the acoustic tubercle are enlarged and pale-staining in Mouse #96050, but the lamination is clear; these dorsal nuclei are much better developed in this specimen than in the brain of Mouse #96836. Neuroglia are numerous ventrally in the caudal two-thirds of the tubercle, and dorsally as well as ventrally, (sparing a middle portion lying between), in the rostral third. The location of the glia corresponds a great deal to the distribution of fibers in the dorsal cochlear nucleus of Mouse brain #96835. The posterior subdivision of the ventral cochlear nucleus is largely degenerated; typical cells are found in a strip through the middle of the nucleus. The anterior subdivision of the ventral cochlear nucleus in this specimen exhibits more degeneration laterally than in Mouse #96836, but far rostrally, the left ventral tip is better preserved in this mouse. The anterior end of the ventral cochlear nucleus is severely affected on the right.

Degeneration is found ventrally throughout the entire primary auditory region on the left side and far rostrally, all but a narrow zone dorsally is atypical. The caudal sixth of auditory koniocortex is delaminated on the right side, as is most of the posterior part of

the middle third. The anterior half of the right primary auditory area is typical except along the dorsal border. The secondary auditory region is almost completely degenerated on the left. On the right, the caudal third and the remainder of the dorsal portion of this region are typical.

The degeneration ventrally in the acoustic tubercle and in the posterior subdivision of the ventral cochlear nucleus, and the delamination caudally in the right auditory koniocortex and rostrally in the secondary areas for hearing indicate some loss of low tones. There should be impairment (if not actual loss) of high tones, also, because of the location of glia in the acoustic tubercles and in the posterior subdivision of the ventral cochlear nucleus, and due to the degeneration at the rostral end of the left koniocortex and in the caudal part of the left secondary auditory area. This animal was not tested with the electrical equipment for range of hearing.

3. Comparison of degeneration in the medial geniculate nucleus with that of the auditory cortex.

Several comparisons may be made to show the relationship which exists between the degeneration within the medial geniculate nucleus and in the auditory areas. The general points of agreement in degeneration of these portions of the acoustic pathway in Mouse #96835 are as follows. On the right side, pars principalis of the medial geniculate nucleus has a triangular-shaped caudal tip, and caudally in the corresponding auditory koniocortex, there are few fibers (even in layer VI). The degeneration lessens gradually in pars principalis, involving first the dorsal two-thirds and finally the dorsal portion and the ventrolateral border. The fibers are delicate at first throughout the rest of the caudal third of the primary auditory area, and then they become more

numerous except at its dorsal border; at the zone of transition between caudal and middle thirds of the area, only the dorsal and ventral borders are atypical. In the middle third of the extent of the right pars principalis, degeneration spreads from the dorsal and lateral borders, invading deeper portions of the nucleus. There is general improvement posteriorly in this third of the corresponding auditory koniocortex but the midportion becomes affected shortly; more rostralward, all but the dorsal part of the area is atypical. On the left side near the midpoint of pars principalis, only the dorsal portion appears degenerated, and near the middle of the auditory koniocortex only the dorsal border is delaminated. However, the rostral end of the nucleus appears to be more affected than the corresponding part of the primary auditory area; it is on this side that the very rich fiber supply is observed dorsally in the auditory cortex.

The fibers are extremely delicate caudally in the left pars principalis of Mouse brain #96362, and approximately the caudal sixth of the left primary auditory area is abnormal. At the anterior end of the caudal third of pars principalis, the nucleus is atrophied, and the fibers are extremely delicate in the corresponding part of the left auditory koniocortex. In general, the most typical part of the pars principalis lies just anterior to its midpoint, and it is at a similar level of the primary auditory area that the fibers are most numerous in Layers II-III and IV. The right pars principalis and the right primary auditory cortex are less affected than the left. Anteriorly in the middle third of the right pars principalis and in the rostral third, there is improvement of the nucleus so that only the dorsolateral portion is chiefly affected; far rostrally, the ventral border is

degenerated. The most typical parts of the right auditory koniocortex are located ventrally at the transition from the middle to the rostral third and in the midportion of the area more rostralward.

Both pars principalis and the auditory koniocortex are more degenerated on the left than on the right in Mouse #96836. The cells of pars principalis become crowded orally and it is difficult to trace the nucleus far rostralward on the right side; the ventral border and the entire anterior end of the right primary auditory area are delaminated. The caudal end of pars principalis and that of the auditory koniocortex are more affected on the left than on the right. Near the midpoint of the extent of the left pars principalis, this nucleus broadens for a short distance. Lamination of the left primary auditory area is observed for about 50μ just anterior to the midpoint, although there are no knobs in the fourth layer. It is extremely difficult to trace the left pars principalis rostralward; it is more degenerated than the right nucleus. The anterior third of the left auditory koniocortex is atypical to its oral tip.

In the case of Mouse #96050, the right pars principalis and the right primary auditory area are better preserved caudally than in the previous brain. The rostral third of the nucleus is rather typical in appearance on this side also, and the rostral third of the auditory koniocortex is well represented except posteriorly and at the anterior tip. The caudal ends of both pars principalis and the primary auditory area are more affected on the left than on the right. The anterior half of the nucleus is rather typical in appearance, and the rostral half of the auditory koniocortex is laminated except at its far dorsal border.

A comparison of the degeneration of pars magnocellularis with that in the secondary auditory area gives the following information: The right pars magnocellularis of Mouse brain #96835 exhibits a good fiber supply anteriorly in the caudal third and posteriorly in the middle third. The fibers are few in number elsewhere in the nucleus but are not completely lacking. In the right secondary auditory area, the fibers are most numerous ventrocaudally, in the dorsal portion of the middle and caudal thirds, and far rostrally. The nucleus is better represented caudally on the left, and the left secondary area for hearing is, in general, typical. There are few fibers caudally in the right pars magnocellularis of Mouse #96362, but anteriorly they become numerous. The anterior half of the right secondary auditory area is laminated, but caudally, the fibers are few and reach only the deepest layer of the cortex. The left pars magnocellularis of this brain is more degenerated than the right, and is well represented only near the midpoint and at the anterior end. Delicate fibers occasionally extend up through Layer II+III dorsally in the anterior portion of the secondary auditory area, but the laminae are usually confluent on this side.

The right pars magnocellularis of the medial geniculate nucleus is defined as a separate nuclear mass for a few sections in the middle third of its extent; the secondary auditory area is differentiated through its caudal half except for its dorsal border on this side. The left pars magnocellularis is most distinct in its middle third. The ventral part of the left secondary auditory area is typical anteriorly in its middle third and near its rostral end. In Mouse #96050, the caudal half of pars magnocellularis on the right and the caudal two-thirds of this nucleus on the left appear to be the least affected portions;

most of the secondary auditory area is delaminated on the right and is differentiated only in its caudal third and along the dorsal border of the area anteriorly on the left side of this brain.

There is a great deal of general agreement between the degeneration of the auditory koniocortex and of pars principalis, so that a caudorostral relationship is apparent. Such a relationship is not so evident between pars magnocellularis and the secondary auditory area. One feature of the degeneration in the secondary area for hearing is that it sometimes appears in an exactly reversed location from that in the primary area. For example, on the right side of Mouse #96836, the ventral border of the auditory koniocortex anteriorly and the dorsal border of the secondary auditory area posteriorly are degenerated; on the left, the ventral part of the primary and the dorsal part of the secondary area for hearing are affected. In Mouse #96050, on the left, the dorsal border of the primary and the ventral border of the secondary auditory area are atypical throughout. Whether or not this indicates a projection from auditory koniocortex to the secondary area for hearing cannot be stated at this time.

The lamination of pars principalis observed in higher forms is not so evident in this material. The ventral and ventromedial portions of the nucleus are generally less degenerated than the dorsal portion and the lateral border; yet, the ventral part of the primary auditory area is often more affected than the dorsal border. The dorsal third, and sometimes more, of pars principalis is usually degenerated and sometimes is atrophic. The dorsomedial cells and fibers are included in this atypical portion. This may indicate that, in the rodent, the cells which project to the ventral part of the primary auditory area are more dorsomedially situated than they are in higher forms. One

example in which the dorsomedial part of pars principalis is rather typical is found on the left side of Mouse brain #96362 near the transition from middle to rostral thirds of the nucleus and continuing for a short distance into its rostral third. The corresponding levels of the ipsilateral auditory koniocortex exhibit clusters ventrally in the fourth cortical layer.

4. Other nuclei associated with the auditory pathway.

A study of the various accessory auditory nuclei--the nucleus of the trapezoid body, the nuclear complex of the superior olive, the nuclei of the lateral lemniscus, and of the inferior colliculi--associated with the auditory pathway in these mice is inconclusive with respect to their specific relationship to the acoustic system. All of these nuclei are affected to some degree but none, except for the parolivary nuclei, are completely degenerated in the brains of the totally deaf mice.

Some of the fibers of the trapezoid (or ventral acoustic) decussation appear to be internuclear components passing between the nuclei of the trapezoid body. There is a heavy decussation between the two nuclei, which lie near the midline, even in the brains of the animals which had been found to be completely deaf. There also appears to be a rather thick internuclear bundle between the inferior and superior nucleus of the lateral lemniscus, for these fascicles are also largely present in the abnormal mouse brains.

5. Hereditary nerve deafness in man.

Several studies have been made of hereditary nerve deafness in man. Among these studies may be mentioned the work of Stephens and

Dolowitz ('49), Dean and Bunch ('23), and Popov ('35). Such deafness is very frequently progressive in nature and appears within the first, second, or third decade of life. Usually, also, the extreme ends of the range of hearing become defective initially. The paper of Stephens and Dolowitz was of particular interest. These workers reported a study hereditary familial nerve deafness in which the onset of the disease is in the early twenties although the loss of hearing increases as the individuals become older. The high tones are affected first in these cases. The authors postualted that a "premature aging" of the acoustic nerve is responsible for the deafness. They demonstrated that this tendency to "premature aging" is inherited in a dominant manner. However, it is possible that these individuals are suffering from demyelinization of the acoustic nerve which is similar to that reported here in the case of the abnormal epileptic waltzing mice. Popov believed that there is demyelinization of the auditory nerve in cases of hereditary nerve atrophy.

It is interesting to note, in connection with the type of loss first observed in these mice and in some cases of deafness in man--that is, defects at the ends of the scale of hearing--that Mc Crody ('35) found the more middle portion of the cochlea of the opossum to be the first part to develop an organ of Corti and the first portion to function. The organ continues to develop in both directions, apically and basally, from this site. The last portions of the cochlear nerve to myelinate in the opossum, then, are those fibers from the apex and from the base of the cochlea, and fibers from these same parts of the cochlea are the first to degenerate in these abnormal mice.

6. The epileptic behavior.

The extreme behavior observed in the abnormal mice in response to audiogenic stimuli--waltzing, dashing, and loss of consciousness--appears to be similar to the "grand mal" type of epilepsy. During the seizure, the animals fall on their sides, sometimes with the forelimbs flexed and the hind limbs extended. The mouse may be picked up and handled during this time. There is no resistance to passive movement of its limbs. It recovers from the seizure quickly, but its movements are not well coordinated at first and the animal seems sluggish. The exciting cause of a convulsive seizure in these mice is an auditory stimulus and, hence, the locus of the disease appears to be within the degenerating auditory area of the cerebrum. The argument for favoring this locus is strengthened by the fact that the epileptic symptoms and seizures cease once the animal is old and deaf.

SUMMARY

1. The deafness of the abnormal mice is due to a selective demyelinization of fibers in the acoustic pathway.
2. From previous studies by Dice ('35) and Watson ('39), it is known that this tendency to demyelinization is inherited as a mendelian recessive.
3. The location of degeneration within the acoustic pathway in relation to tonal losses indicates a pattern of organization of this pathway in the rodent.
4. The demyelinization may be related to cases of hereditary nerve deafness in man.
5. The waltzing and epileptic behavior appear to be similar to the "grand mal" type of epilepsy. The locus of the disease is in the auditory cortex.

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ABBREVIATIONS FOR FIGURES

Acoustic tub. - Acoustic tubercle

Area insul. - Area insularis

Brach. pont. - Brachium pontis

Caud. tip of the sup. ol. nuc. - Caudal tip of the superior olivary nucleus

Cereb. ped. - Cerebral peduncle

Corp. trap. - Corpus trapezoides

Dec. of brach. conj. - Decussation of brachium conjunctivum

Degen. vent. portion of the tub. - Degeneration ventral portion of the tubercle

Desc. root of trig. N. - Descending root of trigeminal nerve

Dors. group of pars princ. - Dorsal group of pars principalis

Fib. from the acoustic tub. - Fibers from the acoustic tubercle

Fib. from the "tail" of the vent. coch. nuc. - Fibers from the "tail" of the ventral cochlear nucleus

Fib. from the vent. coch. nuc. - Fibers from the ventral cochlear nucleus

Genu of the fac. N. - Genu of the facial nerve

In. str. of Layer V - Inner strata of Layer V

Inf. nuc. of the lat. lem. - Inferior nucleus of the lateral lemniscus

Inf. quadrig. brach. - Inferior quadrigeminal brachium

Lam. zona. - Lamina zonalis

Large pyra. cells of Layer V - Large pyramidal cells of Layer V

Lat. group of pars princ. - Lateral group of pars principalis

Lat. lem. - Lateral lemniscus

Main mass of pars princ. - Main mass of pars principalis

Nuc. of the inf. coll. - Nucleus of the inferior colliculus

Nuc. of the oculomot. N. - Nucleus of the oculomotor nerve

Nuc. of the troch. N. - Nucleus of the trochlear nerve

Out. str. of Layer V - Outer strata of Layer V

Pars magnocell. - Pars magnocellularis

Periph. gr. - Peripheral gray

Roots of the coch. N. - Roots of the cochlear nerve

Roots of fac. N. - Roots of facial nerve

Roots of the oculomot. N. - Roots of the oculomotor nerve

Roots of the vest. N. - Roots of the vestibular nerve

Sec. aud. area - Secondary auditory area

Sup. coll. - Superior colliculus

Sup. nuc. of the lat. lem. - Superior nucleus of the lateral lemniscus

Sup. ol. nuc. - Superior olivary nucleus

"Tail" of the post. subdiv. of the vent. coch. nuc. - "Tail" of the posterior subdivision of the ventral cochlear nucleus

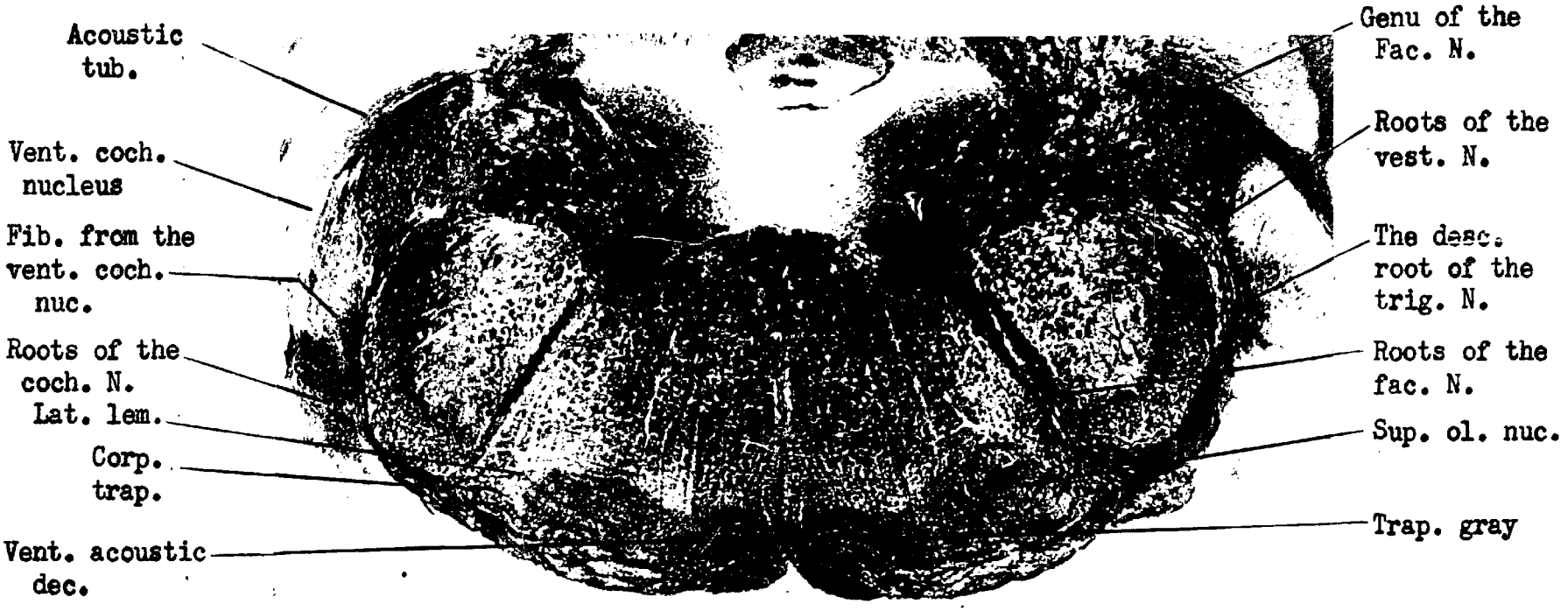
Trans. from aud. cort. to area pariet. - Transition from auditory cortex to area parietalis

Trap. gr. - Trapezoid gray

Vent. acoustic dec. - Ventral acoustic decussation

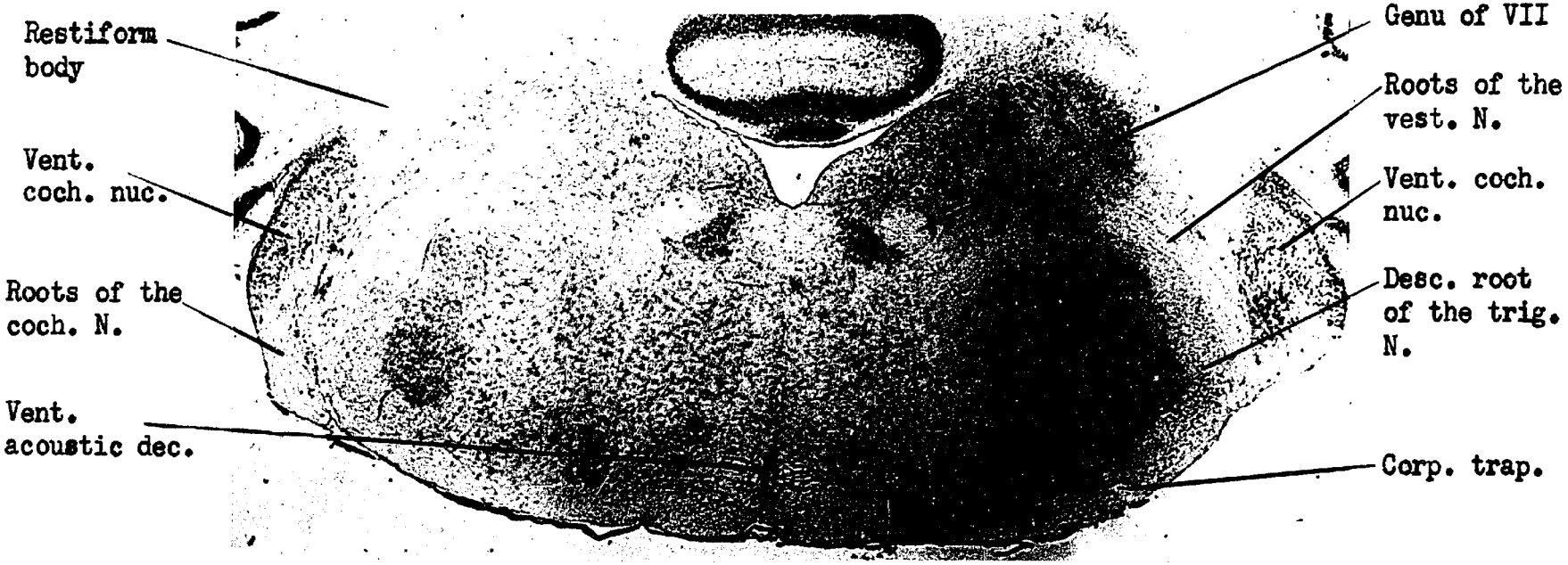
Vent. coch. nuc. - Ventral cochlear nucleus

Vent. portion of the post. subdiv. of the vent. coch. nuc. - Ventral portion of the posterior subdivision of the ventral cochlear nucleus.



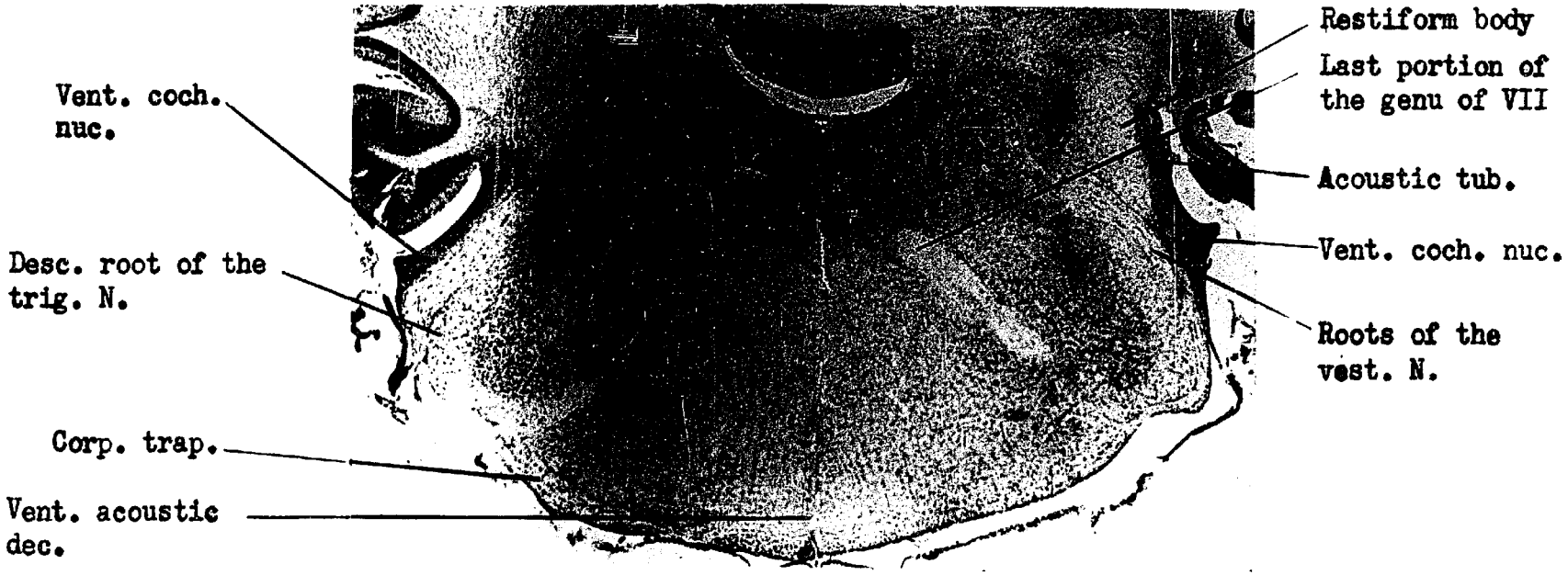
Mouse brain #87932, normal. Section at the level of the roots of the facial N.

Plate 1



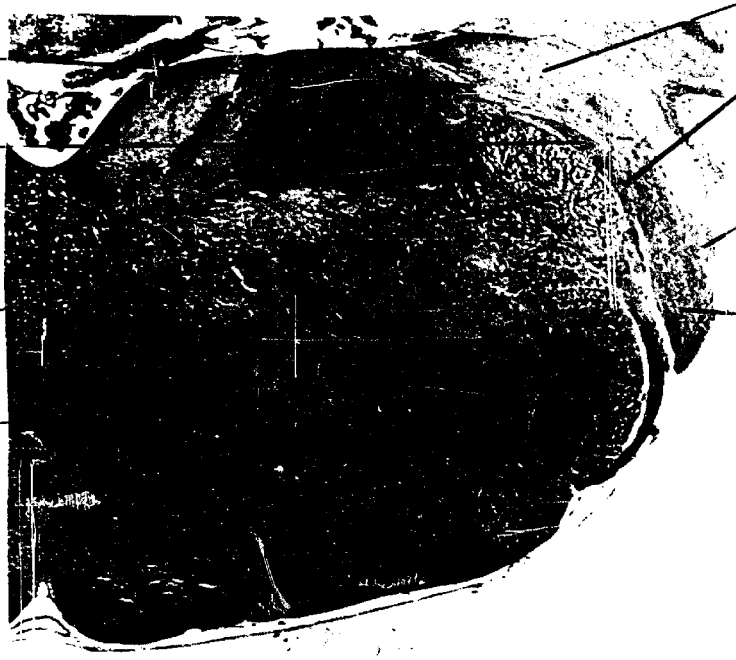
Mouse brain #87120, normal. Section at the level of the genu of VII.

Plate 2

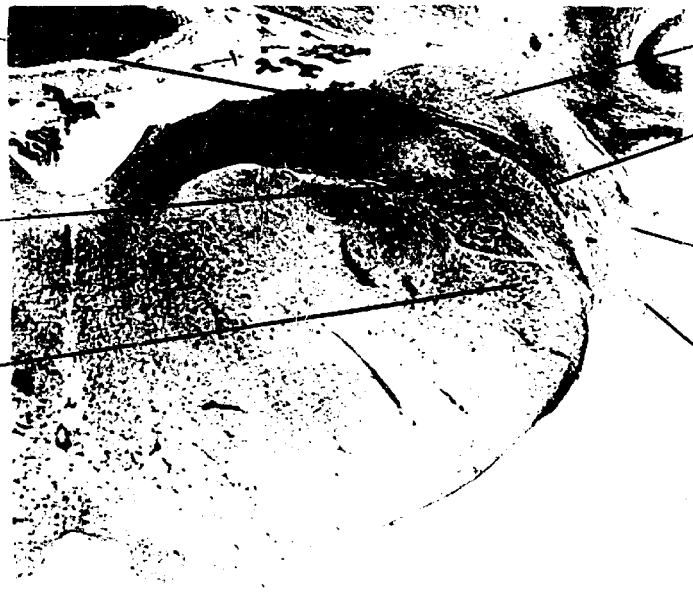


Mouse brain #85836, deaf. Section slightly rostral to the genu of VII.

Plate 3



Mouse brain #96835
Section through the posterior
subdivision of the ventral cochlear nucleus.



Mouse brain #96362
Section through the posterior
subdivision of the ventral cochlear nucleus.

Plate 4



Mouse brain #96835, abnormal. Section at the level of the genu of VII.

Plate 5

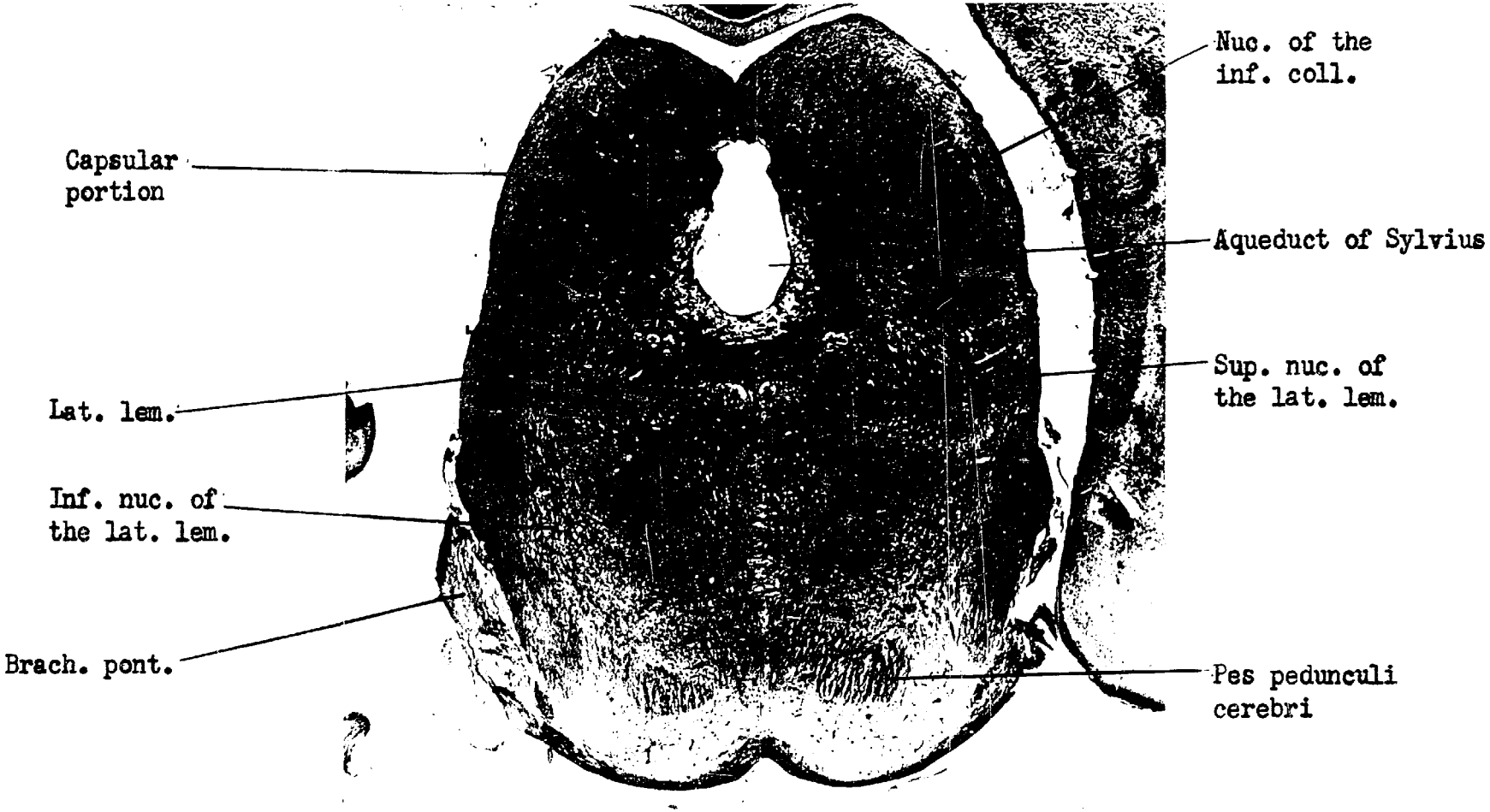


Mouse brain #87932

Section at midbrain level through the

inferior colliculus.

Plate 6



Mouse brain #96835

Section at midbrain level through the inferior colliculus.

Plate 7

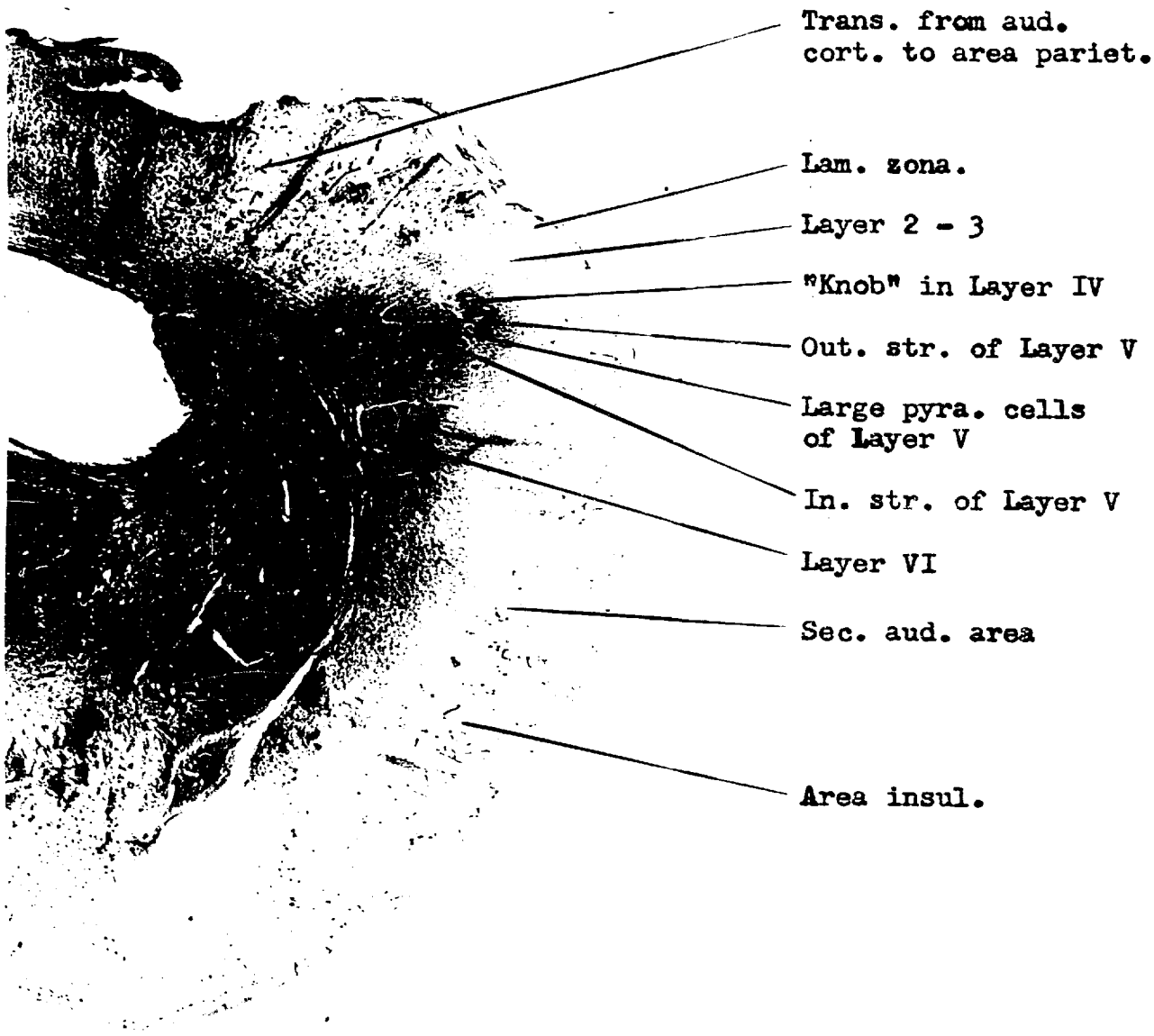


Mouse brain #96835
Section through the caudal third of the medial geniculate nucleus.



Mouse brain #96362
Section through the caudal third of the medial geniculate nucleus.

Plate 8



Mouse brain #96362

Section through the primary and the secondary auditory areas, anteriorly in the caudal third. Light appearing portions exhibit few fibers; note location of knobs in Layer IV of auditory koniocortex.

Plate 9