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THE ORIGIN OF THE WEVER AND BRAY PHENOMENON.

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Introduction.

In 1911 there was published by Witmaack [1911] what appears to have been the first adequate account of the histological changes resulting in the mammalian cochlea from section of the trunk of the VIIIth nerve. According to Witmaack the consequence of this operation in the cat was the production within a few months of a widespread degeneration of the ganglion cells and nerve fibres of the peripheral cochlear neurones distal to the point of section. Witmaack's conclusion that the behaviour of the peripheral cochlear neurones under these circumstances displayed a striking lack of conformity with the classical laws of Wallerian degeneration met with some objection in the published discussion of his results; Siebenmann [1911] pointing out that the attachment to these results of any neural significance was stultified by the vascular disturbance consequent upon the concomitant section of the internal auditory artery inevitably occurring in the operation of nerve section.

Witmaack defended his views firstly on the technical ground that section of the artery was prevented by division of the nerve by pressure with a blunt dissector, significant injury to the more resilient blood vessel being thus avoided.

In addition he pointed out that in conformity with the Wallerian law the cells and fibres of the peripheral vestibular neurones showed comparative absence of degenerative change, a result which, in view of the common blood supply to both vestibular and cochlear neurones by the internal auditory artery, was not compatible with the view that the degenerative changes observed in the case of the latter could properly be attributed to section of this artery.

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Since Witmaack's work further evidence bearing upon the question has resulted from observations by Crowe [1929] and Gray [de Kleyn and Gray, 1932] upon the histological changes engendered in the internal ear by tumours involving the VIIIth nerve. Both report degenerative changes disproportionately greater in the cochlear than in the vestibular neurones, findings which support the views of Witmaack. In addition the effects of experimental section of the VIIIth nerve have recently been more closely studied in the rabbit by Kaida [1931]. As a result of a number of such operations carried out in the manner employed by Witmaack, Kaida describes two widely differing types of histological result. Firstly there may occur gross degeneration of all the neural elements and sensory epithelium of the cochlea with collapse of the membranes and disappearance of Corti's organ; the vestibular portion of the internal ear exhibiting changes comparable in type and degree. These histological findings are correlated by Kaida with division of the internal auditory artery concomitant with that of the VIIIth nerve. In some cases, however, Kaida was able to demonstrate changes more in accordance with those described by Witmaack. In these were found disappearance of the cells of the spiral ganglion and of the nerve fibres within the modiolus. The sensory epithelium and membranes were nevertheless well preserved. In these cases Kaida believed that the integrity of the vascular supply had been maintained, a view supported by the fact that the fibres of the peripheral vestibular neurones and the cells of Scarpa's ganglion showed little observable change.

Though Witmaack states that the sensory cells of Corti's organ may show some degeneration, these may, according to Kaida, present an appearance indistinguishable from normal.

The investigations described in the present paper have had a twofold objective: Firstly, the confirmation of the possibility indicated by the work of Witmaack and Kaida of bringing about in the manner described by them of a clear-cut degeneration of the neural elements of the cochlea. And secondly, the employment of such a preparation *in vivo* for the adduction of evidence bearing upon the problem of origin of the Wever and Bray phenomenon.

Part I.

The histological effects of section of the VIIIth nerve in the cat.

Technical methods. Under nembutal anæsthesia, section of the VIIIth nerve was carried out in a number of adult cats. Adequate access to the nerve was obtained by opening the skull immediately above the superior

occipital crest to one side of the mid-line. Owing to the extreme thinness of the dura mater below the tentorium cerebelli no attempt was made to effect a clean opening into the subarachnoid space, a fine blunt-ended dissector being passed blindly into the internal auditory meatus (which was found to be readily distinguishable by touch) and the nerve divided. The operative mortality of this procedure proved to be negligible, and after early difficulties in the identification by touch of the internal auditory meatus it was found possible in nearly all cases to effect a satisfactory division of the VIIIth nerve, such success being manifested by complete facial paralysis and the classical signs of unilateral labyrinthine destruction. The signs of acute vestibular disturbance, rolling movements and nystagmus, passed off within a few days as described by Magnus [1924] in the case of the rabbit. The rotated posture of the head and facial paralysis were, however, conspicuously persistent in all cases.

The temporal bones of a series of such animals were examined histologically, the animals being killed at periods varying from 3 days to 6 months after division of the VIIIth nerve. Fixation was by the method of *intra vitam* injection, and celloidin was employed for embedding.

The histological preparations obtained in this way showed that in the majority of cases an anatomical picture resulted which approximated closely to the first class of result obtained by Kaida. There was complete disappearance of all nerve elements and sensory epithelium, with collapse of the membranes, vestibular and cochlear portions of the internal ear being equally involved. In some cases gross necrosis of the entire cochlear contents had occurred with the formation of masses of heterotopic new bone. These results are typified by the photo-micrograph shown in Text-fig. 1. In three of the fifteen cases examined there were, however, obtained results of a radically different order, results corresponding closely to what Witmaack and Kaida described as exemplifying the effect of division of the VIIIth nerve without disturbance of the vascular supply, the rods and hair cells of Corti's organ being well preserved, although little remained of the nerve fibres and cells of the spiral ganglion. A marked feature of the sections was the presence of well-preserved capillaries containing fresh blood cells. The cells of Scarpa's ganglion, however, showed little alteration in number and appearance, as also the epithelium of the maculæ and cristæ of the vestibular apparatus and their associated nerve fibres.

Discussion of results. It will be seen that the results described conform with Kaida's view that it is possible to bring about an isolated

degeneration of the neural elements of the cochlea by the operation of section of the trunk of the VIIIth nerve.

In view of the demonstration in such cases of the presence of capillaries with normal red cell contents, also of the preservation, relatively unchanged, of the corresponding elements of the peripheral vestibular neurones, the explanation given by Siebenmann of the changes produced in the cochlear neurones, namely that they are of purely vascular origin, cannot be considered altogether adequate.

An anatomical feature of the trunk of the VIIIth nerve which appears worthy of note is the somewhat unusual degree of protrusion into it of

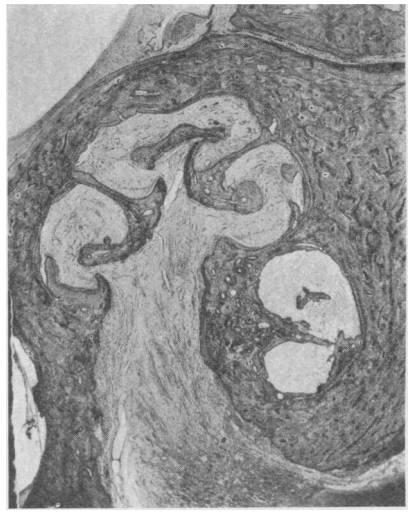

Fig. 1. Cochlea of cat 6 months after section of VIIIth nerve and of the internal auditory artery. Showing total necrosis of the cochlear contents and the formation of masses of heterotopic new bone. ($\times 20$ *circa.*)

neuroglial tissue from the brain stem; in practice, the operation of section being effected in the region of the neuroglial-neurilemmal junction. It is difficult, however, to understand in what way such an anatomical feature can be held to account for the facts in connection with the degenerative changes found to occur after section, the empirical acceptance of which facts must therefore for the present be considered as unavoidable.

It will be understood that preservation or otherwise of the internal auditory artery at the time of nerve section must be determined largely by chance factors inevitably associated with an operative procedure of this type.

Part II.

In view of the possibility shown by preliminary investigation of obtaining, in the manner described, preparations exhibiting a histologically clear-cut degeneration of the neural elements of the cochlea, it has been considered desirable to investigate the electrical responses of the cochlea in animals treated in this way.

This was accordingly carried out in three fully grown cats six months after unilateral section of the VIIIth nerve by the technique already described.

The method of investigation employed was as follows:

After decerebration under ether the tympanic cavities were exposed and platinum electrodes disposed symmetrically upon the round window margins of the two ears. Silver silver-chloride electrodes were also placed in position in the auditory tracts of the exposed brain stem. By a suitable switch mechanism arrangements were made for leading any one of these electrodes to the input grid of an amplifier, and the response of either cochlea or corresponding auditory tract was finally recorded, after amplification, upon fast moving ciné-bromide, employing a Cossor, Type C, cathode ray oscillograph. (For details of the technical methods employed, operative and electrical, reference should be made to a previous publication [Hallpike and Rawdon-Smith, 1934].)

Experimental findings. In all three animals the middle and external ears were found to be normal. Reflex contractions of the tympanic muscles in response to sound stimulation were observed to be brisk upon the unaffected side, and absent upon the side of nerve section. Photographic records of the electrical response of the cochlea upon the unaffected side and of the corresponding auditory tracts showed responses of high amplitude in all three animals investigated. On switching over to input leads from the cochlea of the affected side and its corresponding auditory tracts, no response could be elicited to any frequency within the range 200–6000 ~, even when employing intensities of sound some 40 decibels above the level used for the stimulation of the responsive ear and an increase of some tenfold of the voltage amplification employed (Text-fig. 2). Following the electrical investigation of the tract and cochlear responses, intra-vital fixation was carried out, Witmaack's solution at 37° C. being injected into the aorta *via* an incision in the wall of the left ventricle at a pressure of some 60 mm. Hg. A counter opening for the return of the injection fluid was made in the right auricle. The flow of the fixing solution was continued for 4 min. and was immediately

preceded by Ringer's solution at the same temperature and pressure for 30 sec. The temporal bones were then removed, and after further fixation, hardening and decalcification, embedded in celloidin, the total period of preparation being 6–7 months.

Histological findings. In two of the three animals electrically investigated the cochlea on the side of the nerve section was found to be in a condition corresponding to the first type of result described by Kaida. Total necrosis of the cochlear contents had occurred and the cochlear

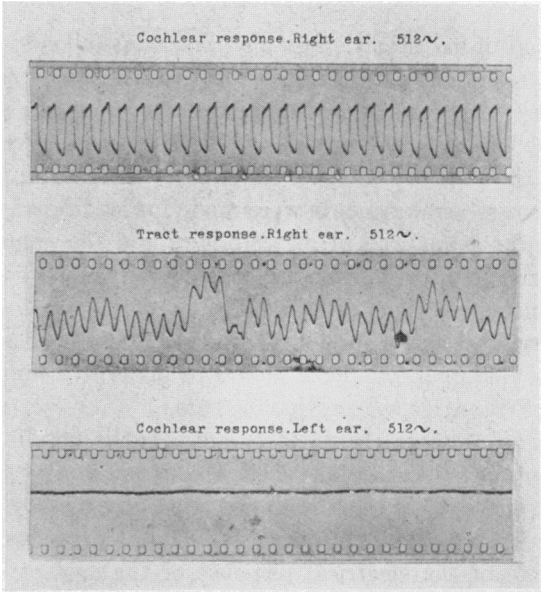

Fig. 2. Cathode ray oscillograph records. Showing cochlear and tract responses. 512~. Records 1 and 3 were taken with active electrodes disposed symmetrically upon the round window margins of the right and left ears respectively; without alteration of stimulus intensity or amplifier gain. Increase of stimulus intensity (40 decibels) and of voltage gain of the amplifier (× 10) yielded no response from the left cochlea.

cavities were found to be filled with loose connective tissue interspersed with masses of newly formed bone. These preparations were therefore deprived of any possible significance in respect of the problem in view and will not be further considered. In the third animal, however, the cochlea on the affected side presented an appearance corresponding to the second type of result described by Kaida. The central canal of the modiolus and the canal of Rosenthal were occupied chiefly by loose connective tissue

and neurilemmal remnants. Medullated fibres were few, and of the spiral ganglion only a few scattered and atrophic members could be observed.

In contrast to the neural elements, all other anatomical features of the cochlea, the membranes, stria vascularis, rods of Corti and hair cells were well preserved and indistinguishable from their counterparts in the opposite normal cochlea, in which, however, nerve fibres and ganglion cells were present in normal numbers and preservation.

Regarding the depression of the membrane of Reissner to be seen in some of the cochlear whorls (Plate I, fig. 2) the degree of deviation is within the limits normally imposed by the technical difficulties in connection with the process of preparation, in spite of the use of gas-free solutions; and it is not considered possible to attach to this deviation any pathological significance.

Conclusions derived from the experimental results. The experimental data provided show the electrical response to be absent in a cochlea in which the only morphologically distinguishable departure from normal was a gross deficiency in the neural elements. As stated in a previous publication [Hallpike, 1934] it is logical to describe these findings as constituting evidence which, with due regard to the limitations of morphology, appears to suggest that the neural theory of origin of the Wever and Bray phenomenon cannot yet be discarded.

Discussion.

The experimental results described invite comment chiefly in respect of their relation to other published observations upon the possible sources of origin of the Wever and Bray phenomenon.

It will be recalled that following the advancement by Wever and Bray [1930*a*] of the view that the potential changes should be regarded as true action potentials generated in the fibres of the auditory nerve, Adrian pointed out [1931 *a*] in objection to this view that the potential changes were not confined to the auditory nerve but spread diffusely about the temporal bone. Moreover, injection of acetic acid into the nerve was without effect in causing their cessation.

In these two fundamental respects, therefore, it has since been agreed that the Wever and Bray effect fails to accord with the characteristics of an action potential.

Davis and Saul [1932] later succeeded in demonstrating in the brain stem potential changes which, while reproducing the frequency of a

stimulating sound, were characterized by strict localization to the auditory tracts and by reversible deletion by anæsthetics.

In a later paper [Davis *et al.* 1934] the results of measurements made on the latency of response of the tract potentials have been published, the figure given being some 2σ. Although the view of Davis and Saul that the tract potentials should be regarded as true auditory action potentials must be considered well substantiated by the experimental evidence adduced by these observers, opinion has continued to oppose the neural hypothesis of origin of the cochlear effect, chiefly in view of its diffuse distribution and its resistance to anæsthesia. Additional evidence which has been considered to contra-indicate the neural theory of origin of the cochlear effect has also been provided by the observations of Davis and his collaborators [1934] upon:

(*a*) The latent period of the cochlear effect, the figure arrived at being approximately $0{\cdot}1\sigma$.

(*b*) The absence of any quantal characteristics exhibited by the continuously variable amplitude of the cochlear effect in response to changes in intensity of the stimulating sound.

Of the various experimental findings generally considered to weigh against the neural theory of origin of the cochlear response, the most important is that which concerns its diffuse distribution. It should be noted that diffused potential changes around any set of active neural elements in the body do not ordinarily permit of experimental assessment owing to the unfavourable electrical conditions, *i.e.* the conducting nature of the surrounding tissues, any pair of recording electrodes in the neighbourhood being effectively short-circuited.

That such conditions do not obtain in the cochlea is clearly visualized by Adrian [1931 *b*], who suggests that the intracochlear generators of the potentials in question are insulated from the surrounding tissues by the bony cochlear wall. It seems likely that any source of potential change so insulated would give rise to an electrical disturbance spreading diffusely *via* localized low-resistance pathways such as the round window, and equally so whether such a source were neural or non-neural. Thus supposing the potential changes to be the response of the cochlear nerve endings then the auditory nerve at any point distal to the brain stem would be the seat of a dual electrical disturbance; firstly, true action potentials passing along it at the rate of the normally conducted nervous impulse with a relatively high latent period, and secondly, the spread of the same potential changes in the cochlear nerve endings employing the nerve now as a simple conductor; the latent period being very low and the

speed of conduction that of an electric current, the effect rapidly failing on passing beyond a point where insulation by the bony cochlear wall is effective in preventing loss from short-circuiting. Thus, granting the insulating action of the bony cochlear wall it is difficult to regard the diffused distribution of the cochlear effect as radically opposing the possibility of its neural origin.

Reaction of the cochlea effect to anæsthesia. The marked reaction of the potential changes in the auditory tracts to anæsthesia evoke agreement with Davis and Saul in regarding these as true action potentials. That there should, however, be a conspicuous difference in reaction to anæsthesia between action potentials in the mid-brain and potentials arising in the terminal fibres of the cochlear nerve cannot be regarded as wholly surprising in view of the presence of synaptic junctions between these points. The relatively insignificant effect upon the cochlear response of anæsthesia up to the point of circulatory failure may be no more than the expression of the difference in sensitivity to blood-borne narcotic substances between synaptic junctions and nerve fibres, death of the animal due to junctional involvement supervening before the attainment in the blood of a concentration level sufficient to affect terminal nerve fibres.

The latent period of the cochlear response. Although the period $0{\cdot}1\sigma$ found by their measurements to elapse between the arrival at the tympanic membrane of the head of a short train of sound waves and the initiation of the cochlear response is tentatively ascribed by Davis and his co-workers to lag in transmission by the ossicular chain, it is difficult to share their disinclination to attribute any of this period to true latency of the cochlear effect. Though the true latent period of the cochlear effect may have a value even less than $0{\cdot}1\sigma$, this, accepting the neural view of its origin, would make necessary the attribution to the terminal fibres of the cochlear nerve exceptional, but not, it is thought, inconceivable characteristics in respect of latency.

The absence of quantal characteristics exhibited by the cochlear effect in respect of intensity variations. It seems worthy of note that the terminal network of the cochlear nerve endings have an anatomical constitution differing significantly from such structures as nerve bundles in which quantal characteristics have been classically demonstrated. In these structures nerve elements are relatively few and as anatomical entities better defined. The density of a neural network as found in the terminal ramifications of the cochlear nerve makes it likely that even at low intensities of stimulation considerable numbers of neural elements are in-

volved. Any physiologically effective increase in intensity of the stimulus would involve fresh nerve elements whose numerical ratio to the sum total of those already in operation would be so small that the resulting step in amplitude of the total response would be beyond the resolving power of available means of experimental assessment. In addition, if the existence of an extra-neural tuning mechanism, direct evidence of which [Hallpike and Rawdon-Smith, 1934] has recently been adduced, be accepted, it seems worthy of note that such a mechanism would operate in the direction of bringing into play in response to intensity increases a smoothly increasing number of units of the finely subdivided network of the cochlear nerve endings.

Regarding possible sources of a non-neural character of the cochlear effect, suggestions which have been advanced include:

(*a*) The membrane hypothesis [Hallpike and Rawdon-Smith, 1934] whereby the potential changes are conceived as being engendered by movements of polarized membranes, *e.g.* that of Reissner or the tectorial membrane; though the evidence of such polarization cannot be regarded as more than circumstantial. This hypothesis is not supported by the results of the present investigation in view of the absence of cochlear response with normal morphology of the membranes in question and of the stria vascularis, to whose secretory activity was attributed the maintenance of polarization of the membrane of Reissner.

(*b*) The sensory cell hypothesis put forward by Davis and his collaborators [Davis *et al.* 1934]. This hypothesis regards the potential changes as being engendered by mechanical deformation of the sensory cells of Corti's organ. The use of the term sensory cell in this sense is not free from ambiguity. It is possible to take the view that a sensory cell can only be so considered in respect of its normally associated nerve-ending complex. Thus a "sensory cell response" might well be supposed to include potential changes engendered by the nerve-ending complex, and so be said to have a neural origin. That no such neural significance is attached by Davis and his co-workers to their use of the term "sensory cell response" is indicated by their further hypothesis that to this response is to be attributed the initiation of the action potentials in the nerve-ending complex itself. Thus they clearly accept the possibility of the cells of Corti's organ giving rise to the potential changes in question in the absence of such nerve-ending complexes.

This belief is not supported by the results of the present investigation in view of the failure of the cochlear response in the presence of morphologically normal sensory cells with absence only of neural elements.

SUMMARY.

The histological changes in the internal ear resulting from intracranial section of the VIIIth nerve in the cat are described.

The results support the views of Witmaack and of Kaida that it is possible by means of this procedure to bring about in some cases an isolated degeneration of the neural elements of the cochlea, with preservation of the vascular supply, in spite of the fact that the point of section is central to the spiral ganglion.

The electrical responses of the cochlea and auditory tracts were found to be absent in a series of cats, six months after section of the corresponding VIIIth nerve, and in one of them, histological examination revealed the presence of such an isolated degeneration of the neural elements.

Since the structure of the cochlea seemed otherwise unchanged, this finding provides evidence which, though of a purely morphological character, apparently supports the neural view of origin of the Wever and Bray phenomenon. Some of the arguments against this view are examined and thought to be inconclusive.

ADDENDUM.

At the time of going to press, Guttman and Barrera[1] have published results of experiments of a similar type in which section of the VIIIth nerve was carried out in a number of cats. Degeneration of the neural elements of the cochlea ensued as described by Wittmaack. It is stated that in some cases the internal auditory artery was cut at the operation of nerve section and in other cases not. Nevertheless, in all cases following this operation and at intervals after it of 10 days to 6 weeks, the cochlear response was found to have undergone no significant reduction. It is the common experience that the immediate results of section of the VIIIth nerve with concomitant section of the internal auditory artery is a rapid fall of the cochlear response to the post-mortem level[2].

Rapid and considerable decrease of the cochlear response resulting from section of the internal auditory artery with the VIIIth nerve appears therefore to be a well-attested fact. It would appear, further, that such abolition must be ascribed to changes in the cochlea which are in effect the early stages of the massive necrosis of the cochlear contents, a later

[1] *Amer. J. Physiol.* 1934, **109**, 704.

[2] *Vide* Wever, E. G. and Bray, C. W. (1930), *J. exp. Psychol.* **13**, 5. Davis, H., Derbyshire, A. J., Lurie, M. H. and Saul, L. J. (1934), *Amer. J. Physiol.* **107**, 316. Hallpike, C. S. and Rawdon-Smith, A. F. (1934), *J. Physiol.* **81**, 401.

stage of which is represented in Text-fig. 1. It is difficult to envisage any stage in the development of these necrotic changes in which, as seems indicated by the results of Guttman and Barrera, the cochlear response could be restored to its original level. The histological changes found in the cochleæ of some of the animals dealt with in Part I of this paper come within the period mentioned by Guttman and Barrera (10 days to 6 weeks after the operation of section of the VIIIth nerve and of the internal auditory artery). These changes, though stopping short of the formation of masses of new bone, show, nevertheless, a degree of cochlear disorganization which does not appear compatible with the possibility of a normal electrical response.

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EXPLANATION OF PLATES.

Plate I.

Fig. 1. Right cochlea. Normal. The neuroglial-neurilemmal junction in the trunk of the nerve is shown. (× 30 *circa*.)

Fig. 2. Left cochlea. Side of nerve section. Showing site of section. The canal of the modiolus contains neurilemmal remnants with scattered medullated fibres. (× 30 *circa*.)

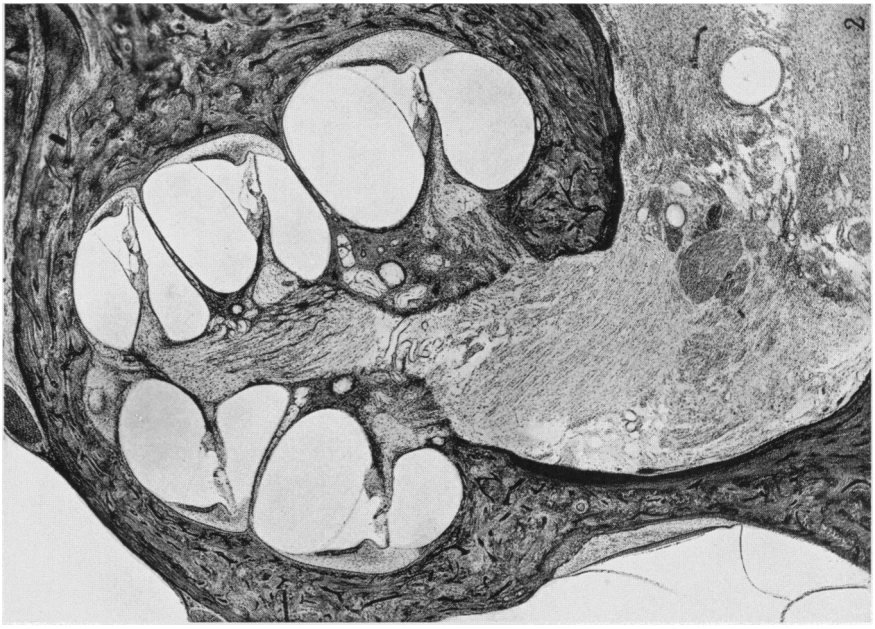
Plate II.

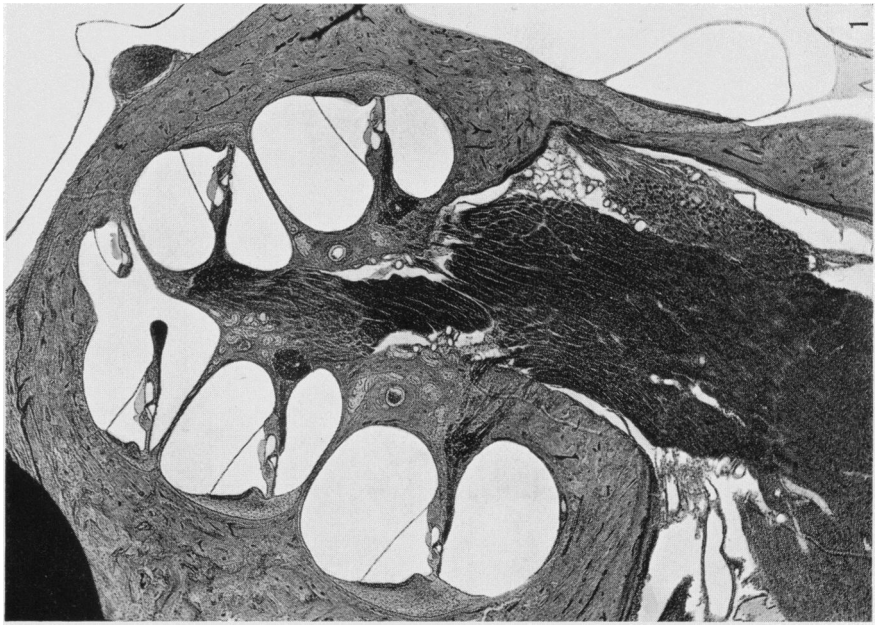
Fig. 1. Right cochlea. Ductus cochlearis and spiral ganglion. Normal. (× 75 *circa*.)

Fig. 2. Left cochlea. Side of nerve section. Showing absence of cells of the spiral ganglion. Numerous blood containing capillaries are present. Organ of Corti and stria vascularis normal. (× 75 *circa*.)

Fig. 3. Right cochlea. Organ of Corti. Normal. (× 250 *circa*.)

Fig. 4. Left cochlea. Side of nerve section. Showing absence of nerve fibrils crossing the tunnel of Corti and of medullated fibres in the osseous spiral lamina. Hair cells, rods of Corti, and tectorial membrane normal. (× 250 *circa*.)





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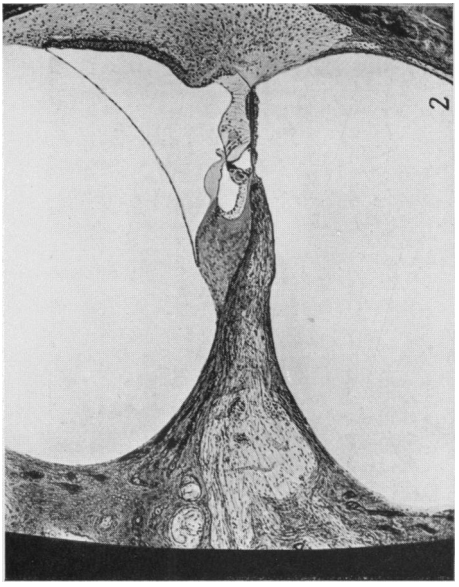

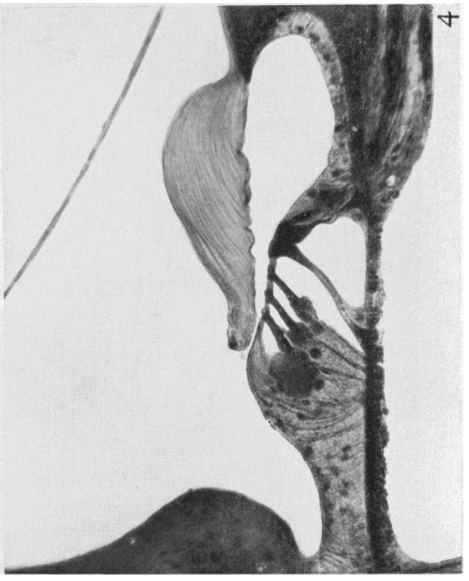

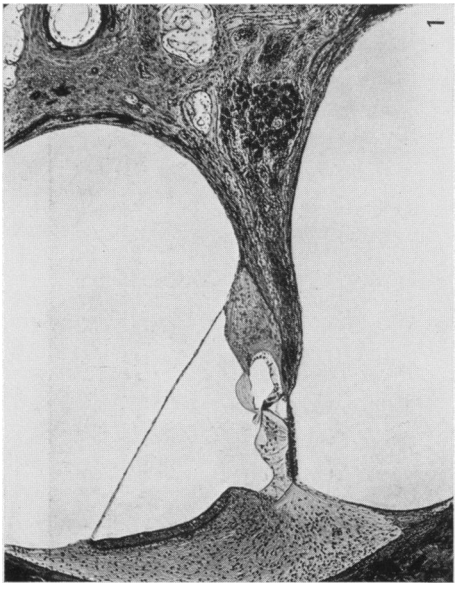

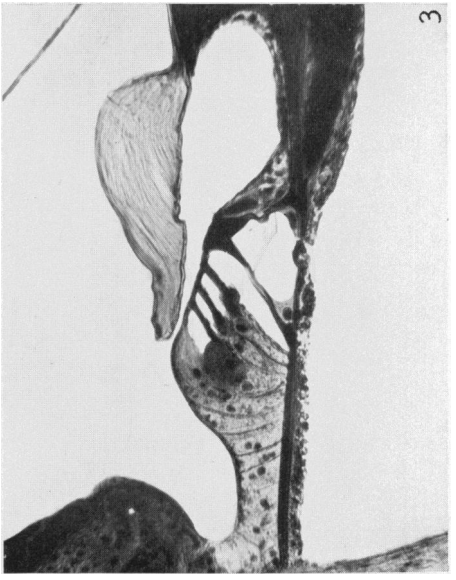

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