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TRANSNEURONAL CELL DEGENERATION IN THE AUDITORY RELAY NUCLEI OF THE CAT

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INTRODUCTION

Transneuronal cell degeneration was first recognized in the dorsal nucleus of the lateral geniculate body after removal of the eye (Minkowski, 1913), and despite several claims for its occurrence at other sites in the central nervous system it is still generally considered that the lateral geniculate nucleus might be the only site for its unequivocal demonstration (cf. Torvik, 1956). It is possible, however, that it may occur in the relay nuclei of other sensory pathways as well as in certain cerebral and brain-stem systems. This possibility is of interest for two reasons, one relevant to the degenerative process itself and the other to its use as an experimental technique.

First, little is known about either the factors initiating the degeneration or about those influencing the severity of the cellular change. It has been shown, for example, that the cellular degeneration in the lateral geniculate nucleus following removal of the eye is both more rapid in onset and more severe in the macaque than in the cat and rabbit (Matthews, Cowan & Powell, 1960), but it is not known whether the time-course and degree of cellular change is the same in different afferent sensory systems of the same species. It is also not clear to what extent the cellular change is affected by such factors as the morphology of the afferent nerve endings or the size of the cell. Secondly, if transneuronal cell degeneration is found to occur in other systems it might be possible to use it as an experimental technique, not only for analysing more precisely the organization of the projection of the peripheral receptors upon the central relay nuclei, as was done by Le Gros Clark & Penman (1934) for the projection of the retina, but also for tracing connexions in systems where it is difficult to determine whether fibres are actually terminating or simply passing through a nucleus.

A study of transneuronal cell degeneration in the primary auditory relay nuclei of the cat should give answers to some of these questions. For example, the results of the detailed study of this form of cellular degeneration in the lateral geniculate nucleus of the cat by Cook, Walker & Barr (1951) can be used for a comparison of the degeneration in two afferent systems, and in addition there are, within the cochlear nuclei, distinct differences in both the type of afferent nerve ending and in the size of the cells. The value of the possible application of this cellular degeneration as an experimental technique for elucidating the connexions of the auditory system need hardly be stressed. Apart from the need for defining more precisely the topical organization of the projection of the basilar membrane upon the cochlear nuclei it is necessary to determine the main sites of termination of the primary auditory fibres (cf. Galambos, 1954).

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MATERIAL AND METHODS

Ten mature cats of both sexes were used in this study. In all the animals the bulla was exposed on one side and the cochlea destroyed. After being allowed to survive for periods varying from 30 to 359 days, (the intervals having been chosen to correspond in general with those of Cook *et al.* (1951)) the animals were killed and the brains and temporal bones fixed in 70% alcohol and 2% acetic acid. The brain of one normal animal was used as a control. Blocks of the brain stem were embedded in paraffin wax and cut transversely at 25 μ. A one in five series of sections was mounted and stained with thionine.

The severity and the extent of the transneuronal cell degeneration and glial reaction were studied qualitatively in the cochlear nuclei, the nuclei of the superior olive and the trapezoid and lateral lemniscal nuclei. Quantitative studies were made of the degree of the cellular degeneration in all but the last of these nuclei in nine animals. In the tenth animal the cochlear nuclei had been inadvertently damaged at operation.

Cell shrinkage was estimated by drawing, on mm. graph paper with the aid of a camera lucida, the outlines of the cell, nucleus and nucleolus of fifty neurons on the normal and atrophied sides. The linear magnification was adjusted to exactly 1000 times so that a measurement in μ^2 was obtained of the nucleolar, nuclear and total cell area by counting the number of squares contained within each outline. The samples were taken at comparable levels on the two sides of the brain stem and at corresponding levels in each animal. Thus, for the medial trapezoid nucleus, the lateral superior olive and the dorsal cochlear nucleus two sections at the middle of the rostro-caudal extent of the nuclei were used, and for the postero-ventral and the antero-ventral nuclei the seventh and eighth sections from their caudal and rostral ends respectively were taken. Sample fields were taken at random throughout the cross-sectional area of the nucleus, and the only criterion used for selection of the cells was the presence of a distinct nucleolus.

In one experiment (survival period 319 days) an estimate was made of the total number of cells in the ventral cochlear nucleus and the lateral superior olive on the normal and atrophied sides. The areas of the nuclei in every section of the series (125 μ apart) were measured from projection drawings on 1 in. graph paper at a magnification of fifty times. The volume of the nucleus was then calculated (Dornfeld Slater & Scheffe, 1942). Counts of the number of cells per unit area of section were made throughout the length of these nuclei using an oil immersion objective and a field of known diameter. Only neurons with a distinct nucleolus were counted, and the size of the sample was of the order of 2% of the total cell population of the ventral cochlear nucleus and 7% of that of the lateral superior olive.

In the female animals the nucleolar sex satellite was very conspicuous, and in two animals—one short and one long survival period—the position of the satellite in relation to the nucleolus or the nuclear membrane was determined in approximately 500 cells of the lateral superior olive and the ventral cochlear nucleus on the normal and atrophied sides.

In order to determine the extent of the lesion the temporal bones from *one* animal (survival period 319 days) were decalcified and sectioned, and alternative series were

stained with haematoxylin and eosin and Bodian's protargol method. The bones from other animals were not cut because the distribution of the degeneration in the brain stem was the same in all animals.

RESULTS

After destruction of the cochlea, with severe degeneration or complete atrophy of the cochlear nerve, unequivocal changes are found in the neurons of certain of the primary and secondary auditory relay nuclei. In some, but not in all, a glial reaction accompanies the neuronal degeneration. On the ipsilateral side of the brain-stem cellular changes are seen in the ventral cochlear nucleus, in the lateral superior olive and in the pre-olivary nuclei. On the contralateral side the cells of the medial trapezoid nucleus and of the nuclei of the lateral lemniscus are affected. It is difficult to be certain about any neuronal degeneration in the dorsal cochlear nucleus, but definite gliosis is present.

The findings are presented in two sections. In the first section the appearance of both the normal and degenerated nuclei is described and each nucleus is considered separately. Only a brief account of the normal morphology of these nuclei is given because detailed accounts are already available (Cajal, 1909; Fuse, 1913); reference is made mainly to those points relevant to an understanding of the degenerative changes. The quantitative data are given in the second section in the form of tables and graphs and here most of the nuclei are treated together.

Qualitative description of the degeneration

The dorsal cochlear nucleus lies dorsal to the posterior part of the ventral cochlear nucleus and in Nissl-stained preparations is seen to be distinctly laminated (Pl. 2, fig. 5). Immediately beneath the outer ependymal layer is the molecular layer in which are a number of small round cells and a few medium-sized neurons. Deep (or ventral) to it is the characteristic 'spindle-cell layer' which is two or three cells thick. The cells are spindle or pyramidal in shape and are quite deeply staining; they are arranged regularly with their long axes perpendicular to the surface and they have well-defined dendritic processes. The deep polymorph layer is the thickest but is sparsely populated; most of the cells are medium-sized but there is an occasional larger pyramidal cell. No appreciable cellular degeneration is seen in this nucleus at any time up to 359 days after destruction of the cochlea. The cells of the spindle layer certainly show no change, but the possibility of some alteration in those of the polymorph layer cannot be excluded because of their sparse distribution and variation in size. There is, however, a marked increase in the number of glial cells in the polymorph layer. It is more pronounced after the shorter survival periods and becomes progressively less intense after survival periods of several months.

Ventral cochlear nucleus. It is generally accepted that the ventral cochlear nucleus can be divided into an anterior (antero-ventral) and a posterior (postero-ventral) portion (Rose, Galambos & Hughes, 1959). The cells are of medium size, rounded, with short processes and have a relatively large amount of cytoplasm. In the majority the Nissl material is fine and evenly distributed but in some it is aggregated into larger clumps. In the anterior part of the nucleus a further medial and lateral

Text-fig. 1. Diagrammatic representation of the distribution of the cellular degeneration and gliosis in the auditory relay nuclei after destruction of the cochlea. The drawings were made by means of a projection apparatus of transverse sections of the brain stem stained with thionine. The relay nuclei which show cellular shrinkage and gliosis are indicated in black, those in which cell atrophy occurs without accompanying gliosis are indicated by stippling, and those where gliosis is found without appreciable cell change by hatching.

subdivision can be recognized in transverse sections of the brain stem. In the medial part, which is triangular in cross-section, the cells are smaller, rounder and paler-staining than in the lateral part and they are more compactly arranged (Pl. 1, fig. 1). In sagittal sections Rose *et al.* (1959) describe the oral part of the antero-ventral nucleus as having small cells which are more closely packed than in the caudal part of this element, and it is probable that this rostral portion corresponds to the medial subdivision described here. The cells of the lateral subdivision are of the same order of size as those in the postero-ventral part of the nucleus but they are more uniform in size. To facilitate the description of the results these two portions of the antero-ventral cochlear nucleus will be called the medio-ventral and latero-ventral nuclei, respectively. Destruction of the cochlear nerve results in clear-cut changes in all subdivisions of the ventral nucleus (Text-fig. 1). Thirty days after operation the cells are more compactly arranged but otherwise show no change; severe gliosis is present throughout the nucleus but is most obvious at the level of entry of the nerve. After 60 days the nucleus is distinctly smaller in its cross-sectional area, and all subdivisions appear to be equally affected. The cells are more densely packed than on the normal side and are definitely shrunken (Pl. 1, fig. 2 Table 10). They are also more uniform in size and shape and have less prominent dendritic processes. Many of the cells are slightly paler than normal, and their Nissl material is more homogeneous in its distribution. The nucleus and nucleolus are shrunken but are not altered in position. There does not appear to be any cell loss. After longer survival periods the appearance of the cells remains essentially the same, but the glial reaction diminishes.

Superior olivary nuclei

The lateral superior olive is S-shaped in transverse section and is found at a level corresponding approximately to the middle of the rostro-caudal extent of the antero-ventral nucleus (Text-fig. 1). Most of the cells are spindle-shaped, have prominent dendrites at each end and lie with their long axes at right angles to the corresponding part of the nucleus; a few are round or pyramidal in section (Pl. 3, fig. 9). There is a moderate amount of Nissl material in the form of fine granules evenly distributed. Thirty days after destruction of the cochlea this nucleus shows no appreciable change. After 60 days, however, severe shrinkage and pallor of the cells are quite obvious even at low magnifications. At higher magnifications the nuclei of the cells are also found to be smaller, and the Nissl material is seen to be considerably reduced and to have a homogeneous appearance. The nucleus as a whole shows no diminution in its cross-sectional area, and there is no gliosis. Not only is there no compacting of the cells, but indeed they are more widely spaced apart. After longer survival periods the appearance of the nucleus remains the same, pallor and shrinkage of the neurons being the only change (Pl. 3, fig. 10). At no stage is there any sign of cell loss or glial reaction.

The medial superior olive is formed of a narrow band of cells which extends obliquely in a ventro-lateral direction on the medial side of the lateral superior olive. Long, well-defined dendrites extend medially and laterally from the cell bodies. This nucleus shows no change after destruction of the cochlea.

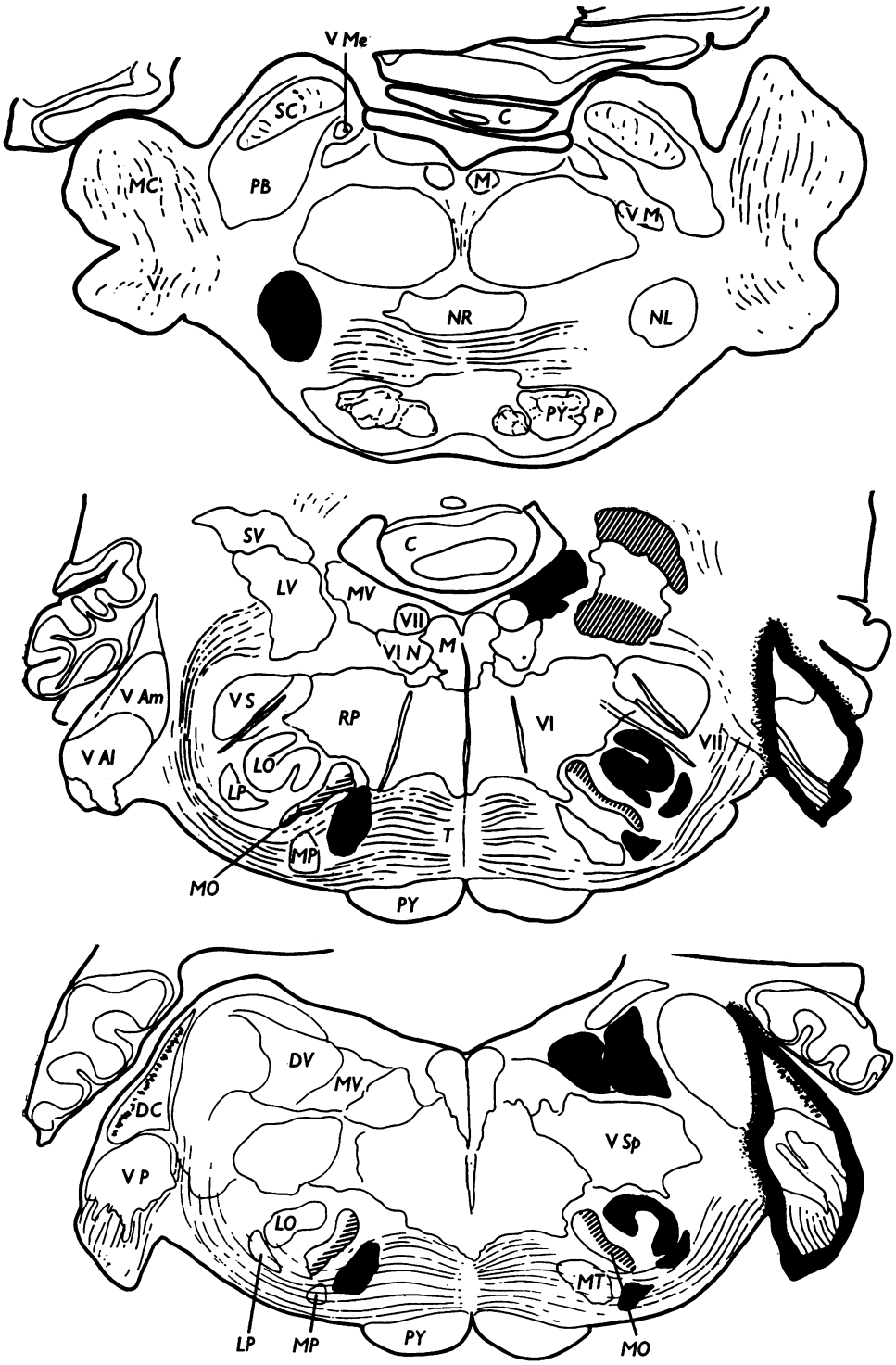
The medial trapezoid nucleus lies ventro-medial to the medial superior olive, with

its cells scattered amongst the deeper fibres of the trapezoid body. It is triangular in transverse section with its apex directed dorsally (Text-fig. 1). The neurons, which are quite deeply staining, are medium-sized and round or triangular in shape. In the nucleus of the contralateral side the neurons undergo definite changes following destruction of the cochlear nerve. After 30 days the cells are slightly smaller and paler than on the ipsilateral side, and these changes become more pronounced from 60 days onwards (Pl. 2, fig. 8). Examination at higher magnifications shows that the cell bodies are smaller but that there is no shrinkage of the nucleus, with the result that the nuclear-cytoplasmic ratio is considerably raised; as in the lateral superior olive, there is no compacting of the cells nor is there any gliosis. Furthermore, no gliosis can be seen amongst the fibres of the trapezoid body.

The ventral and lateral pre-olivary nuclei and lateral lemniscal nuclei. The preolivary nuclei are small groups of cells amongst the fibres of the lateral part of the trapezoid body and lie ventral to the medial and lateral superior olivary nuclei, respectively (Text-fig. 1). The dorsal and ventral nuclei of the lateral lemniscus are found more rostrally as two groups of cells interspersed amongst the ascending lemniscal fibres. In the pre-olivary nuclei of the ipsilateral side and in the lateral lemniscal nuclei of the contralateral side the cells show changes similar in appearance and time course to those found in the contralateral medial trapezoid nucleus. Furthermore, these nuclei are similar in showing neither gliosis nor any compacting of the cells.

A careful search was made in the region dorsal to the medial superior olive for evidence of retrograde cell degeneration (in the form of cell shrinkage or cell loss) because of Rasmussen's observation (1946) that the centrifugal fibres to the cochlea originate here, but in none of the experiments was there any evidence suggestive of retrograde degeneration. This is in no way in conflict with Rasmussen's evidence as the cells in question may be resistant to axonal section or they may have recovered within 30 days (the shortest survival period in this series). In all these experiments the vestibular nerve was not affected and there is no change in the cells of the vestibular nuclei.

In one experiment, A8, in addition to destruction of the cochlea, the dorsal and ventral cochlear nuclei were inadvertently destroyed. The survival period was 60 days. Following the involvement of the primary relay nuclei, the proximal parts of the trapezoid body and of the dorsal and intermediate striae show intense gliosis; but as these tracts are traced towards and across the mid-line the gliosis decreases so that the contralateral lemniscus shows only a moderate, diffuse glial reaction. The lateral superior olive and pre-olivary nuclei of the same side, and the medial trapezoid and lateral lemniscal nuclei of the opposite side all show essentially similar changes (Text-fig. 2). These nuclei are all reduced in cross-sectional area and are severely gliosed; their constituent cells are shrunken, paler than normal and more densely packed together. The gliosis in the contralateral medial trapezoid nucleus is particularly conspicuous. The changes in the medial superior olive of both sides is quite characteristic. The involvement of the cochlear nuclei has resulted in severe gliosis amongst the dendrites on the lateral side of the cell bodies of the ipsilateral nucleus and amongst those on the medial side of the cell bodies on the contralateral side. The cells do not appear to be altered on either side. In this experiment the vestibular nerve has been damaged and intense gliosis can be seen extending from



Text-fig. 2. Diagrammatic representation of the distribution of the cellular degeneration and gliosis in the secondary auditory relay nuclei and in the vestibular nuclei after destruction of the cochlear nuclei and vestibular nerve. The extent of the lesion is indicated by a thick black line, the nuclei which show cell atrophy accompanied by gliosis in black, and those in which only gliosis occurs by hatchings.

the nerve into most of the cross-sectional area of the superior vestibular nucleus and into the ventral part of the lateral vestibular nucleus of the same side (Text-fig. 2). A more diffuse and less severe glial reaction has occurred in the medial and descending nuclei. In the medial and descending nuclei definite shrinkage and pallor of the cells can be seen; in the affected part of the lateral nucleus some of the cells are smaller but the giant pyramidal cells show no change. There is no appreciable alteration of the cells of the superior vestibular nucleus.

Quantitative observations

The data on the mean areas of the cells, nuclei and nucleoli, together with standard errors of the means, are presented in Tables 1–6. The figures for each nucleus are given separately and in each case they are arranged in order of increasing survival periods. Measurements of the cells in the postero-ventral nucleus after 120 days, and in the latero-ventral nucleus after 200 days, were not made because the lateral parts of these nuclei were damaged during removal of the brain. The cellular degeneration in the pre-olivary and lateral lemniscal nuclei was not studied quantitatively. In Tables 7–9 the percentage changes in the areas of the cells, nuclei and nucleoli at each survival period are given, together with the results of the *t*-test for the significance of each comparison. Each percentage change is calculated with reference to the unaffected nucleus in that experiment. The accompanying graphs (Text-fig. 3) showing the time-course of the degeneration in the auditory relay nuclei are constructed from these data, and, for the sake of comparison, a similar graph has been drawn for the lateral geniculate nucleus from the results of the study by Cook *et al.* (1951).

These tables show that although the mean values of the areas of the normal cell, nucleus and nucleolus in the auditory relay nuclei vary between different animals the relative sizes of these structures usually remain similar. The largest cells are found in the postero-ventral nucleus and the smallest in the lateral superior olive; the cells in the latero-ventral nucleus, those of the spindle-cell layer of the dorsal cochlear nucleus and those of the medial trapezoid nucleus are all of the same order of size. In general, the quantitative data confirm the qualitative impressions of the degeneration in the respective nuclei, and a comparison of the qualitative descriptions with Table 7 makes it clear that a shrinkage of approximately 20% of the cell body must occur before any diminution in size can be detected qualitatively. With the exception of the medial trapezoid nucleus, in which the nuclei and nucleoli do not undergo any shrinkage and which will be considered separately, the degenerative process in the cells of the different relay nuclei follows the same time-course and is of the same degree of severity. The slight differences found between individual nuclei in the same animal and between the degree of shrinkage of the cells of the same nucleus at different survival periods (after the appearance of degenerative changes) can probably be accounted for in part by technical difficulties of sampling and measuring, by 'biological variation' and possibly by minor differences in the extent of the lesion.

Apart from the postero-ventral nucleus, marked shrinkage of the cell body, nucleus and nucleolus is only found after survival periods of 60 days or longer. In the postero-ventral nucleus, however, a shrinkage of 17% of the total cell area is found as early

Tables 1–6. *Mean areas for 50 neurons from normal and atrophied auditory relay nuclei at different survival times after unilateral destruction of the cochlea, and of the nuclei of the two sides of a normal control*

Table 1. *Postero-ventral nucleus*

(Fifty neurons in each sample.)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.
Control	348·7 (normal)	14·21	352·3 (atrophied)	13·03	74·48 (normal)	1·57	77·5 (atrophied)	1·66	7·64 (normal)	0·18	7·34 (atrophied)	0·22
30	471·1	14·20	389·9	18·92	85·8	2·08	88·7	2·92	7·8	0·24	7·9	0·28
60	422·7	20·40	344·3	16·86	81·9	2·67	76·4	2·37	8·2	0·23	7·0	0·20
90	465·5	18·18	307·1	13·11	79·1	1·82	73·4	2·46	5·6	0·17	4·5	0·17
140	362·7	13·70	269·1	10·23	81·2	1·97	68·8	1·94	4·6	0·13	4·1	0·14
201	482·7	19·96	307·1	12·35	84·9	1·85	69·2	1·87	4·8	0·13	4·3	0·14
272	361·9	14·41	264·7	12·81	79·9	1·49	67·3	1·63	5·1	0·16	4·5	0·18
319	467·1	23·32	304·3	14·20	83·3	2·27	65·5	2·37	5·0	0·15	4·2	0·19
359	359·5	16·93	284·7	13·35	70·0	1·60	64·7	1·45	6·5	0·14	5·6	0·16

Table 2. *Latero-ventral nucleus*

(Fifty neurons in each sample.)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.
Control	349·1 (normal)	9·20	333·5 (atrophied)	9·21	83·6 (normal)	1·47	79·7 (atrophied)	1·51	6·9 (normal)	0·14	6·8 (atrophied)	0·17
30	337·9	8·81	304·7	7·90	85·0	1·44	88·3	1·42	4·5	0·10	4·2	0·12
60	355·1	13·82	233·1	7·37	73·8	2·55	59·7	1·55	4·7	0·15	4·0	0·13
90	417·9	11·11	315·1	11·22	88·6	1·81	75·9	1·76	5·3	0·14	4·6	0·16
120	355·9	11·80	267·1	8·05	82·1	2·15	64·4	1·58	4·2	0·08	3·6	0·12
140	375·5	12·63	265·9	6·11	91·7	1·99	75·4	1·25	6·04	0·19	5·2	0·15
272	335·7	8·67	229·7	6·48	72·7	1·73	59·3	2·14	4·31	0·10	3·5	0·12
319	409·9	17·67	265·9	10·26	88·9	3·07	65·4	2·46	5·3	0·21	3·9	0·12
359	330·7	16·42	263·1	10·45	93·7	2·64	71·1	2·07	5·8	0·19	4·6	0·16

Table 3. *Medio-ventral nucleus*

(Fifty neurons in each sample.)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E
Control	263·5 (normal)	8·0	267·5 (atrophied)	6·69	68·3 (normal)	1·42	67·0 (atrophied)	1·29	6·4 (normal)	0·21	6·4 (atrophied)	0·19
30	262·7	8·81	257·1	9·10	71·3	2·03	65·5	1·55	6·2	0·19	6·1	0·20
60	253·5	9·40	215·1	7·81	77·6	1·49	64·6	1·33	6·2	0·19	5·9	0·18
90	329·9	8·54	240·3	7·20	75·4	1·16	62·4	1·14	6·0	0·19	5·1	0·15
120	259·5	8·63	207·5	5·42	63·4	1·66	56·8	1·16	5·4	0·16	5·0	0·15
140	331·9	7·24	216·3	6·24	79·7	1·45	64·1	1·24	4·8	0·14	4·0	0·10
201	247·9	6·33	172·5	5·50	55·9	1·53	46·3	1·37	3·8	0·09	3·3	0·10
272	249·1	8·02	205·5	6·08	76·5	1·65	66·4	1·09	4·8	0·12	4·2	0·12
319	310·3	12·98	217·9	6·31	70·6	2·19	63·0	1·43	4·6	0·16	4·1	0·12
359	225·9	5·61	169·5	4·49	61·3	1·26	52·4	1·18	5·0	0·19	4·5	0·20

Table 4. *Lateral superior olive*

(Fifty neurons in each sample.)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.
Control	227·5 (normal)	8·66	235·1 (atrophied)	7·91	55·9 (normal)	1·63	55·4 (atrophied)	1·40	6·7 (normal)	0·18	6·3 (atrophied)	0·19
30	237·9	9·10	207·9	7·22	53·1	1·86	48·4	1·52	4·5	0·10	4·2	0·12
60	278·7	11·34	197·1	7·81	66·6	2·30	49·2	1·85	7·4	0·28	6·2	0·21
90	258·3	8·36	201·1	7·18	56·1	1·43	45·9	1·38	7·9	0·23	6·8	0·22
120	204·3	6·73	151·1	4·73	52·9	1·61	41·4	1·15	6·6	0·21	5·4	0·21
140	182·3	6·16	129·5	6·46	41·0	1·51	34·7	1·53	5·4	0·16	4·9	0·17
201	231·1	10·49	166·9	7·47	42·3	1·68	33·5	1·43	4·0	0·9	3·3	0·12
272	192·7	8·26	149·1	4·79	44·0	1·73	37·0	1·18	4·6	0·18	3·9	0·16
319	208·3	13·05	140·7	6·9	42·1	1·68	32·9	1·57	5·0	0·19	3·7	0·14
359	205·5	9·84	159·5	12·34	39·1	1·95	31·0	1·64	4·1	0·16	2·8	0·14

Table 5. *Medial trapezoid nucleus*

(Fifty cells in each sample)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.	Right	S.E.	Left	S.E.
Control	328·7 (normal)	9·50	314·3 (atrophied)	7·54	45·6 (normal)	1·52	44·1 (atrophied)	1·48	5·5 (normal)	0·14	5·8 (atrophied)	0·15
30	390·6	12·38	316·0	10·68	66·1	1·83	67·0	1·97	4·4	0·09	4·1	0·09
60	368·7	11·43	307·9	9·52	56·0	1·81	59·5	1·70	4·0	0·08	3·7	0·13
90	392·7	12·66	301·5	9·49	58·2	2·36	59·6	1·43	6·4	0·23	6·7	0·18
120	370·7	11·79	286·3	9·96	58·4	1·87	57·6	1·47	3·6	0·10	3·8	0·13
140	308·3	11·93	254·7	10·17	49·4	1·77	50·1	1·37	3·5	0·11	3·7	0·14
201	318·3	11·33	261·5	10·12	36·2	1·97	37·2	1·48	4·0	0·14	4·0	0·14
272	273·9	11·98	213·1	6·63	40·2	1·97	40·7	1·60	3·7	0·15	3·7	0·12
319	341·5	12·30	258·3	10·31	45·6	1·64	48·1	1·76	4·2	0·12	4·4	0·12
359	321·3	14·19	218·5	9·38	62·9	2·83	59·7	2·33	3·5	0·18	3·5	0·14

Table 6. *Dorsal cochlear nucleus*

(Fifty cells in each sample.)

Survival time (days)	Cell areas (μ^2)				Nuclear areas (μ^2)				Nucleolar areas (μ^2)			
	Normal	S.E.	Atrophied	S.E.	Normal	S.E.	Atrophied	S.E.	Normal	S.E.	Atrophied	S.E.
319	383·5	20·95	364·3	17·87	73·9	2·58	79·0	2·21	5·5	0·19	5·3	0·23
359	365·1	16·23	363·1	14·0	90·2	2·98	89·6	2·50	6·6	0·26	6·5	0·24

as 30 days after destruction of the cochlea, and after the same period a slight but significant degree of shrinkage occurs in the cells of the latero-ventral and lateral superior olivary nuclei amounting to approximately 10%. After survival periods of longer than 60 days, even up to 1 year, the shrinkage is more or less constant.

Tables 7–9 show the percentage changes in area of cell body, nucleus and nucleolus in neurons of the auditory relay nuclei at different survival periods after unilateral

destruction of the cochlea. Asterisks indicate level of significance by the *t*-test. *significant at 5% level; **significant at 1% level; ***significant at 0·1% level.

In all the nuclear groups for which quantitative data are available, and at almost all survival periods, the shrinkage of the total cell area is proportionately greater

Table 7. *Percentage change of cell area from normal*

Survival time (days)	Postero-ventral nucleus	Latero-ventral nucleus	Medio-ventral nucleus	Lateral superior olive	Medial trapezoid nucleus	Dorsal cochlear nucleus
Control	+ 1·0	− 4·6	+ 1·5	+ 2·4	− 4·5	—
30	−17·2**	− 9·8*	− 2·1	−12·6*	−19·1***	—
60	−18·5**	−34·3***	−15·1**	−29·4***	−16·5***	—
90	−34·0***	−24·6***	−27·1***	−22·1***	−23·2***	—
120	—	−24·9***	−20·0***	−26·0***	−22·7***	—
140	−25·8***	−29·1***	−34·8***	−28·9***	−17·3**	—
201	−36·3***	—	−30·4***	−27·7***	−17·8***	—
272	−26·8***	−31·6***	−17·5***	−22·6***	−22·1***	—
319	−34·8***	−35·1***	−29·7***	−32·4***	−24·3***	−5·0
359	−20·8***	−20·4**	−24·9***	−22·4***	−32·0***	−0·6

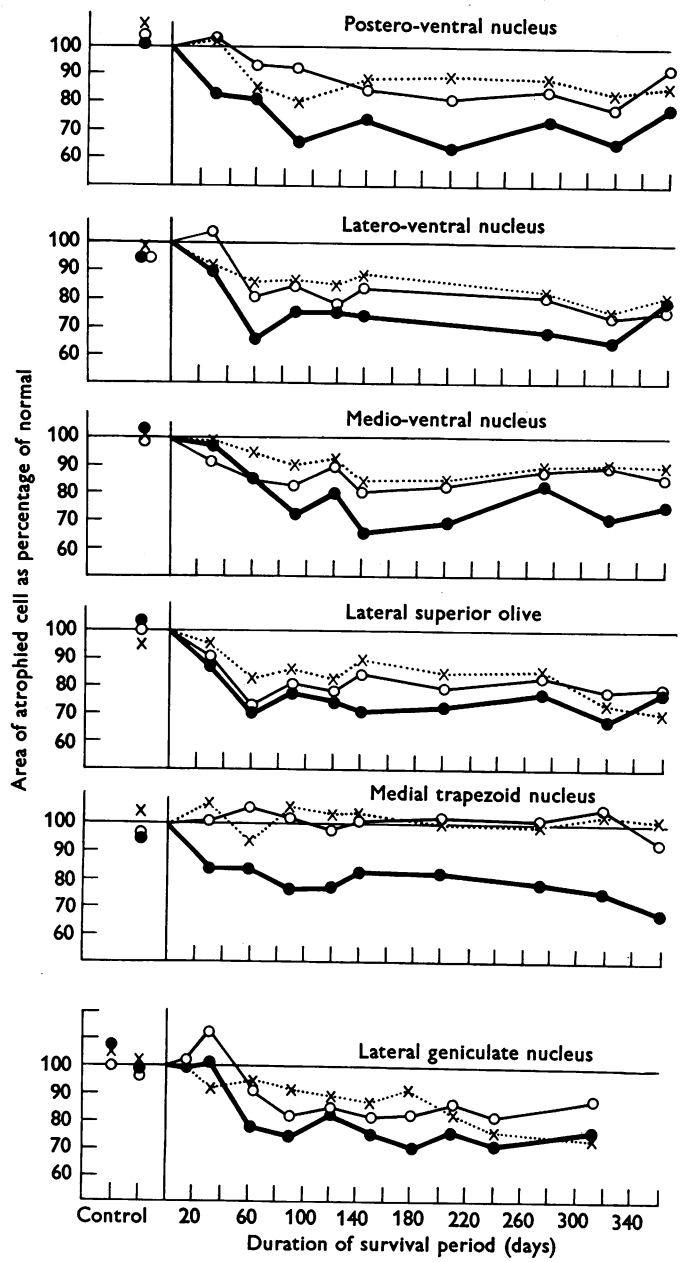
Table 8. *Percentage change of nuclear area from normal*

Survival time (days)	Postero-ventral nucleus	Latero-ventral nucleus	Medio-ventral nucleus	Lateral superior olive	Medial trapezoid nucleus	Dorsal cochlear nucleus
Control	+ 4·0	− 5·0	− 1·8	− 0·9	−3·4	—
30	+ 3·3	+ 4·0	− 8·1*	− 9·0	+1·2	—
60	− 6·7	−19·0***	−16·2***	−26·1***	+6·1	—
90	− 7·2*	−14·3***	−17·3***	−18·1***	+2·4	—
120	—	−21·4***	−10·0**	−21·7***	−1·3	—
140	−151·1***	−17·7***	−19·5***	−15·2**	+1·4	—
201	−18·5***	—	−17·1***	−20·8***	+2·5	—
272	−15·6***	−18·3***	−11·8***	−15·8**	+1·2	—
319	−21·4***	−26·0***	−10·7**	−21·8***	+5·4	+6·9
359	− 7·5*	−24·0***	−14·3***	−20·8***	−5·0	−1·3

Table 9. *Percentage change of nucleolar area from normal*

Survival time (days)	Postero-ventral nucleus	Latero-ventral nucleus	Medio-ventral nucleus	Lateral superior olive	Medial trapezoid nucleus	Dorsal cochlear nucleus
Control	+ 8·1*	− 0·9	0	− 5·3	+4·4	—
30	+ 1·2	− 7·0*	− 1·0	− 4·8	−7·1*	—
60	−13·9***	−13·9**	− 5·1	−17·1***	−6·0	—
90	−19·8***	−13·1**	−14·8***	−13·6**	+5·9	—
120	—	−14·6***	− 7·0	−17·2***	+3·2	—
140	−11·3*	−12·9**	−15·4***	−10·2*	+3·9	—
201	−10·3*	—	−13·2**	−15·5***	0	—
272	−11·5*	−17·5***	−11·6**	−15·5**	0	—
319	−16·9***	−25·1***	− 9·9*	−26·0***	+3·2	−2·9
359	−14·2**	−20·0***	−10·0*	−30·1***	0	−0·9

than that of the nucleus or nucleolus. For the ventral nuclei and the lateral superior olive this decrease in size amounts to between 20 and 35% of the normal area. At most of the intervals studied after 60 days the nuclear shrinkage is found to be between 10 and 25% and is usually more severe in the lateral superior olive than in



Text-fig. 3. Graphs to show the time-course of the changes in the mean cell, nuclear and nucleolar areas in the ventral cochlear, lateral superior olivary and medial trapezoid nuclei following destruction of the cochlea, and in the lateral geniculate nucleus after eye enucleation. Each mean value for the atrophied neurons is plotted as a percentage of the mean normal value for that animal. The graph of the lateral geniculate nucleus is constructed from the results of Cook *et al.* (1951). ● = cell area, ○ = nuclear area, × = nucleolar area.

the other nuclear groups. In two nuclear groups, the postero-ventral and latero-ventral, a slight increase in size of the nuclei is seen after 30 days similar to that found in the lateral geniculate nucleus by Cook *et al.* (1951). The time-course of the nuclear change in the cells of a particular nucleus usually parallels that of the cell area. Most commonly the nucleolus is found to undergo the least degree of shrinkage, and it was usually between 10 and 15%. It should be emphasized, however, that these estimates of nucleolar area are the least accurate of all the measurements partly because of the difficulty in outlining the nucleolus precisely, and partly because of the relatively large error in measuring such small areas outlined. No double nucleoli were observed either in the normal or atrophied cells.

The measurements of the neurons of the medial trapezoid nucleus show that there are distinct differences in the degenerative process at this site. The most obvious difference is that at almost all of the intervals studied there are no significant changes in the size of the nucleus and nucleolus despite the unequivocal and constant shrinkage of the cell area. Although the degree of shrinkage of the cell area is slightly less than that in the cells of the other nuclei, being between 15 and 25%, the time of onset of the degeneration of these cells appears to be earlier as they are found to have undergone a decrease in size of 19% at 30 days. Because of these exceptional findings many of the measurements of the cells of this nucleus were repeated, but with the same results.

Table 10. *Total volumes, mean numbers of cells per unit volume and total cell counts of normal and atrophied ventral cochlear and lateral superior olivary nuclei* 319 *days after destruction of the cochlea*

Nucleus	Volume (cell mass)			Mean number of cells per unit volume			Estimated total cell count		
	Normal	Atrophied	Difference (%)	Normal	Atrophied	Difference (%)	Normal	Atrophied	Difference (%)
Ventral cochlear nucleus	11·46	7·53	−34·3	4·78	7·6	+59	75,897	79,210	+4·2
Lateral superior olive	1·21	1·08	−10	4·86	5·22	+ 7·4	7,787	7,505	−3

The characteristic spindle cell layer of the dorsal cochlear nucleus shows no change in area of the cells, nuclei or nucleoli after the two longest survival periods, thus confirming the qualitative impression that these cells do not undergo trans-neuronal atrophy.

The data on the volumes and cell counts of the normal and degenerated ventral cochlear nucleus and lateral superior olive at 319 days are presented in Table 10. The volume of the ventral cochlear nucleus on the operated side is reduced by 34·3%, but the mean cell density, i.e. the number of cells/unit volume is increased by 60% so that the total cell counts differ by the statistically insignificant figure of 4·2%. The decrease in volume of the lateral superior olive is much less, being only 10% of the normal, and as the mean density of the cells increased by only 7·5% the difference in the total population of the cells between the normal and atrophied nuclei is only 3% which is again not significant. In these nuclei in the cat, therefore, no cell loss occurs up to 300 days after destruction of the primary auditory nerve

fibres. The counts of the nucleolar sex satellite in these two nuclei in female cats at 319 and 60 days also show no difference in incidence or in position. The satellite is present in between 90 and 94% of cells, and most frequently it is found immediately adjacent to the nucleolus.

The sections of the temporal bones of the cat which survived 319 days after operation show that the basal parts of the cochlea have been completely destroyed and that the basilar membrane of the middle and apical turns is degenerated. The Bodian-stained sections show clearly that the cochlear division of the VIIIth cranial nerve is almost totally degenerated, only a few fibres remaining in the nerve and a comparable number of bipolar cells in the ganglion. The vestibular division is quite unaffected.

DISCUSSION

The results of the experiments which have been described show that after destruction of the cochlea there is a marked transneuronal atrophy of the cells of the ipsilateral ventral cochlear and lateral superior olivary nuclei, and that definite degenerative changes are also found in the cells of the ipsilateral pre-olivary nuclei and in those of the contralateral medial trapezoid and lateral lemniscal nuclei. The morphological changes in the cell bodies of the neurons undergoing transneuronal degeneration in the ventral cochlear and lateral superior olivary nuclei are essentially similar to those which have been described in other sites in the cat and other species. All three of the major components of the soma—the cytoplasm, nucleus and nucleolus—are reduced in size, the cytoplasm showing the maximum degree of change and the nucleolus the least. There is also a slight reduction in the amount of Nissl material and the granules become finer and have a more homogeneous appearance. It should be understood, however, that apart from these changes the cells appear remarkably healthy so that the degeneration would almost certainly not be detected if the normal cells of the corresponding group of the other side were not available to serve for comparison. In the ventral cochlear nucleus these cellular changes are accompanied by gliosis which is most severe after the shorter survival periods and which becomes progressively less intense after longer intervals. In the lateral superior olivary nucleus, on the other hand, the cellular atrophy occurs without any gliosis being seen at any interval after operation. In the contralateral medial trapezoid nucleus (and possibly in the affected pre-olivary and lateral lemniscal nuclei where quantitative studies were not made) the changes in the size of the cell bodies and in the Nissl material are similar to those already described, but the nucleus and nucleolus differ in showing no shrinkage.

The data obtained from the quantitative studies indicate that both in the time-course and in the degree of the degeneration, the cells of the different auditory relay nuclei closely resemble each other and those of the lateral geniculate nucleus of the same species. In both these afferent systems of the cat little appreciable change is seen in the cells before a period of approximately 60 days has elapsed, and after this period little further change occurs, the degenerative process appearing to remain more or less stationary. The factors which are known to influence the rate of onset of transneuronal degeneration have been fully discussed in an earlier paper (Matthews *et al.* 1960); the marked difference in time of onset of this type of degeneration in the

lateral geniculate nucleus of different species was emphasized, and particularly the more rapid occurrence of the cellular changes in this nucleus in primates as compared with that of the cat. What is surprising, and very difficult to understand, however, is the slow development of detectable morphological change in the lateral geniculate and auditory relay nuclei of the cat. The nerve fibres and afferent terminals to these nuclei degenerate within a few days (Glees, 1941; De Robertis, 1956; Powell & Cowan, 1962). It is difficult to explain why the cells do not atrophy soon after the break up of the afferent fibres or for that matter what factors are operating to cause the atrophy when it ultimately does appear.

The finding that the time-course and severity of the degeneration of the cells in the different subdivisions of the ventral nucleus and lateral superior olive are essentially the same indicates that both the size of the cell body and the morphology of the afferent terminals do not influence appreciably the degenerative process. The distinct differences in the size of the cell body in the subdivisions of the ventral cochlear nucleus and lateral superior olive are shown in Tables 1 to 4, from which it can be seen that although the cells of the postero-ventral nucleus are normally considerably larger than those in the medio-ventral nucleus and lateral superior olive, in transneuronal degeneration both types of cells are affected to the same degree. Furthermore, it is known that the auditory nerve fibre bifurcates upon entering the brain stem into two branches. The ascending branch passes to the antero-ventral nuclei to end as the characteristic endings of Held (Held, 1891, 1983; Cajal, 1909) and the descending branch terminates on the cells of the postero-ventral nucleus as pericellular endings and boutons.

This difference in the morphology of the afferent nerve terminal is probably not a significant factor in determining the onset or severity of the degeneration, however, as the only difference between the degeneration of the cells of the different subdivisions of the ventral cochlear nucleus, of the lateral superior olive and of the lateral geniculate nucleus is the slightly earlier onset of change in the postero-ventral nucleus. It has already been mentioned that this difference could well be within the limits of error of the technique of cell measurement, particularly in view of the greater variation in the size of the cells in the postero-ventral nucleus as compared with those of the other nuclei.

There is no qualitative evidence of any cell loss in the auditory relay nuclei even 1 year after destruction of the cochlea, and this is confirmed by the counts of the ventral cochlear and lateral superior olivary nuclei. This agrees with the observations, in the same species, of Cook *et al.* (1951) on the lateral geniculate nucleus and of Hamlyn (1954) on the superior cervical ganglion of the rabbit. The only appreciable cell loss found in this type of degeneration in adult animals is that described in the human lateral geniculate and trigeminal nuclei (Goldby, 1957; Penman & Smith, 1950). In view of these findings it is difficult to explain the statement of Carpenter, Bard & Alling (1959) that chromatolysis and cell loss is found in the cochlear nuclei 13–17 days after labyrinthectomy.

While the finding of transneuronal degeneration in the cells of the ventral cochlear nucleus is not particularly surprising the absence of any such change in the characteristic spindle-cell layer of the dorsal cochlear nucleus is one of the unexpected features of these experiments. Because of their variable size and low

density the absence of transneuronal changes cannot be excluded for the cells of the deeper polymorph layer of this nucleus. There are at least three possible explanations for the lack of occurrence of this form of atrophy in the spindle cells. The first and most obvious one is that there are no primary auditory fibres projecting to this nucleus as Stotler (1949) and Rasmussen (1957) have claimed. That the classical description of the descending branch of the auditory nerve fibre going on to terminate in the dorsal nucleus is the more correct, however, is confirmed by the finding of definite gliosis in the deeper polymorph layer in these experiments, by the presence of preterminal degeneration in the same layer after shorter survival periods (Powell & Cowan, 1962) as well as by the recent electrophysiological evidence of Rose *et al.* (1959). The second possibility is that the primary auditory fibres which pass to the dorsal nucleus terminate exclusively in its deep polymorph layer and do not make direct contact with the spindle cells. Against this interpretation is the description by Cajal (1909) of Golgi material, that the terminals of the descending branch form an elaborate plexus in relation to the deep dendrite and soma of the spindle cell, and this is confirmed by experimental studies (Powell & Cowan, 1962). The third and most likely explanation is that although the central processes of the spiral ganglion do terminate upon the spindle cells they form only a small proportion of the total number of afferents to these cells. For transneuronal cell degeneration to occur it is probable that a high proportion of the afferents must be destroyed. The exact figure is not known—and this may vary with the site in the nervous system and the relative functional importance of the afferents—but Torvik (1956) found cellular degeneration in the inferior olivary nuclei of kittens, even though approximately 50% of the afferent fibres were still intact. In this connexion it is significant that in Golgi material Lorente de Nó (1933) has described many centrifugal fibres to the dorsal nucleus. It is generally accepted, although without any real quantitative evidence, that the size of the cell body of a neuron is proportional to the amount of its axoplasm. It is also possible that the size of the soma and the extent of its dendritic processes are proportional to the number of afferent fibres terminating upon them, and that the shrinkage found in transneuronal degeneration is simply a reflection of the decrease in the number of afferents.

The occurrence of transneuronal degeneration in the lateral superior olive is another unexpected finding because it is generally accepted that this is a secondary relay nucleus (Stotler, 1953) and not directly related to the auditory nerve fibres (cf. Held, 1893). The remarkable similarity in the time-course and in the severity of the degeneration in the cells of this nucleus and those of the cells of the ventral cochlear and lateral geniculate nuclei might be taken as evidence for a primary projection to this nucleus. That this is incorrect, however, is suggested by two important differences between the degeneration in this nucleus and the ventral cochlear nucleus: the absence of gliosis at any interval after destruction of the cochlea is particularly striking, and in addition there is a lack of compacting of the cells and shrinkage of the nucleus as a whole. Furthermore, fibre degeneration studies, after long and short survival periods, have failed to show any direct connexion to this nucleus, and the findings in the brain in which the cochlear nuclei were destroyed confirm the results of Barnes, Magoun & Ranson (1943) and Stotler (1953) in showing that this nucleus receives the majority of its afferents from the

cochlear nuclei. It must be concluded, therefore, that the cellular changes in this nucleus after destruction of the cochlea are not due to the interruption of direct afferents, but that they are secondary to the changes which have occurred in the cochlear nuclei. In other words, the cells of the lateral superior olive have atrophied following a lesion which is separated from them by two synapses. It is surprising that the time-course and the severity of the degeneration are so similar to those in the cells separated by only one synapse, but the criteria for degeneration used here —of change in size and depth of staining—are relatively crude, and it is possible that electronmicroscopic or electrophysiological studies might show differences between the degenerated cells of these two nuclei.

A similar problem arises in the interpretation of the changes found in the contralateral medial trapezoid and lateral lemniscal nuclei and the homolateral pre-olivary nuclei. The possibility of a direct projection of some auditory nerve fibres to the contralateral medial trapezoid nucleus was admitted by Cajal (1909) and Winkler (1921), and Lewy & Kobrak (1936) produced evidence from Marchi experiments in the rabbit for such a connexion. On the other hand, no fibre degeneration was found in this nucleus at either short or long survival periods after destruction of the cochlea (Stotler, 1953; Powell & Cowan, 1962). The presence of dense gliosis in all three of these nuclei, together with loss of afferent fibres to the pre-olivary and medial trapezoid nuclei after additional involvement of the cochlear nuclei, indicate that the latter nuclei are indeed the origin of their afferent fibres as described by Stotler (1953). It would appear, therefore, that the cellular degeneration found in these nuclei after destruction of the cochlea is similar to that found in the lateral superior olive in being secondary to that occurring in the cells of the ventral cochlear nucleus or to the de-afferentation of the dorsal cochlear nucleus. It is also interesting to note that the degenerative process is qualitatively different, as shown by the absence of change in their nuclei and nucleoli.

The only secondary relay nucleus in which cellular changes do not occur on one or other side is the medial superior olive. The probable explanation for the absence of change here lies in the approximately equal proportion of afferents which this nucleus receives from the cochlear nuclei of each side (Stotler, 1953; Powell & Cowan, 1962). In view of Torvik's (1956) finding of transneuronal degeneration in the inferior olive of kittens even though at least one-half of the afferents are intact it would be of interest to repeat these experiments in younger animals.

In addition to the finding of unequivocal transneuronal degeneration in the auditory relay nuclei, there is the incidental observation that this type of degeneration also occurs in two of the vestibular nuclei after interruption of the primary vestibular fibres. Thus transneuronal cellular degeneration has now been demonstrated in most of the main afferent systems (visual, olfactory, auditory, trigeminal) and in the inferior olivary nucleus. If the survival periods after operation in experimental animals were made longer, and if the possibility of this type of degeneration occurring were considered it would almost certainly be found even more frequently, and it could provide an additional technique for tracing connexions in the central nervous system. That this is so is indicated by some unpublished observations in this laboratory: distinct shrinkage of the cells of the pontine nuclei and the substantia nigra has been found at survival periods of 2 months after lesions of the cerebral

cortex, and the distribution of the cellular changes in these nuclei is found to vary according to the site of the lesion.

SUMMARY

1. A qualitative and quantitative study has been made of the transneuronal cell degeneration which occurs in the auditory relay nuclei of the cat following destruction of the cochlea.

2. The most obvious cell atrophy occurs in the ipsilateral ventral cochlear and superior olivary nuclei, but definite degenerative changes are also found in the cells of the ipsilateral pre-olivary nuclei and in those of the contralateral medial trapezoid and lateral lemniscal nuclei. No change is seen in the spindle cell layer of the dorsal cochlear nucleus.

3. In both the time-course and severity of degeneration the cells of the different auditory relay nuclei closely resemble each other and those of the lateral geniculate nucleus of the same species. Little change is found after survival periods of less than 60 days, and after this period the degenerative process appears to be more or less stationary.

4. There is no evidence of any cell loss in the auditory relay nuclei up to 359 days after destruction of the cochlea.

5. The cellular atrophy which occurs in the ventral cochlear nucleus is due to the interruption of the direct auditory afferent fibres which terminate in this nucleus. The cellular changes which are found in the other auditory relay nuclei, however, are considered to be secondary to those in the ventral cochlear nucleus.

6. In one experiment in which the vestibular nerve was incidentally involved, transneuronal cell degeneration was seen in the medial and descending vestibular nuclei.

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REFERENCES

BARNES, W. T., MAGOUN, H. W. & RANSON, S. W. (1943). The ascending auditory pathway in the brain stem of the monkey. *J. comp. Neurol.* **79**, 129–152.

CAJAL, S. R. Y (1909). *Histologie du Système Nerveux de L'Homme et des Vertébrés.* Paris: A. Maloine.

CARPENTER, M. B., BARD, D. S. & ALLING, F. A. (1959). Anatomical connexions between the fastigial nuclei, the labyrinth and the vestibular nuclei in the cat. *J. comp. Neurol.* **111**, 1–26.

COOK, W. H., WALKER, J. H. & BARR, M. L. (1951). A cytological study of transneuronal atrophy in the cat and rabbit. *J. comp. Neurol.* **94**, 267–292.

DE ROBERTIS, E. (1956). Submicroscopic changes of the synapse after nerve section in the acoustic ganglion of the guinea pig. An electron microscope study. *J. biophys. biochem. Cytol.* **2**, 502–512.

DORNFELD, E. J., SLATER, D. W. & SCHEFFE, H. (1942). A method for accurate determination of volume and cell numbers in the small organs. *Anat. Rec.* **82**, 255–259.

FUSE, G. (1913). Das ganglion ventrale und das acusticum bei einigen Säugern und beim Menschen. *Arb. hirnanat. Inst. Zurich*, **7**, 1–210.

GALAMBOS, R. (1954). Neural mechanisms of audition. *Physiol. Rev.* **34**, 497–528.

GLEES, P. (1941). The termination of optic fibres in the lateral geniculate body of the cat. *J. Anat., Lond.* **75**, 434–440.

GOLDY, F. (1957). A note on transneuronal atrophy in the human lateral geniculate body. *J. Neurol. Psychiat.* **20**, 202–207.

HAMLYN, L. H. (1954). The effect of preganglionic section on the neurones of the superior cervical ganglion in rabbits. *J. Anat., Lond.*, **88**, 184–191.

HELD, H. (1891). Die zentralen Bahnen des Nervus acusticus bei der Katze. *Arch. Anat. Physiol. Lpz., Anat.* Abt., 271–288.

HELD, H. (1893). Die centrale Gehörleitung. *Arch. Anat. Physiol., Lpz.*, Abt., 201–248.

LE GROS CLARK, W. E. & PENMAN, G. G. (1934). The projection of the retina in the lateral geniculate body. *Proc. roy. Soc.* B, **114**, 292–313.

LEWY, F. H. & KOBRAK, H. (1936). The neural projection of the cochlear spiral on the primary acoustic centres. *Arch. Neurol. Psychiat*, **35**, 839–852.

LORENTE DE NÓ, R. (1933). Anatomy of the eighth nerve. III—General plan of structure of the primary cochlear nuclei. *Laryngoscope*, **43**, 327–350.

MATTHEWS, M. R., COWAN, W. M. & POWELL, T. P. S. (1960). Transneuronal cell degeneration in the lateral geniculate nucleus of the macaque monkey. *J. Anat., Lond.*, **94**, 145–169.

MINKOWSKI, M. (1913). Experimentelle Untersuchungen über die Beziehungen der Grosshirnrinde und der Netzhaut zu den primären optischen Zentren besonders zum Corpus Geniculatum externum. *Arb. hirnanat. Inst. Zurich*, **7**, 255.

PENMAN, J. & SMITH, M. C. (1950). Degeneration of the primary and secondary sensory neurons after trigeminal injection. *J. Neurol. Psychiat.*, **13**, 36–46.

POWELL, T. P. S. & COWAN, W. M. (1962). An experimental study of the projection of the cochlea. *J. Anat., Lond* **96**, 269–284.

RASMUSSEN, G. L. (1946). The olivary peduncle and other fibre projections of the superior olivary complex. *J. comp. Neurol.* **84**, 141–220.

RASMUSSEN, G. L. (1957). *Selective Silver Impregnation of Synaptic Endings. New Research Techniques of Neuroanatomy.* C. C. Thomas: Springfield, Ill.

ROSE, J. E., GALAMBOS, R. & HUGHES, J. R. (1959). Microelectrode studies of the cochlear nuclei of the cat. *Johns Hopk. Hosp. Bull.* **104**, 211–251.

STOTLER, W. A. (1949). The projection of the cochlear nerve on the acoustic relay nuclei of the medulla. *Anat. Rec.* **103**, 561.

STOTLER, W. A. (1953). An experimental study of the cells and connexions of the superior olivary complex of the cat. *J. comp. Neurol.* **98**, 401–423.

TORVIK, A. (1956). Transneuronal changes in the inferior olive and pontine nuclei in kittens. *J. Neuropath.* **15**, 119–145.

WINKLER, C. (1921). *Manuel de Neurologie, Tome* 1, *Anatomie du système nerveux*, Part 2. Haarlem: de Erven F. Bohn.

ABBREVIATIONS

C	Cerebellum
DC	Dorsal cochlear nucleus
DV	Descending vestibular nucleus
LO	Lateral superior olive
LP	Lateral pre-olivary nucleus
LV	Lateral vestibular nucleus
M	Medial longitudinal bundle
MC	Middle cerebellar peduncle
MO	Medial superior olive
MP	Medial pre-olivary nucleus
MT	Medial trapezoid nucleus
MV	Medial vestibular nucleus
NL	Nucleus of the lateral lemniscus
NR	Nucleus reticularis tegmenti pontis
P	Pontine nuclei
PB	Nucleus parabrachialis
PY	Pyramidal tract
RP	Nucleus reticularis pontis caudalis
SC	Superior cerebellar peduncle
SV	Superior vestibular nucleus
T	Trapezoid body
V	Vth cranial nerve
V*Am*	Medio-ventral cochlear nucleus
V*Al*	Latero-ventral cochlear nucleus
V*M*	Motor nucleus of Vth cranial nerve
V*Me*	Mesencephalic nucleus of Vth cranial nerve
V*P*	Postero-ventral cochlear nucleus
V*S*	Sensory nucleus of Vth cranial nerve
V*Sp*	Spinal nucleus of Vth cranial nerve
VI	VIth cranial nerve
VI*N*	Nucleus of VIth cranial nerve
VII	VIIth cranial nerve

EXPLANATION OF PLATES

All sections were cut transversely, were 25 μ in thickness and were stained with thionine.

PLATE I

Figs. 1, 2. Low-power photomicrographs to show the shrinkage of the antero-ventral cochlear nucleus and its constituent cells 359 days after destruction of the cochlea (Fig. 2) as compared with the nucleus of the normal side (Fig. 1). $\times 38$.

Figs. 3, 4. Photomicrographs of normal (Fig. 3) and degenerated (Fig. 4) cells of the antero-ventral nucleus 359 days after destruction of the cochlea. $\times 180$.

PLATE 2

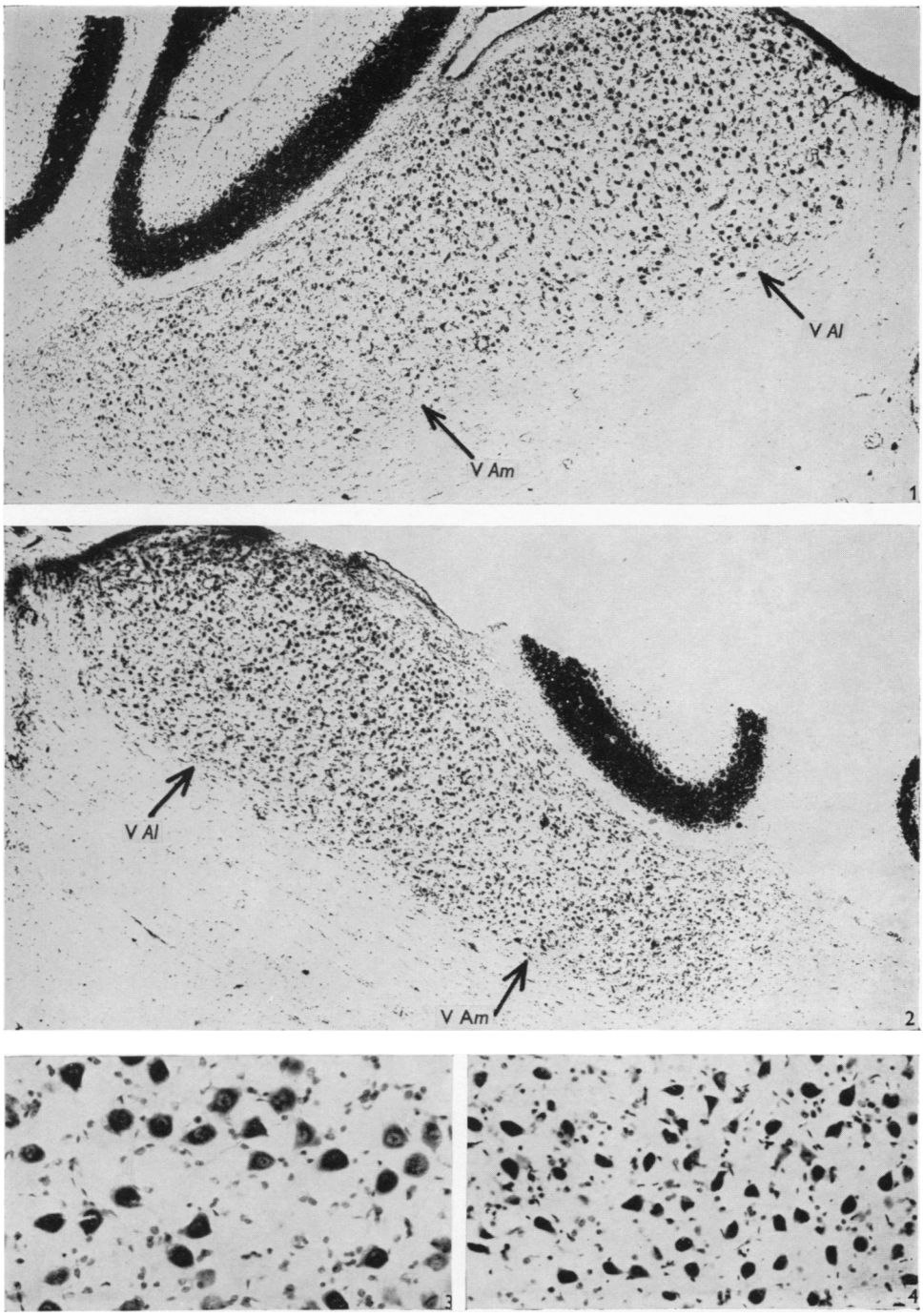
Figs. 5, 6. Photomicrographs of normal (Fig. 5) and degenerated (Fig. 6) postero-ventral and dorsal cochlear nuclei 60 days after destruction of the cochlea. Severe gliosis is seen throughout the postero-ventral nucleus and in the deep polymorph layer of the dorsal nucleus. $\times 33$.

Figs. 7, 8. Photomicrographs to show the shrinkage of the cells of the contralateral medial trapezoid nucleus (Fig. 8) 120 days after destruction of the cochlea as compared with those of ipsilateral side (Fig. 7). $\times 86$.

PLATE 3

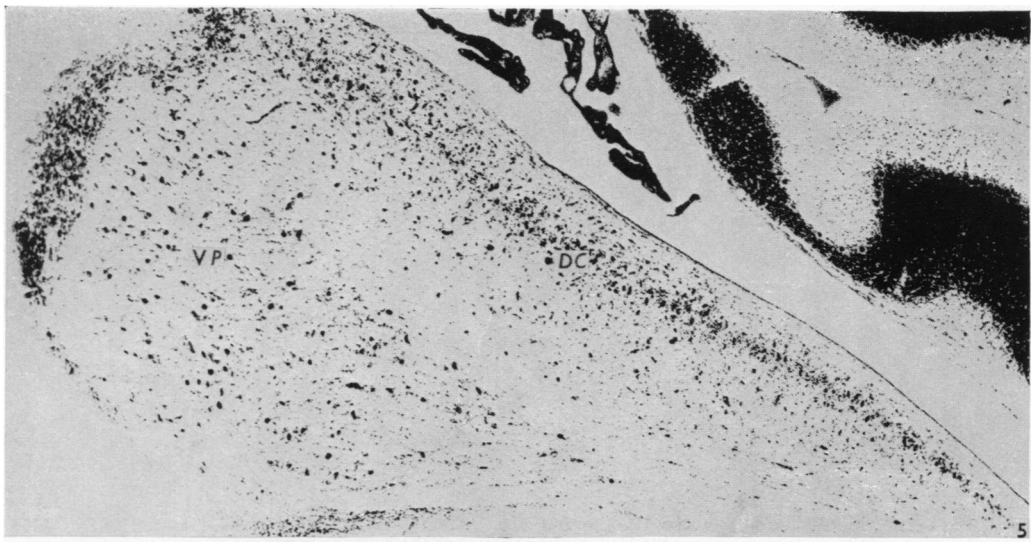
Figs. 9, 10. Photomicrograph to show the atrophy of the cells in the lateral superior olive 359 days after destruction of the cochlea (Fig. 10) as compared with the normal side (Fig. 9). $\times 78$.

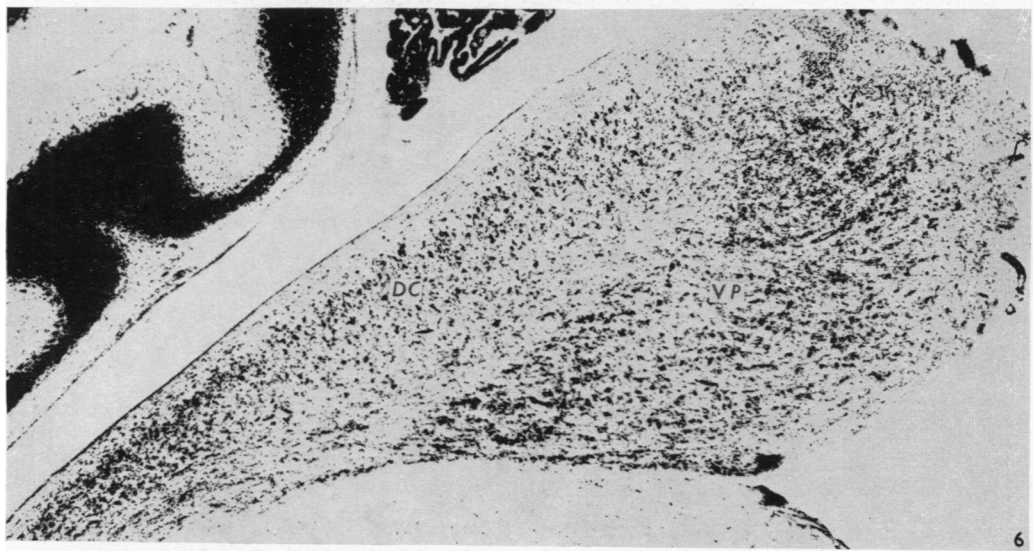
Figs. 11, 12. Normal (Fig. 11) and atrophied (Fig. 12) neurons of the lateral superior olive 359 days after destruction of the cochlea. $\times 875$.

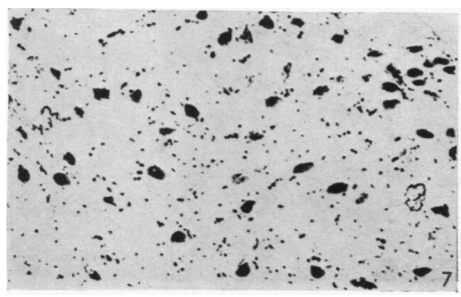


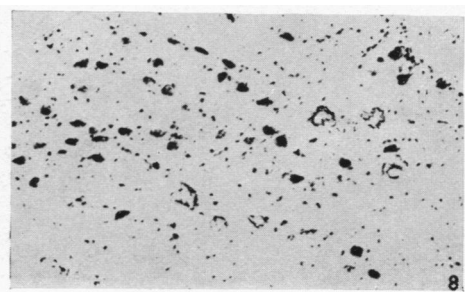
POWELL AND ERULKAR—TRANSNEURONAL CELL DEGENERATION IN THE CAT

(*Facing p.* 268)

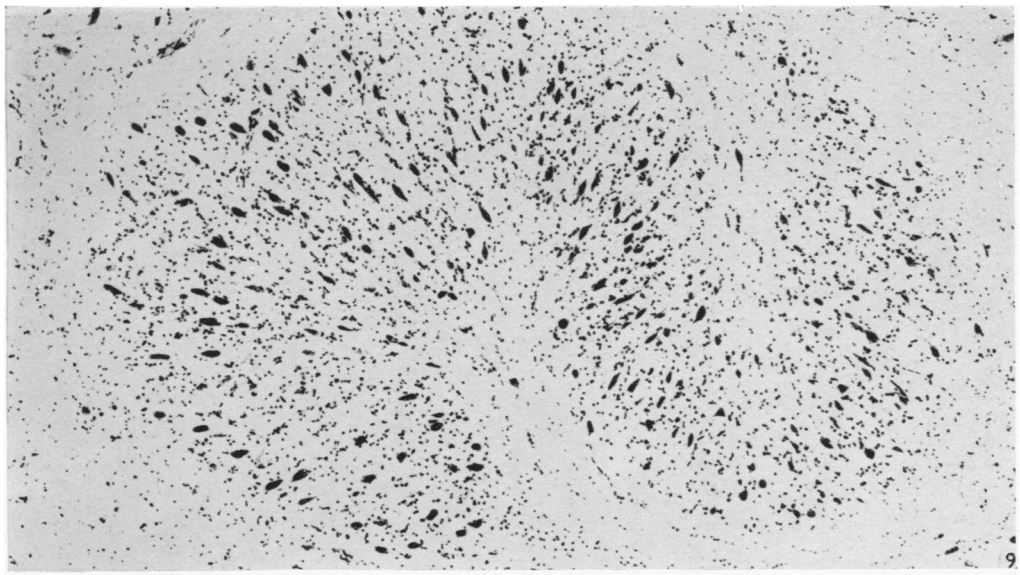


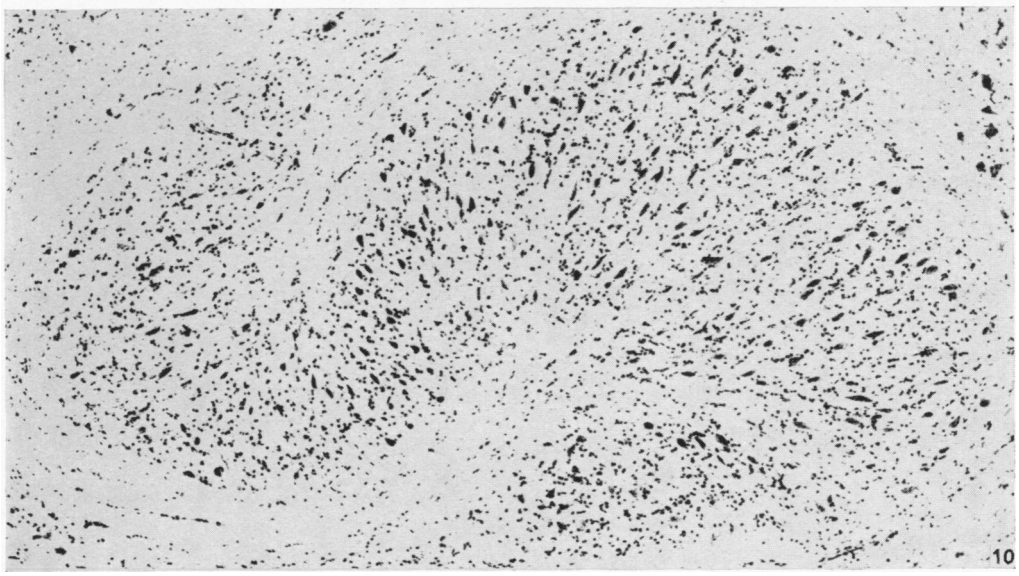


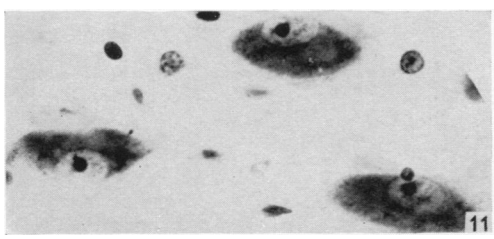


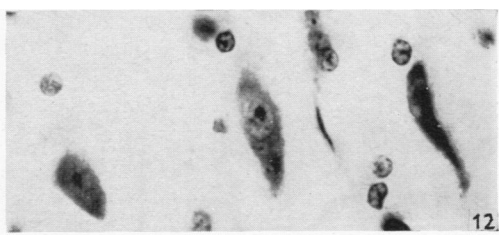


POWELL AND ERULKAR—TRANSNEURONAL CELL DEGENERATION IN THE CAT









POWELL AND ERULKAR—TRANSNEURONAL CELL DEGENERATION IN THE CAT