J. Anat., Lond. (1963), 97, 3, pp. 429–449
With 2 plates and 5 text-figures
Printed in Great Britain

The rate of secondary degeneration in the central nervous system

I. The pyramidal tract of the cat

By H. van CREVEL and W. J. C. VERHAART
Institute of Neurological Sciences, Leiden University

INTRODUCTION

Although the tracing of secondary degeneration has been a basic method of neuro-anatomy for over a century, little is known about the process of degeneration itself and the factors influencing it. Yet to ignore these factors in the interpretation of hodological data may result in erroneous conclusions being drawn as to the number, origin or direction of the fibres in a nerve tract.

The fibres in a severed nerve tract do not degenerate simultaneously. At first no degenerated fibres are visible, then gradually more and more fibres disintegrate, until at last the degeneration is complete. Thus, for an exact determination of the amount of degeneration following a lesion, two data are required. First, the 'degeneration time' (the time-interval between severance of the fibres and death of the specimen) and secondly, the 'degeneration rate' (the relation between the number of degenerated fibres and the degeneration time).

This rate is determined by many factors. Among these, fibre size (the outer transverse diameter of the fibre) is one of the most important. However, the evidence is contradictory in this respect: some workers state that large fibres degenerate at a higher rate than those of small size, while others maintain the opposite (see Discussion). The present work is a quantitative study of the degeneration rate and of the relation between fibre size and degeneration rate in the central nervous system.

In a series of experiments, the pyramidal tract of the cat was completely severed unilaterally by hemidecortication. The animals were killed after different degeneration times, varying from 3 days to 30 weeks. In each degenerating pyramid, the number of degenerated fibres of each size was determined as described below. In this way the time course of secondary degeneration resulting from 'one' lesion was followed, and the degeneration rate for each fibre size could be determined.

Since degenerated fibres vanish sooner or later by resorption, to count those still visible is misleading. Moreover, since degenerated fibres are swollen, to measure them is of little value. These difficulties were overcome by Verhaart (1947). Instead of the degenerated fibres, the non-degenerated fibres in a severed tract are counted and measured. The same is done in the contralateral, normal tract of the same specimen. Comparison of both sets of data reveals the number and size of the degenerated fibres. This will be called the 'indirect' method.

It will be clear that this method requires a staining technique which permits: (1) differentiation between normal and degenerated fibres, and (2) exact measuring and counting of normal fibres. Therefore, the Häggqvist modification of the Alzheimer–Mann methylblue-eosin stain was chosen (see Methods).

METHODS

Staining

Häggqvist (1936) modified the Alzheimer–Mann technique for paraffin sections by aftermordation in bichromate. This technique, using methylblue-eosin, stains myelin sheath and nucleolus a bright red, axons, cells and glial tissue blue. Häggqvist and his associates used it mainly for counting and measuring normal fibres (Häggqvist, 1936, 1948; Rexed, 1944). However, the Alzheimer–Mann stain was originally used for neuropathological purposes; and Doinikow (1911), Jakob (1912), Spatz (1921) and Spielmeyer (1922, 1929) gave beautifully coloured pictures of it in their studies of secondary degeneration. Its usefulness in this field was almost forgotten, until it was re-introduced by Verhaart (1947). The technique used has been recently described by Busch (1961) as follows:

(1) Further fixation of the blocks (*exp. mat.*) or the entire brain (*norm. mat.*) in Baker's formol-calcium fixative, made up of 10 ml. commercial formalin, 10 ml. of a 10 % aqueous solution of calcium chloride (anhydrous) and 80 ml. distilled water. Fix for 3–4 weeks, preferably in the incubator at 40° at night and during the day at room temperature. Change the fluid once.

(2) Wash overnight in running water.

(3) Mordation for 3–4 weeks, at the same temperatures as in fixation, in dichromate-calcium solution, made up of 90 ml. 10 % potassium dichromate with 10 ml. 10 % aqueous calcium chloride (anhydrous).

(4) Rinse in running water for one night, dehydrate and embed in paraffin.

(5) Cut sections 5–6 μ, mount according to Masson's gelatin-formalin vapour method.

(6) Deparaffinize and bring to distilled water.

(7) Transfer to 10 % phosphomolybdic acid for 1–2 hr. at room temperature.

(8) Wash well in distilled water.

(9) Stain for 3–4 hr. at room temperature in a solution containing equal parts of 0·5 % methylblue (preferably Bayer) and 0·1 % eosin in distilled water. Add 15 drops of concentrated acetic acid per 1000 ml. staining solution.

(10) Immediately after staining, pass rapidly through 96 % alcohol and 100 % alcohol, clear in two baths of xylol. Mount in Canada balsam. Dehydration must be rapid to prevent loss of eosin.

Because the method is not well known, its criteria for degeneration will be discussed here at some length. The first signs of degeneration are most conspicuous in thick fibres. The axon swells, sometimes becoming red instead of blue. Hyperchromatic axons can often be observed in large fibres. Then the axon becomes pale and granular, and often reticular or vacuolated. Later, only a semilunar part of it is left; and finally it is resorbed. The myelin sheath also swells, and becomes cloudy and irregular in outline (Pl. 1, figs. 1–3). In thin degenerated fibres a blue axon

can no longer be distinguished. In transverse sections only a seemingly luminous disc of a more vicious red is left. The fibres are swollen and irregular. The intermediate stages of degeneration can seldom be observed in thin fibres. This is probably due to the rapid resorption of thin fibres, once they are degenerated (see Discussion). In addition to fibre degeneration, glial proliferation is clearly visible. Areas of old degeneration are blue, because of the abundance of glial tissue. Fresh degeneration shows up red, owing to the disappearance of blue axons.

In the present work, fibres were regarded as degenerated: when a blue axon was lacking or (in larger fibres) when the axon was obviously hyperchromatic, granular, or partly resorbed. In properly fixed material, artefacts are rare. They can be distinguished from true degeneration by the use of serial sections; or, in experimental material with strictly unilateral lesions, by comparison with the contralateral side of the section.

Fibre analysis

The 'fibre pattern' of a tract is the percentage frequency distribution of the fibre sizes. Determination of the fibre pattern by counting and measuring was termed 'fibre analysis' by Häggqvist (1936). Fibre analysis may be performed in various ways. In the present study, the normal fibres in samples of normal and degenerating pyramids were counted and measured directly from the microscope, with the aid of a net-ocular micrometer. Then the whole surface area was determined and the total number of fibres calculated by multiplication. The advantages of this method are its speed and the possibility of judging degeneration through the microscope. Both are lost when photomicrographs are used.

Sampling. In each pyramid, ten fields under oil immersion were used for fibre analysis. This is about one-twentieth of the total surface. Increasing the number of samples did not enhance the accuracy. As the pyramid shows no periodicity or density gradient, interval sampling was used, instead of random sampling.

Measuring. The fibres were measured and counted simultaneously with the aid of a net-ocular micrometer (Text-fig. 1). The distance between two tiny lines corresponds to 1μ under oil-immersion magnification. The outside diameter of the fibres was measured and the fibres were distributed in the following groups: 0–2, >2–4, >4–6 and $>6\mu$.

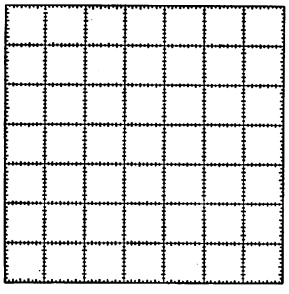
Counting. A differential counting machine was used, so that each fibre could be allocated to its size group when it was measured. In this way, double counting and overlooking of fibres are reduced to a minimum. Fibres on the outer lines of the square were counted at two of the four sides only.

Surface measuring. This was also done through the microscope, the advantage being that the border between pyramid and medial lemniscus can be defined by direct inspection of the fibre pattern (Pl. 1, fig. 4). While the mechanical stage was moved along parallel paths, the number of squares belonging to the pyramid was determined with the net-ocular.

Error of the method. The histological techniques of fixing, embedding, cutting and staining cause several errors, of which shrinkage is the most obvious. It amounts to some 25%, but it is remarkably constant, thick and thin fibres shrinking in the same proportion (Rexed, 1944). Another histological source of error is the deformation of the circular shape of transected fibres. Here Häggqvist's rules were

followed: in oval and polygonal cross-sections the smallest diameter is taken, while in pyriform shapes the base is measured.

However, the observer himself is a greater source of error than the histological imperfections of his material. In the present study, errors could be made in four operations (apart from sampling): measuring, counting, surface measuring and judging degeneration. Since the fibres were measured directly under the microscope, duplicate counts to determine the standard deviation could not be performed. Nor could the error made in counting be dealt with statistically. Double counting is infrequent, but overlooking of fibres probably happens to a considerable extent. However, our final values of interest (percentages of non-degenerated fibres) are quotients of two counts. Therefore, these final results are influenced far less by this inexactness than are the absolute numbers themselves. Surface measuring was always performed twice, and the average used for calculation. The difference was in the order of 1%, which is very satisfactory. Finally, fallacies made in judging degeneration are unavoidable, and cannot be estimated by statistical means.



Text-fig. 1. Net-ocular micrometer (see text for explanation).

Fortunately, these various errors are not correlated. Moreover, they can be reduced by training and tend to reach a constant level when work of this kind has been done for some time. Furthermore, since a large number of observations was made, the values obtained for the proportion of non-degenerated fibres are at least comparable. As thin fibres are much more numerous in the pyramid than thick ones, and as the standard error is inversely proportional to the root of the number of observations, the data concerning thin fibres are more exact than those on thick fibres. The error cannot be expressed in statistical language, but is estimated at some 10% for thick, and rather less for thin fibres.*

MATERIAL

Both normal and experimental adult cats were used (Table 1). The former were studied to decide whether in normal cats number and pattern of the fibres in the pyramid of both sides differ significantly. The latter constitute the series of cats with a unilateral total removal of the cells of origin of the pyramid, killed after different degeneration times. Since all, or nearly all fibres of the medullary pyramid

* For a more detailed discussion of the Häggqvist technique and fibre analysis, see van Crevel (1958).

arise from the cerebral cortex (see van Crevel, 1958, and references), several other cases could be added to the series of hemidecortications. These are: some hemispherectomies, some unilateral severances of the cerebral peduncle, and one case of unilateral severance of the medullary pyramid.

Table 1. *Normal and degenerating pyramids on which fibre analysis was performed*

Slide	Cat no.	Deg. time	Lesion
1	H 542	—	Normal pyramids
2	H 2505	—	Normal pyramids
3	H 544	—	Normal pyramids
4	H 3519	—	Normal pyramids
5	H 3518	—	Normal pyramids
6	H 3513	—	Normal pyramids
7	H 3513	—	Normal pyramids (different level)
8	H 3513	—	Normal pyramids (different level)
9	H 536	30 weeks	Hemispherectomy
10	H 536	30 weeks	Hemispherectomy (Glees method)
11	H 2721	28 weeks	Hemidecortication
12	H 2722	24 weeks	Hemidecortication
13	H 2723	20 weeks	Hemidecortication
14	H 2802	20 weeks	Hemidecortication
15	H 2746	16 weeks	Hemidecortication
16	H 3520	16 weeks	Hemidecortication
17	H 2810	16 weeks	Hemispherectomy
18	H 2891	12 weeks	Hemidecortication
19	H 539	12 weeks	Hemispherectomy
20	H 2760	10 weeks	One peduncle severed
21	H 2887	8 weeks	Hemidecortication
22	H 2800	8 weeks	Hemispherectomy
23	H 2892	6 weeks	Hemidecortication
24	H 3022	4 weeks	Hemidecortication
25	H 2635	4 weeks	One peduncle severed
26	H 2889	3 weeks	Hemidecortication
27	H 3521	3 weeks	Hemidecortication
28	H 3459	2 weeks	One pyramid severed
29	H 2890	2 weeks	Hemidecortication
30	H 3095	8 days	Hemidecortication
31	H 2794	7 days	Hemispherectomy
32	H 2806	5 days	Hemispherectomy
33	H 2790	3 days	Hemispherectomy
34	H 3135	16 months	Leukotomy (see text)

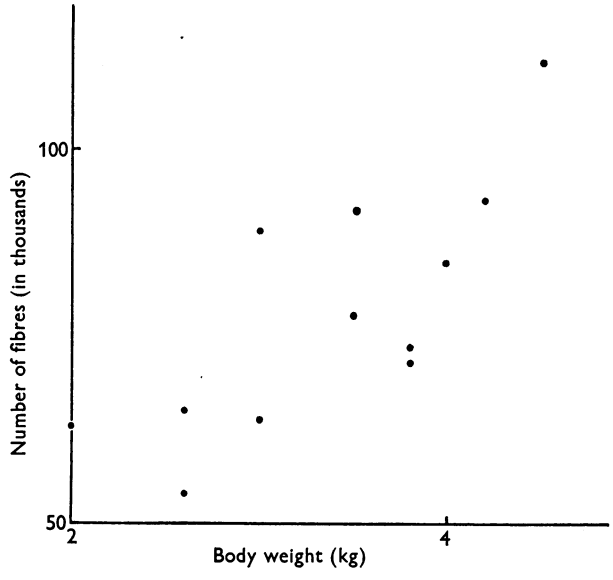
All operations were performed under intraperitoneally administered hexobarbitone anaesthesia. The cortex was removed by suction. The animals were killed in deep anaesthesia by perfusion with a 10% formalin solution through the aorta. In this way the central nervous system is fixed and hardened *in situ*. In some hemidecortications, small bits of basal, cingular, or occipital cortex were left intact; but no pyramidal fibres originate in these areas (van Crevel, 1958, and references). Unless stated otherwise, all slides were stained with the Häggqvist technique.

RESULTS

Normal pyramids

The pyramids of the normal cats (slides 1–8) as well as the normal pyramids of the experimental cats (slides 9–33) of Table 1 fall within this group. Only the former were used in deciding whether in normal cats number and pattern of the fibres in the pyramid of both sides differ significantly. To determine the normal range of number and pattern of the pyramidal fibres on either side, the latter group also was taken into account.

The number of fibres averaged about 80,000. It varied widely (between 56,000 and 106,000) in this group of thirty cats. In twelve cats whose weights were known, the number of fibres was found to be significantly correlated with weight (Text-fig. 2; t test: $P < 0{\cdot}005$). No significant correlation with the sex of the animals could be established; neither could it be determined whether the number of fibres drops slightly with advancing age, this factor being unknown in our cats.

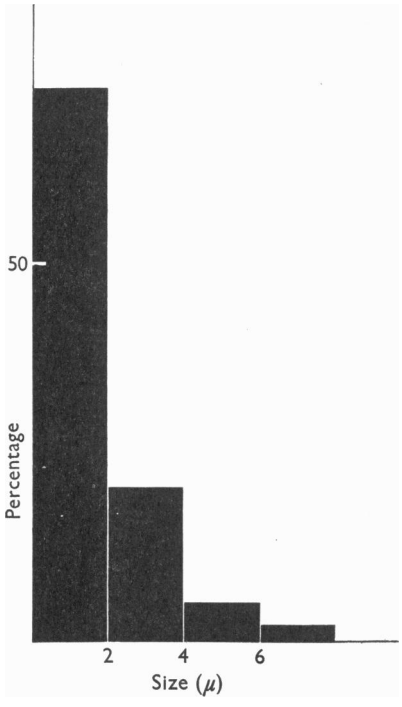


Text-fig. 2. Correlation diagram showing relationship between body weight and number of fibres in the pyramid of the cat.

Since it is impracticable to transect all the pyramids at exactly the same level, three different medullary levels were counted in one cat (slides 6, 7 and 8). From cranial to caudal, they correspond to Jansen & Brodal's (1954) levels XV, X and IV–V in the inferior olive. The numbers found (average of both sides) were 90,835 and 88,775 and 87,650 respectively. Consequently, the difference between the extreme levels used in counting in this study accounts for only a small percentage of the total variation.

The fibre pattern proved to be homogeneous over the whole area of the pyramid, and to differ much less than the total number of fibres in different individuals. The

average values found were 73% (0–2μ), 20% (>2–4μ), 5% (>4–6μ) and 2% (>6μ) (Text-fig. 3). Variations from this pattern are in the order of a few per cent only; and when groups 1 and 2 are added, their total shows even less variation. No doubt part of the variability is 'real', i.e. biological (as can be verified from the slides), but the observation just mentioned also demonstrates the subjective error involved in measuring fibres, especially those about 2μ in diameter. Comparison of three different levels in one individual (slides 6, 7 and 8) showed only slight and inconsistent differences in pattern: the middle level had fewer fibres of group 1 than both the upper and lower olivary levels.



Text-fig. 3. Percentage histogram of fibre sizes in the pyramid of the cat.

The majority of the fibres in group 1 are about 1μ in diameter. Some are thinner (about 0·75μ), and preparations were studied with the electron microscope (Philips EM 100) to find out whether large numbers of fibres below 1μ in diameter occur in the pyramid. This was found not to be the case. The largest fibres in the pyramid were 10μ; in some cats a few larger ones (12–14μ) were found (Pl. 1, fig. 3; Pl. 2, fig. 5). It should be remembered that the four size groups do not contain fibres averaging 1, 3, 5 and 7μ respectively.

Comparison of right and left pyramid. As the values for the proportion of degenerated fibres were obtained by comparing the two sides in one cat, it was felt necessary to test the assumption that in a normal individual the pyramids of the two sides are equal as to both number and size-frequency distribution. Hence the fibres of both pyramids of six normal cats were counted and measured. The results

are presented in Table 2. The numbers of fibres actually measured were used to compare the patterns. With the exception of the fibre pattern in a single slide (slide 1), neither the total number of fibres ($t = 0{\cdot}054$, D.F. 5) nor the fibre patterns (see χ^2) showed significant differences between the two sides. It soon became evident that initially the subjective errors are very large and inconsistent (see Methods), and this single difference in pattern was attributed to inexperience in counting and measuring. Consequently, it was decided that there is no reason to reject the hypothesis that number and pattern of the pyramidal fibres of both sides in a normal cat are the same.

Table 2. *Comparison of right and left (normal) pyramids*

(For D.F. 3, $P = 0{\cdot}05$ that $\chi^2 > 7{\cdot}81$.)

Slide	Number of fibres		Distribution in size groups: fibre pattern								χ^2
	L	R	L				R				
1	102,840	110,710	3,166	877	134	50	3,482	668	122	51	42·64
2	84,600	81,010	2,744	555	122	69	2,560	582	144	78	7·009
3	109,680	106,130	2,615	602	143	74	2,607	672	150	83	3·757
4	103,010	101,080	1,773	543	112	77	1,820	496	127	72	4·714
5	79,200	81,940	2,786	496	103	45	2,630	510	104	39	1·920
6	88,720	86,580	2,295	549	122	66	2,230	534	135	64	1·032

Degenerating pyramids

The most surprising feature of the whole series of degenerating pyramids was the great length of time needed for total degeneration. It is usually assumed that fibres degenerate more or less synchronously, and that all fibres have degenerated about one month after severance; but both these assumptions proved to be wrong. The first degenerated fibres in the pyramid were seen after 3 days; but after several weeks many apparently normal fibres could be observed. Even without quantitative analysis it was evident that thin fibres are strikingly more resistant to degeneration than larger ones. It takes up to 6 months for all these thin fibres to lose their normal appearance in a transverse section.

About 6 months after a hemidecortication (slides 11 and 12), a few normal fibres of various sizes can still be observed. No further degeneration seems to occur after that time: 16 months after a large lesion through the internal capsule had been made (in a cat 3 weeks old, H 3135), these normal fibres were still present. Since ascending pyramidal fibres could not be found (van Crevel, 1958), these fibres were held to be either lemniscal, or external arcuate, with perhaps a few contralaterally descending pyramidal fibres.

The over-all picture of degeneration in the pyramid changes gradually with time (Pl. 2, figs. 5–8). After 3 days only a few large degenerated fibres are conspicuous; but after 5 days degenerated fibres of all sizes are present. After a week the picture is dominated by red discs, indicating that many medium-sized fibres have degenerated.

After 2–3 weeks only few large fibres are still intact, and the general picture is one of full-blown degeneration. Unlike the thin, the large fibres have acquired unusual and irregular forms. Again, it must be stressed that under oil immersion many

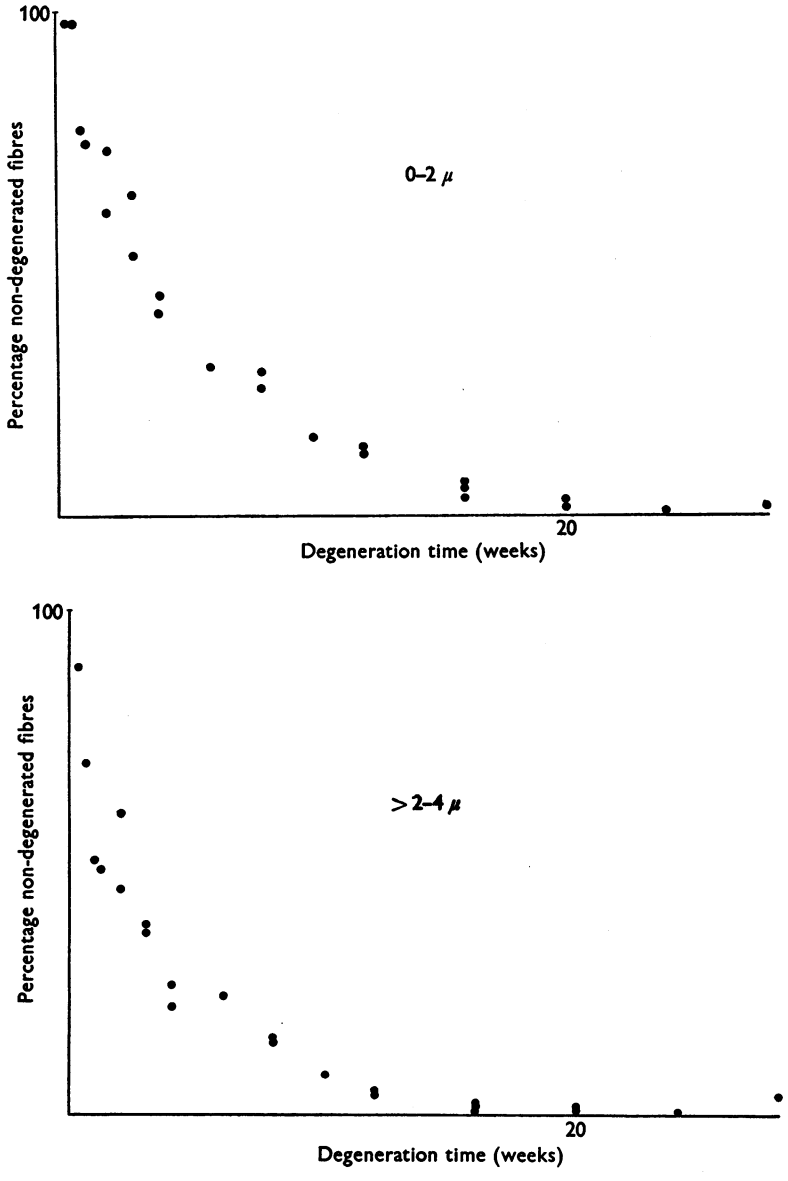
normal fibres are revealed. Six weeks after the operation many large degenerated fibres have been resorbed; but their spaces have not been filled, and relatively large white gaps show in the slide. On the other hand, thin fibres fade out unobtrusively: they are apparently resorbed rapidly, since few showing degeneration are to be seen at any one time. More than 3 months after the operation the pyramid consists for the greater part of glial tissue, with some debris and a few normal fibres. Most of the debris has been cleared away after 4 months, and the glial scar closes (Pl. 2, fig. 8). Shrinkage of the cross-surface area at that time amounts to some 50%, while in later stages it is even more. Quantitative data concerning it, however, show great variation: after 4 weeks it may be 20–25%; but in one case there was no atrophy at all after 8 weeks. It may, perhaps, vary with age; its study was not further pursued.

Table 3. *Percentages of normal fibres in the degenerating pyramid after different degeneration times*

Slide	Time	0–2 μ	> 2–4 μ	> 4–6 μ	> 6 μ
33	3 days	97·8	88·9	81·9	79·4
32	5 days	97·8	69·8	35·1	31·6
31	7 days	77·2	52·1	39·6	27·3
30	8 days	74·4	49·0	37·7	16·4
29	2 weeks	61·2	45·4	26·5	13·4
28	2 weeks	73·6	60·2	24·9	13·6
27	3 weeks	64·5	36·5	12·3	8·0
26	3 weeks	52·7	38·0	10·4	8·7
25	4 weeks	41·5	21·7	10·5	7·1
24	4 weeks	43·7	26·3	16·3	13·0
23	6 weeks	30·4	24·0	4·9	3·7
22	8 weeks	25·7	16·0	4·1	1·7
21	8 weeks	28·6	15·8	5·5	4·2
20	10 weeks	16·3	8·0	1·5	1·4
19	12 weeks	12·8	4·8	1·5	1·3
18	12 weeks	14·0	4·2	0·5	0·0
17	16 weeks	4·0	2·0	0·9	0·0
16	16 weeks	5·9	2·0	0·9	0·0
15	16 weeks	6·4	2·0	0·8	0·0
14	20 weeks	2·1	0·8	0·5	0·0
13	20 weeks	3·4	1·8	0·7	1·2
12	24 weeks	1·2	1·6	1·6	1·5
11	28 weeks	2·3	4·0	4·3	4·2*

* The apparent increase of normal fibres more than 20 weeks after the operation is due to a larger proportion of 'non-pyramidal' fibres in slides 11 and 12. Degeneration has reached a maximum after about 20 weeks; this was confirmed in slides 9 and 10.

Quantitative analysis. As explained before (see Introduction), it is useless for our purpose to count and size degenerated fibres. Therefore the normal fibres in the degenerating pyramid were counted and measured, and these data were compared with the number and pattern of the normal pyramid at the same level in the same animal (the 'indirect' method). The results were expressed as percentages of normal fibres (in the degenerating pyramid) for each size group. The values obtained are represented in Table 3 and (graphically) in Text-figure 4.



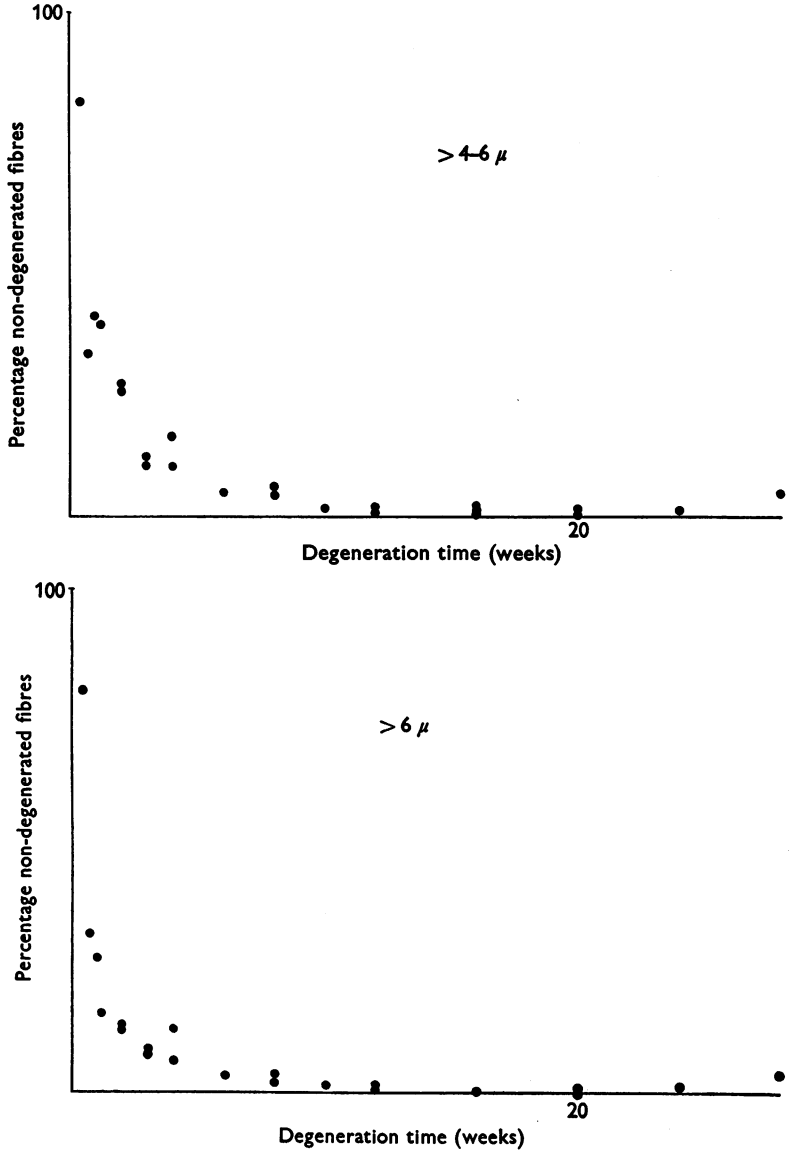
Text-fig. 4. For legend see opposite.

Remembering that percentages of 'not-yet-degenerated' fibres are given rather than percentages of degenerated fibres, it may be concluded from the graphs that:

(1) Fibres of all sizes start degenerating within a week of the lesion being made. Total degeneration takes several months.

(2) Large fibres, as a group, degenerate more rapidly than thin.

(3) Degeneration, considered as a temporal process, follows a continuous course with a steadily decreasing slope: there are no sudden changes of rate.

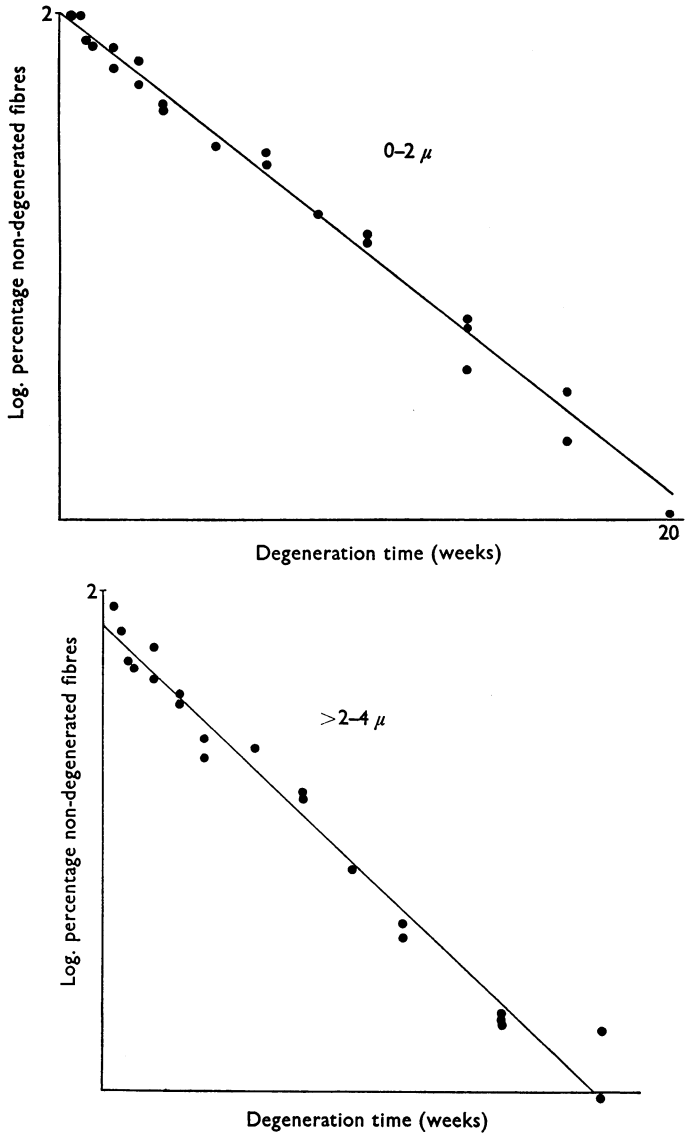


Text-fig. 4. The percentage of non-degenerated fibres in the pyramid plotted against degeneration time.

(4) Initially, large numbers of fibres are degenerating per unit interval of time; later, these numbers decrease progressively—this holds for all size groups.

Another point of interest was derived from the data by plotting the logarithm of percentage-left-intact against degeneration time. A linear relationship seems to exist between the two, indicating that the percentage itself forms a falling exponential function of degeneration time (Text-fig. 5).

The regression of log percentage normal fibres (y) on degeneration time (x) was calculated according to the method of least squares and resulted in equations of the



Text-fig. 5. For legend see opposite.

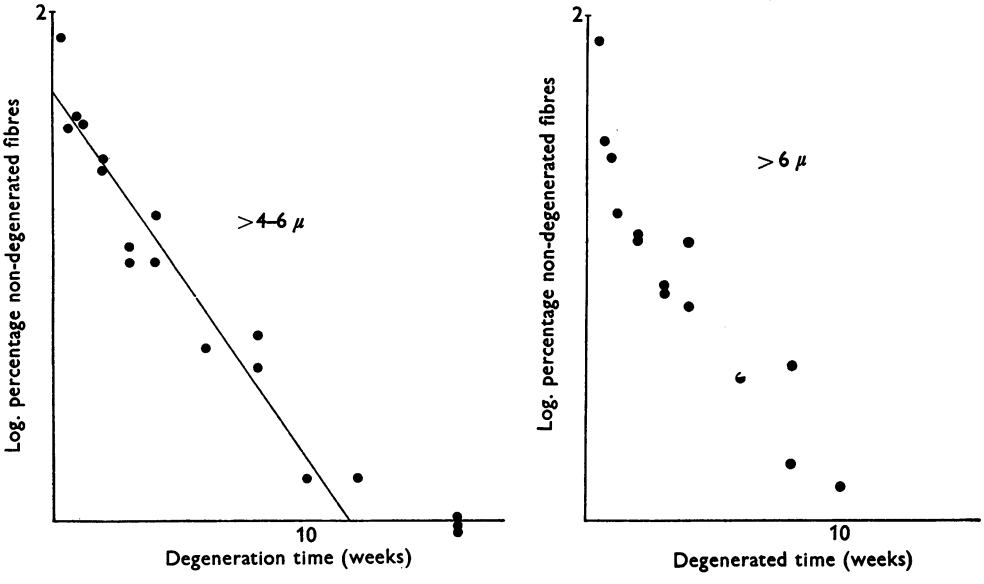
form $y = a+bx$ with $b < 0$.* This was done only for the first three size groups, as the data for the largest fibres were felt not to be sufficiently reliable to justify mathematical operations. The 'goodness of fit' was tested by $t = b/s_b$. The following equations were obtained:

(1) $y = 1{\cdot}994 - 0{\cdot}0111x$. ($x_{\max.} = 140$), $t = 34{\cdot}_{217}$ (0–2μ),
(2) $y = 1{\cdot}862 - 0{\cdot}0134x$. ($x_{\max.} = 140$), $t = 27{\cdot}_{589}$ ($>$ 2–4μ,)
(3) $y = 1{\cdot}703 - 0{\cdot}0210x$. ($x_{\max.} = 84$), $t = 13{\cdot}_{892}$ ($>$ 4–6μ).

* The relation between the percentage normal fibres and degeneration time being $Y = Ae^{bx}$, where A is the natural number of a.

For thicker fibres, the regression lines show a steeper slope and cross the ordinate at lower values of y. The proportion between regression coefficient and its standard deviation demonstrates that the rates of degeneration differ significantly in the three size groups. Thus a simple description of the data can be given as follows:

(5) Within each size group, the number of fibres degenerating in a unit interval of time is proportional to the number present at that time; the thinner the fibres, the smaller this proportion.



Text-fig. 5. The data of Text-fig. 4 plotted semilogarithmically.

DISCUSSION

Scope of the method

The scope of the Häggqvist method as used in fibre analysis of normal material has been discussed exhaustively by Rexed (1944): only its significance for studies of secondary degeneration remains to be evaluated. Therefore, it will be compared here with the routine neuro-anatomical methods: silver impregnations, the Marchi technique and the Weigert stain. (For a comparison with more refined morphological techniques and with chemical and physiological methods, see van Crevel, 1958.)

Disintegration of the axon, as revealed by silver methods, sets in after 3–5 days (Cajal, 1928; Nauta, 1957). Complete degeneration and removal of axonal debris take 4–6 months (Liu & Chambers, 1958). It is not feasible to count the non-degenerated fibres a long time after severance in silver preparations, because differentiation between glial fibres and thin axons is very difficult (Spielmeyer, 1930, own observation). Therefore, exact data about the last stages of degeneration are

difficult to obtain by these methods. The Marchi method reveals degenerated myelin from about 3 days after severance onwards (Glees, 1948). Degeneration is said to be complete in 3 weeks' time (Glees, 1948). However, the Marchi method seems unsuitable to determine the termination of the process of degeneration because normal fibres remain invisible. The Weigert method(s), staining normal myelin, supplements the Marchi method, especially for the late stage of degeneration. With it, total degeneration in the dog's pyramid is seen to require 4–6 months (Morin, Poursines & Maffre, 1951; Maffre, 1953).

Summing up, we may conclude that the over-all picture of degeneration as displayed by the Häggqvist method does not differ substantially from that seen with routine neuro-anatomical methods. The changes in the axon become visible at the same time as when observed in silver impregnations, and those of the myelin sheath correspond to the alterations demonstrable with the Marchi and Weigert methods.

Finally, something should be said about the 'quantitative' nature of the results. As explained before (see Methods), a considerable amount of uncertainty is inherent in all work of this kind. Consequently, the data should not be regarded as absolute values, but rather as approximations or even orders of magnitude.

The normal pyramid

The large variability in the number of fibres of the pyramid is most striking. It has been described in man, both for surface area (van der Bruggen, 1929; Duncan, 1940) and for number of fibres (Verhaart, 1947). It is explained to some extent by the relation between the number of pyramidal fibres and body weight, established in the present study. When no attention is paid to the fact that in carnivores the medial lemniscus covers the whole dorsal border of the pyramid, the former may be included in counts of the latter, as was apparently done by Maffre (1953), in her study of the dog's pyramid. Due attention should also be paid to distinction between nerve fibres and glial fibres in silver impregnations.

The pyramid is often described as containing many unmyelinated fibres (recently: Glees, 1957, De Myer & Russell, 1958). However, the occurrence of unmyelinated fibres anywhere in the nervous system seems to be exceptional (Edgar, 1955, and references). With more precise methods, such as polarized light and electron microscopy, a thin sheath can be detected in nearly all vertebrate nerve fibres. The meaning of the terms 'myelinated' and 'unmyelinated', then, is determined by the histological method used. In Häggqvist slides, a myelin sheath can be seen around all fibres in the pyramid, even those thinner than 1 μ. This made it unnecessary to draw a distinction between unmyelinated and myelinated fibres in the present study.

Lassek & Rasmussen (1940), using the Davenport protargol method, found 186,000 fibres in the pyramid of the cat. They examined two cats, but do not mention the dispersion of the data. Glees (1957) found only 70,000 fibres. Counting from Häggqvist slides, van Beusekom (1955) found 40,000–80,000 at a low medullary level. Our number, 80,000 fibres at a middle medullary level, and ranging from 56,000 to 106,000 in thirty cats, agrees reasonably with the figures quoted above, except those of Lassek & Rasmussen. Possibly these authors were not aware of the topography of the medial lemniscus in the cat.

The preponderance of thin fibres in the pyramid was noted early (Flechsig, 1876) and stressed by Häggqvist in 1936. Lassek (1942), Szentágothai (1941), Verhaart (1947, 1948*a*, *b*) and Brookhart & Morris (1948) found similar patterns. Although their studies are not directly comparable, because neither their methods nor their size groups were the same, all found a maximum number of fibres in the group classified as thin, and consistently smaller numbers in the groups of larger sizes. The pattern found by us (73, 20, 5 and 2% for the groups 0–2, >2–4, >4–6 and >6μ) agrees well with their results. Deviations from this average pattern were in the order of a few per cent only, while none but the first specimen counted showed a significant difference in the patterns of left and right sides.

The degenerating pyramid

The most obvious features of the series of degenerating pyramids (the long time needed for total degeneration, and the asynchronism of fibres in degeneration) have both been known for a long time, but have mostly been disregarded.

The low rate of degeneration in the pyramid was observed by Schaffer (1895), Worotynski (1897) and Ziehen (1899), later mentioned by Verhaart (1953) and described in detail by Morin *et al.* (1951) and Maffre (1953). Levin, von Bonin & Crandall (1952) warn that in 'isolation experiments' (cat) half a year should elapse before all severed pyramidal fibres can be regarded as vanished. Yet the slow pace of degeneration in the pyramid as a whole has often been disregarded, resulting in erroneous conclusions about its site of origin (see van Crevel, 1958).

However, some qualifications must be made here. Degeneration is usually studied from transverse sections. In longitudinal sections it is seen to proceed much faster, because it does not set in simultaneously along the whole fibre, but at random loci. Secondly, only the obvious signs of degeneration were taken into account. When subtler criteria are applied—such as slight swelling or paling of the axon—the degeneration rate is again found to be somewhat higher; but this is impracticable in a study where large numbers of fibres have to be differentiated as normal or degenerated.

Simple inspection shows that the fibres of a severed tract do not degenerate in strict synchronism—it would be most surprising if they did. This asynchronism was described in the last century (Homén, 1885; Stroebe, 1893), and mentioned by many later authors (Doinikow, 1911; Jakob, 1912; Cajal, 1928; Weddell & Glees, 1941); moreover, it was noticed in retrograde cell degeneration (Nissl, 1892; Liu, 1955). However, this simple fact is often ignored in neuro-anatomical studies where degeneration times of a few weeks are used.

Fibre size and degeneration rate. Some authors state that thick fibres degenerate at a higher rate than thin ones, while others maintain the opposite. Our conclusion was that large fibres degenerate faster than thin ones (meaning that a larger proportion of them break down in a unit interval of time). However, sometimes at a late stage more large degenerated fibres are visible than thin ones. This is caused by the slow reabsorption of the debris of large fibres as compared to the rapid disappearance of thin fibres—once they have degenerated. Both observations can be made from the Häggqvist slides, but both have been made with other methods as well. Cajal (1906) found that resorption of large degenerated fibres, as studied in silver

preparations, proceeds more slowly than that of thin fibres; and Duncan (1930) noted that thin fibres are Marchi-positive for only a short time.

In the old literature, no study is found devoted exclusively to the influence of fibre size on degeneration rate. However, Stroebe (1893), Mönckeberg & Bethe (1899), and Marinesco (1907), in their papers on secondary degeneration in general, note that thin fibres are more resistant than large ones. In 1910, van Gehuchten & Molhant, in an elaborate study on this subject, state that the time factor has been entirely neglected in experimental neuro-anatomy, and are of the opinion that their work will cause a revision of neuro-anatomical knowledge. They examined the vagus nerve at various times after section, and conclude that degeneration rate depends on size only, the thinner fibres being the faster ones in degeneration. However, they used the Marchi method, and therefore their 'lois de dégénérescence' are of dubious validity. With this method only debris is stained, and it is not certain that large lumps originate from large fibres and small dust from small ones. Moreover, normal fibres are invisible in Marchi sections, making differentiation between fragmentation and reabsorption by 'indirect' counts impossible. Probably the only thing demonstrated by van Gehuchten & Molhant is that debris of large fibres remains traceable for a longer time than that of thin fibres.

Doinikow (1911) observes that the first fibres to degenerate are large ones, but that the subsequent process develops in the thin fibres at a higher rate. Jakob (1912), working in the same laboratory, states that 'the whole process is faster' in thin fibres than in thick ones. It is not clear what exactly was meant by these authors—both were interested primarily in 'Abbau' and 'Abräumung', rather than in degeneration proper.

Cajal, in his classical work on degeneration and regeneration (1928), concludes that large fibres are the faster to degenerate. Citing van Gehuchten & Molhant, he points out that although the process progresses more rapidly in thin fibres, it starts later. Lassek and Hard, studying the degenerating pyramid with various methods, also conclude that thin fibres have a lower rate of degeneration (Hard & Lassek, 1946; Lassek, 1946*a*, *b*; Lassek & Hard, 1946). Gutmann & Holubár however (1950), come to the opposite conclusion. They studied longitudinal sections because their main criterion for degeneration was discontinuity of the fibres. Nauta, in 1950, wrote that large fibres are slower to degenerate than thin ones, and Combs (1951) reached the same conclusion; in 1957, however, Nauta expressed the contrary opinion.

Summing up, the evidence from the literature is inconclusive and contradictory. Much of the dispute is caused by a lack of clear terms. Thus, 'degeneration' involves two processes—'the fragmentation and loss of normal structure of the nerve fibre severed from its cell of origin, and the reabsorption of the broken and altered material' (Maturana, 1958). The same author continues: 'there is no *a priori* reason for these two processes to proceed at the same rate, and actually there is evidence that they occur at different speeds'. This should be borne in mind when data about the rate of degeneration have to be interpreted, and a definition of the term 'degeneration rate' is a first necessity in those cases. The quantitative data in the present study bear on the first process only: the loss of normal structure of axon and myelin sheath.

However, the distinction between the loss of normal structure of a fibre and its resorption is artificial. Severance of a nerve fibre initiates a complicated process, beginning with the loss of its normal structure, and ending with its disappearance. This proceeds at a higher rate in a thin fibre than in a thick one; but it is quicker to appear in thick fibres than in thin. We defined 'degeneration rate' as the relation between the number of fibres which have lost their normal appearance and the time elapsed since their severance. By that definition, thick fibres degenerate faster than those of small size.

The relation between fibre size and degeneration rate, as established here, explains the slow degeneration of the pyramidal tract as a whole: it consists mainly of very thin fibres. If this relation holds for all fibres in the central nervous system, it might, similarly, explain the old observation that the tracts of the spinal cord degenerate in the order of their myelination (Schaffer, 1895; Worotynski, 1897): other things being equal, the tracts that myelinate first have the greatest proportion of large fibres (Szentágothai, 1941). In other words, the degeneration rate of any tract as a whole would be determined by its fibre pattern.

The exponential law of degeneration. When the results of the counts were plotted, they suggested an exponential curve for each size group. Accordingly, a linear relationship seemed to exist between the logarithm of the percentage of 'not-yet-degenerated' fibres and the degeneration time. Before the (slight) anomalies of the curves are discussed, however, it should be recalled that, although a falling exponential function is a reasonably fitting and compact description of our observations, no proof that it is 'the' description is possible (Sholl, 1948).

The anomalies of the curves are twofold. In the first place, the semilogarithmic graphs do not all run through $y = 2$ for $x = 0$; in other words, degeneration seems to progress at a higher rate during the first few days after the operation than later on. This applies especially to the larger fibres. Three explanations of this phenomenon offer themselves. First, fibres within one size group are not all of the same diameter: the larger ones in the group drag the curve downward at the beginning. Secondly, the phenomenon is well-known in other processes of decay that follow an exponential law. It is related to the relatively large error in the first values of time, and is most striking in fast processes. For some reason or other, perhaps a psychological one, the anomaly is always in the same direction (the zero point should be shifted to the left to get a completely linear relation). In our case, the phenomenon did occur most strikingly in the faster processes, and the shift was in the usual direction. The third explanation is that large fibres do really possess a higher rate of degeneration during the first few days. In this respect Cajal's (1928) observation about 'precocious' degeneration of large fibres, though not supported by counts, should be remembered.

The second anomaly in our curves is located at the other end. There the degeneration seems somewhat 'too slow'. This is, at least to some extent, the result of the presence of foreign fibres in the pyramid, as indicated by the fact that the phenomenon is most prominent in groups 2 and 3 (the lemniscus contains far fewer thin fibres than the pyramid). These fibres vary in number and cause an apparent increase of normal fibres in the degenerating pyramid after 20 weeks. Their influence is detectable only in late stages of degeneration because at that time the number of

normal pyramidal fibres is of the same order. It is also possible that bias has played a part here.

The exponential 'law' means simply that, for each fibre size, the number of fibres degenerating in a unit interval of time is proportional to the number present at that time. Therefore, the degeneration rate of each fibre size could be described by a single constant. For instance, the term 'relative degeneration rate' could be used, in analogy with 'relative growth rate', etc. (Abercrombie & Johnson, 1946). It should be defined as the rate of decrease of the logarithm of the number of surviving fibres, in other words, the slope b of the regression lines of Text-fig. 5. Another way to describe the degeneration rate would be to compute the 'half-life' $T = \log 2/b$ for each fibre size. For the fibres of 0–2 μ this is about 27 days.

An exponential law is well known in other decay processes of unicellular organisms, e.g. bacteria during disinfection (Rahn, 1943) and erythrocytes during exogenous hemolysis (Mendes de Leon, 1954). Its chemical significance appears to be that the process is of the first order, i.e. unimolecular (Booy, 1956). Biologically, it signifies that the cells possess equal resistance. Conversely, divergence from an exponential curve indicates that some elements of the population are more resistant than others, e.g. spores in a sample of bacteria (Rahn, 1943). Thus, the resistance to secondary degeneration may be considered to be equal for fibres of one size group within the pyramidal tract.

SUMMARY

The rate of secondary degeneration and the relation between fibre size and degeneration rate were studied quantitatively in the pyramidal tract of the cat. In a series of twenty-five experiments, the tract was severed unilaterally. The animals were killed after different degeneration times, varying from 3 days to 30 weeks. In each degenerating pyramid, the number of degenerated fibres was determined by the 'indirect' method: comparison of the number of normal fibres in a degenerating tract with the number of fibres in the contralateral (normal) tract. In this way, the degeneration rate (the relation between the number of degenerated fibres and the degeneration time) of each fibre size was determined. In six normal cats both pyramids were analysed to test the assumption that number and pattern of the pyramidal fibres of both sides in a normal specimen are the same. The Häggqvist staining technique, which is suitable for fibre analysis and shows both normal and degenerated fibres, was used throughout.

The following results were obtained:

1. The pyramid of the cat contains some 80,000 fibres; this number, being correlated with body weight, varies considerably. The fibre pattern of the pyramid shows little variation, and averages 73, 20, 5 and 2 % for fibres of 0–2, >2–4, >4–6 and >6 μ respectively. Neither pattern nor number of the fibres in right and left pyramid differs significantly in normal cats.

2. Secondary degeneration in the pyramid is visible with the Häggqvist method from 3 days after decortication onwards. The fibres degenerate asynchronously: normal and degenerated fibres can be seen at the same time. Total degeneration as seen from transverse sections requires several months.

3. The degeneration rate, as defined above, is a function of fibre size, large fibres

degenerating faster than those of small size. Resorption of the debris proceeds more rapidly in thin fibres.

4. The slow degeneration of the pyramidal tract as a whole can be explained by the relation between fibre size and degeneration rate, since it consists mainly of very thin fibres.

5. The time course of secondary degeneration is gradual, and the number of fibres degenerating per time unit declines progressively. Within each size group, the number of fibres degenerating in a unit interval of time is roughly proportional to the number present at that time.

6. This exponential 'law' of degeneration, if confirmed in other tracts, would signify that fibres of equal size possess equal resistance to secondary degeneration.

7. Furthermore, it would allow the degeneration rate of fibres of equal size to be described by a single constant, e.g. the 'relative degeneration rate'.

The authors are deeply indebted to the late Dr D. A. Sholl for statistical advice and criticism.

REFERENCES

ABERCROMBIE, M. & JOHNSON, M. L. (1946). Quantitative histology of Wallerian degeneration. I. Nuclear population in rabbit sciatic nerve. *J. Anat., Lond.*, **80**, 37–50.

BEUSEKOM, G. T. VAN (1955). Fibre analysis of the anterior and lateral funiculi of the cord in the cat. Thesis, Leiden.

BOOY, H. L. (1956). *Inleiding tot de physische biochemie.* Haarlem and Leiden: Erven Bohn and Stenfert Kroese.

BROOKHART, J. M. & MORRIS, R. E. (1948). Antidromic potential recordings from the bulbar pyramid of the cat. *J. Neurophysiol.* **11**, 387–398.

BRUGGEN, J. VAN DER (1929). Over den invloed van cerebrale kinderparalyse op cerebellum en pyramidebaan. Thesis, Amsterdam.

BUSCH, H. F. M. (1961). An anatomical analysis of the white matter in the brain stem of the cat. Thesis, Leiden.

CAJAL, S. R. Y (1906). Notas preventivas sobre la degenerecion y regeneracion de las vias nerviosas centrales. *Trab. Lab. Invest. biol. Univ. Madr.* **4**, 295–301.

CAJAL, S. R. Y (1928). *Degeneration and Regeneration of the Nervous System.* London: Oxford University Press.

COMBS, C. M. (1951). The distribution and temporal course of fibre degeneration after experimental lesions in the rat brain. *J. comp. Neurol.* **94**, 123–176.

CREVEL, H. VAN (1958). The rate of secondary degeneration in the central nervous system. An experimental study in the pyramid and optic nerve of the cat. Thesis, Leiden, Eduard Ydo N.V.

DE MYER, W. & RUSSELL, J. (1958). The number of axons in the right and left medullary pyramids of *Macaca rhesus* and the ratio of axons to myelin sheaths. *Acta morph. neerl. scand.* **2**, 134–139.

DOINIKOW, B. (1911). Beiträge zur Histologie und Histopathologie des peripheren Nerven. *Histol. histopath. Arb.* **4**, 445–630.

DUNCAN, D. (1930). The incidents of secondary (Wallerian) degeneration in normal mammals compared to that in certain experimental and diseased conditions. *J. comp. Neurol.* **51**, 197–228.

DUNCAN, D. (1940). Individual variations in the size of the medullary pyramids. *Anat. Rec.*, **76** (Suppl), 64–65.

EDGAR, G. W. F. (1955). Myelination studied by quantitative determination of myelin lipids. Thesis, Amsterdam.

FLECHSIG, P. (1876). *Die Leitungsbahnen in Gehirn und Rückenmark des Menschen auf Grund entwicklungsgeschichtlicher Untersuchungen dargestellt.* Leipzig: Engelmann.

GEHUCHTEN, A. VAN & MOLHANT, M. (1910). Les lois de la dégénérescence Wallérienne directe. *Névraxe*, **11**, 73–130.

GLEES, P. (1948). The time factor in central nerve fibre degeneration. *Acta anat.* **6**, 447–450.

GLEES, P. (1957). *Morphologie und Physiologie des Nervensystems. Stuttgart*, Thieme.

GUTMANN, E. & HOLUBÁR, J. (1950). The degeneration of peripheral nerve fibres. *J. Neurol.* **13**, 89–105.

HÄGGQVIST, G. (1936). Analyse der Faserverteilung in einem Rückenmarkquerschnitt (Th 3). *Z. mikr.-Anat. Forsch.* **39**, 1–34.

HÄGGQVIST, G. (1948). Faseranalyse und einige dadurch gewonnene Ergebnisse. *Ann. Med. exp. Fenn.* **26**, 1–24.

HARD, W. L. & LASSEK, A. M. (1946). The pyramidal tract. The effect of maximal injury to acid phosphatase content in neurons of cats. *J. Neurophysiol.* **9**, 121–126.

HOMÉN, E. A. (1885). Experimentelle Beiträge zur Pathologie und pathologischen Anatomie des Rückenmarckes speziell mit Hinsicht auf die sekundäre Degeneration. *Fortschr. Med.* **3**, 267–276.

JAKOB, A. (1912). Über die feinere Histologie der sekundären Faserdegenerationin der weissen Substanz des Rückenmarks. *Histol. histopath. Arb.* **5**, 1–181.

JANSEN, J. & BRODAL, A. (1954). *Aspects of Cerebellar Anatomy.* Oslo: Grundt Tanum.

LASSEK, A. M. (1942). The human pyramidal tract. IV. A study of the mature, myelinated fibres of the pyramid. *J. comp. Neurol.* **76**, 217–225.

LASSEK, A. M. (1946*a*). The pyramidal tract. The sensitivity of axons to maximal injury of cells of origin in the cat. *J. comp. Neurol.* **84**, 133–140.

LASSEK, A. M. (1946*b*). The pyramidal tract. The speed of degeneration in axons following ablation of cells of origin in the monkey. *J. comp. Neurol.* **85**, 45–51.

LASSEK, A. M. & HARD, W. L. (1946). The pyramidal tract. The relation of axonal diameters to the rate of degeneration as revealed by the acid phosphatase method in the monkey. *J. Neuropath.* **5**, 374–379.

LASSEK, A. M. & RASMUSSEN, G. L. (1940). A comparative fibre and numerical analysis of the pyramidal tract. *J. comp. Neurol.* **72**, 417–428.

LEVIN, P. M., BONIN, G. VON & CRANDALL, P. H. (1952). The 'isolation technique' in the study of cortical projection systems. *Trans. Amer. neurol. Ass.*, pp. 41–44.

LIU, CHAN NAO (1955). Time pattern in retrograde degeneration after trauma of central nervous system of mammals. In Windle, W. F.: *Regeneration in the Central Nervous System*, pp. 84–93. Springfield: Thomas.

LIU, CHAN NAO & CHAMBERS, W. W. (1958). Intraspinal sprouting of dorsal root axons. *Arch. Neurol. Psychiat.* **79**, 46–62.

MAFFRE, S. (1953). Étude physiologique et morphologique du faisceau pyramidal chez le chien d'après les conséquences de son exclusion 'chronique'. Thesis, Marseille.

MARINESCO, G. (1907). La nature intime du processus de dégénérescence des nerfs. *Pr. méd.* **14**, 105–107.

MATURANA, H. R. (1958). Efferent fibres in the optic nerve of the toad (*Bufo bufo*). *J. Anat., Lond.*, **92**, 21–27.

MENDES DE LEON, D. E. (1954). Haemolytische anaemieën. Thesis, Amsterdam.

MÖNCKEBERG, G. & BETHE, A. (1899). Die Degeneration der markhaltigen Nervenfasern bei Wirbeltieren. *Arch. mikr. Anat.* **54**, 135–183.

MORIN, G., POURSINES, Y. & MAFFRE, S. (1951). Sur l'origine de la voie pyramidale. Documents obtenus par la méthode des dégénérescences descendantes chez le chien. *J. Physiol. Path. gén.* **43**, 75–96.

NAUTA, W. J. H. (1950). Über die sogenannte terminale Degeneration im Z.N.S. und ihre Darstellung durch Silberimpregnation. *Schweiz. Arch. Neurol. Psychiat.* **66**, 353–376.

NAUTA, W. J. H. (1957). Silver impregnation of degenerating axons. In Windle, W. F.: *New Research Techniques of Neuro-anatomy*, pp. 17–26. Springfield: Thomas.

NISSL, F. (1892). Über die Veränderungen der Ganglienzellen am Facialiskern des Kaninchens nach Ausreissung der Nerven. *Allg. Z. Psychiat.* **48**, 197–198.

RAHN, O. (1943). The problem of the logarithmic order of death in bacteria. A critical discussion. *Biodynamica*, **4**, 81–130.

REXED, B. (1944). Contributions to the knowledge of the post-natal development of the peripheral nervous system in man. Thesis, Stockholm.

SCHAFFER, K. (1895). Über die zeitliche Reihenfolge der secundären Degeneration in den einzelnen Rückenmarkssträngen. *Neurol. Zbl.* **14**, 386–390.

SHOLL, D. A. (1948). Quantitative investigations of vertebrate brain and applicability of allometric formulae. *Proc. Roy. Soc.* B, **135**, 243–258.

SPATZ, H. (1921). Über die Vorgänge nach experimenteller Rückenmarksdurchtrennung. *Histol. histopath. Arb.* 49–364.

SPIELMEYER, W. (1922). *Histopathologie des Nervensystems.* I. Band. Berlin: Springer.

SPIELMEYER, W. (1929). Degeneration und Regeneration am peripherischen Nerven. *Handbuch der normalen und pathologischen Physiologie*, IX, 285–338. Berlin: Springer.

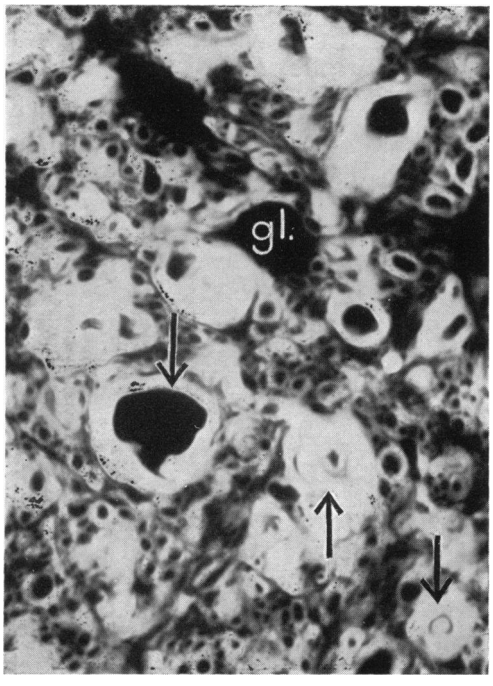


Fig. 1

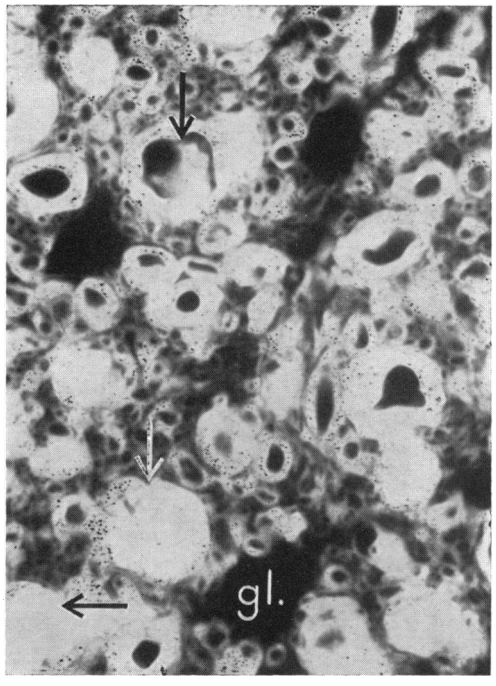


Fig. 2

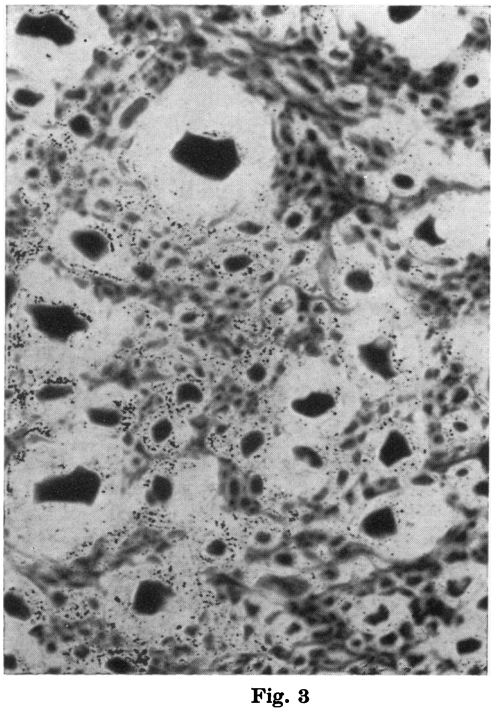


Fig. 3

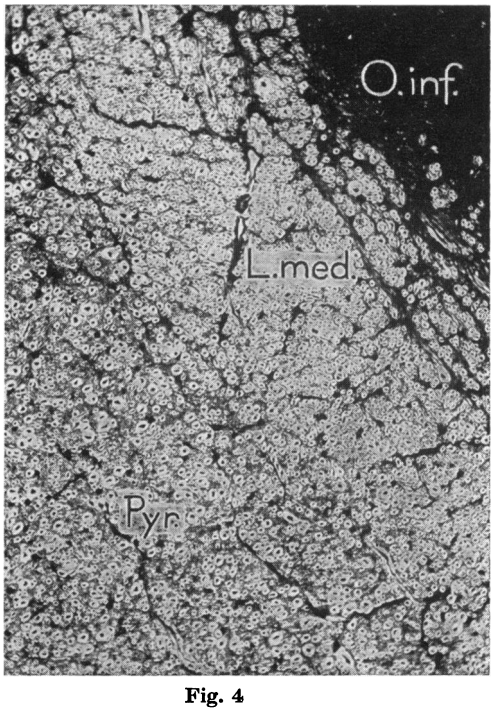


Fig. 4

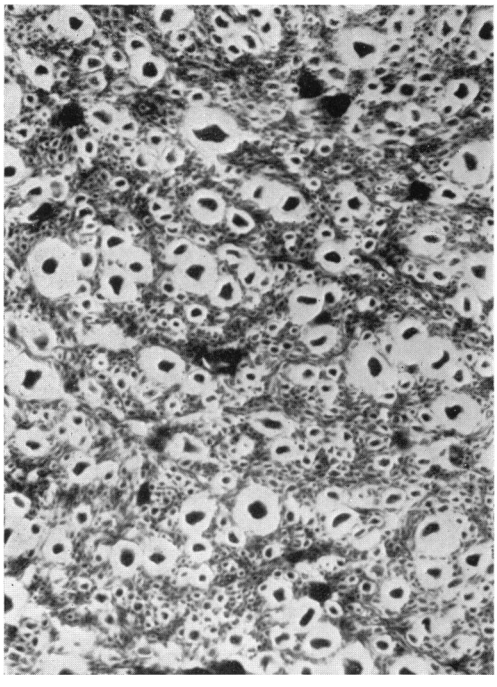


Fig. 5

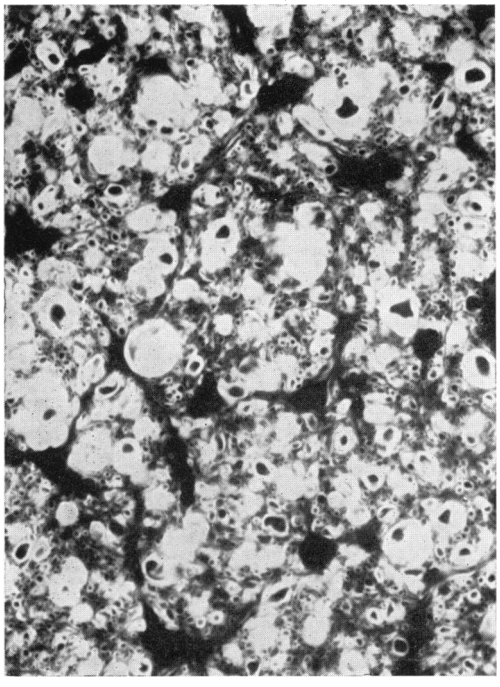


Fig. 6

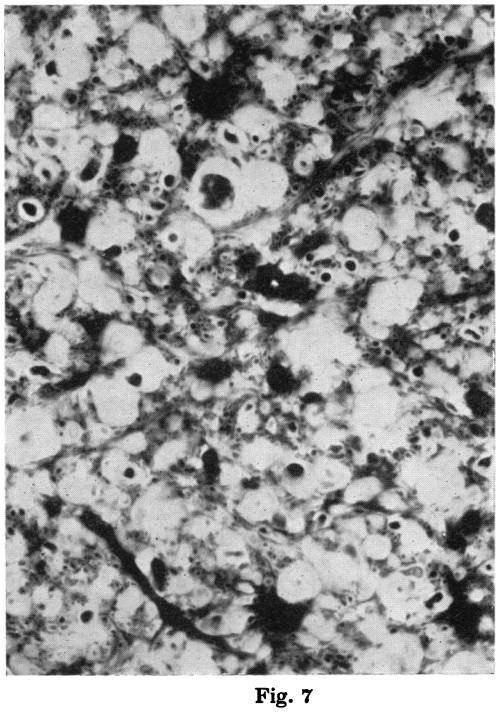


Fig. 7

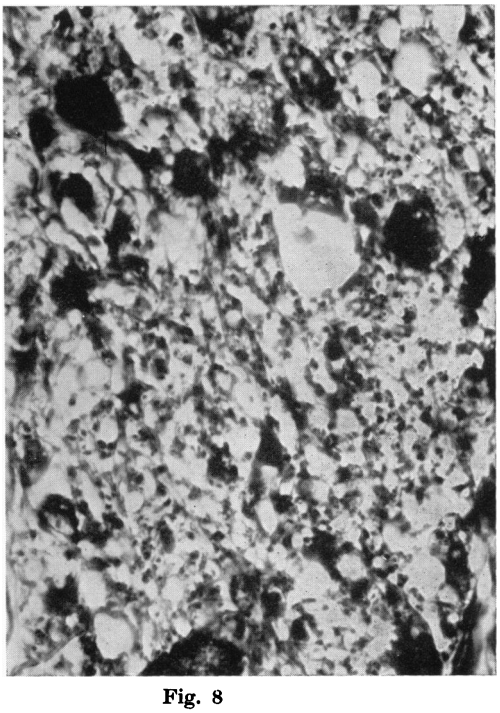


Fig. 8

SPIELMEYER, W. (1930). *Technik der mikroskopischen Untersuchung des Nervensystems.* Berlin: Springer.

STROEBE, H. (1893). Experimentelle Untersuchungen über Degeneration und Regeneration peripherer Nerven nach Verletzungen. *Beitr. path. Anat.* **13**, 160–278.

SZENTÁGOTHAI, J. (1941). Die Bedeutung des Faserkalibers und der Markscheidendicke im Zentralnervensystem. *Z. ges. Anat.* **1. Z. Anat. EntwGesch. 111**, 201–225.

VERHAART, W. J. C. (1947). On thick and thin fibres in the pyramidal tract. *Acta psychiat. neurol.* **22**, 271–281.

VERHAART, W. J. C. (1948*a*). The pes pedunculi and pyramid. *J. comp. Neurol.* **88**, 139–155.

VERHAART, W. J. C. (1948*b*). The pes pedunculi and pyramid in hylobates. *J. comp. Neurol.* **89**, 71–78.

VERHAART, W. J. C. (1953). The anatomy of the pyramidal tract. *Folia psychiat. neerl.* **56**, 923–942.

WEDDELL, G. & GLEES, P. (1941). The early stages in the degeneration of cutaneous nerve fibres. *J. Anat., Lond.*, **76**, 65–93.

WOROTYNSKI, P. (1897). Zur Lehre von den secundären Degenerationen im Rückenmarcke. *Neurol. Zbl.* **16**, 1094–1097.

ZIEHEN, T. (1899). Centralnervensystem. In *Bardelebens Handbuch der Anatomie*, IV. Bd, I. Teil. Jena: Fischer.

EXPLANATION OF PLATES

PLATE 1

The Häggqvist stain: secondary degeneration and fibre patterns.

Fig. 1. Degenerated fibres (mainly large) between normal fibres (mainly thin) in the pyramid. H 2794, ×1400.

Fig. 2. Idem: note hyperchromatosis, swelling and break-down of axons (*gl.* = glial cell). Same cat, same magnification.

Fig. 3. Normal (contralateral) pyramid of the same cat for comparison with figs. 1 and 2. Same magnification.

Fig. 4. Border between the normal pyramid and medial lemniscus: note difference in fibre pattern. Same cat, ×140.

PLATE 2

Degeneration in the pyramid at different times after decortication. ×550.

Fig. 5. Normal pyramid for comparison with figs. 6–8. H 2794.

Fig. 6. Degeneration time 1 week: mainly large fibres degenerated. H 2794.

Fig. 7. Degeneration time 3 weeks: many thin fibres also degenerated. H 2889.

Fig. 8. Degeneration time 16 weeks: nearly all fibres degenerated; glial proliferation. H 3520.