FIBRE DEGENERATION IN THE CEREBRAL CORTEX OF THE CAT AND RABBIT FOLLOWING EXPERIMENTAL CRANIOTOMY

By W. G. HARRIS

Department of Anatomy, University College, London

INTRODUCTION

During the course of a series of experiments on the cats' cerebral cortex it was noted that craniotomy and exposure of the pia mater by incising the dura mater resulted in histologically demonstrable fibre degeneration in the underlying cortex. There had been no interference with the pia mater or the cortex. As experimental craniotomy is frequently performed prior to lesions being made in the cerebral cortex this observation seemed of some considerable importance. Further experiments have been carried out to verify it.

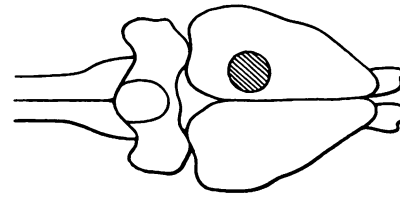
MATERIALS

Three cats and seven rabbits were used, of differing sex and breed. The cats were anaesthetized with intraperitoneal nembutal supplemented with ether when necessary. The rabbits were anaesthetized with intravenous nembutal.

METHOD

(*a*) *Rabbits*

The rabbits were divided into three pairs. In one of each pair craniotomy was performed and the dura incised, thus exposing the pia mater. In the second of each pair after craniotomy the dura was left intact. The seventh animal was the second of a pair in which the first sustained damage to the cortex during operation and has not been included in the results.



Text-fig. 1. Rabbit brain. The shaded area shows the approximate position and extent of the craniotomy.

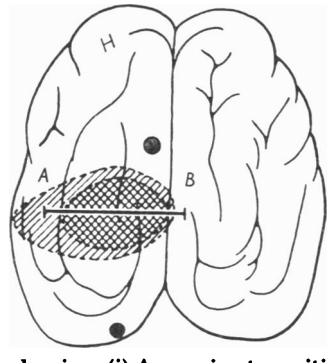
In all rabbits the craniotomy was performed in the same situation on the skull. This is shown in Text-fig. 1 in which the shaded area shows the approximate site and size of the bony defect.

The brains were perfused and removed 4 and 5 days after operation. In each animal the bony defects were measured immediately before the brain was removed.

(*b*) *Cats*

In cat 1 the bony defect was large (Text-fig. 2). The dura beneath was incised and the pia exposed. In each of the second and third cats there were two small craniotomies (Text-fig. 2) and in each of these cats the dura under only one of the defects was incised.

The brain of the first cat was perfused and removed 5 days after operation. Those of the second and third cats were perfused and removed 8 days after operation.



Text-fig. 2. Cat brain. Diagram showing: (i) Approximate position and extent of the bone defect in cat 1; shaded ▨. (ii) Approximate position and extent of the dural defect in cat 1; shaded ●. (iii) Approximate position and extent of the bone and dural defects in cats 2 and 3; shaded ●. (iv) *AB* is the plane of the section drawn in Text-fig. 4.

(*c*) *Method of craniotomy*

(i) The head was shaved.

(ii) A mid-line incision was made from the root of the nose to the external occipital protuberance.

(iii) The occipito-frontalis muscle was incised in the mid-line and the left one retracted laterally.

(iv) The left temporal fascia was incised along its line of attachment to the skull.

(v) The left temporal muscle and periosteum on the left side of the skull were reflected laterally using a rugine.

(vi) A dental burr was used to make a hole in the skull. Care was taken not to leave the burr in contact with bone for more than four or five seconds at any one time. It was found that if it was left longer than this undue heat was generated and it was feared that this would damage the underlying cortex. When the pial vessels could be plainly seen through the bone the burr was discarded and a pair of finely pointed scissors used to pierce this last thin piece of bone and then remove it. Haemorrhage from the bone edges was controlled with bone wax. If enlargement of the skull defect was desired it was done with bone ronguers. All the rabbits and cat 1 had their skull defects enlarged with rongeurs. The defects of cats 2 and 3 were not enlarged in this way.

(vii) If the dura was to be incised it was anchored with a dural hook, raised slightly and a small cut made in it with scissors. This small cut was then enlarged in the form of a cruciate incision. It was found that the arachnoid was always

incised with the dura and C.S.F. leaked from the incision as soon as it was made. The pia mater was left exposed for about 30 sec and then the dura was replaced over the surface of the cortex. No attempt was made to suture the dura.

(viii) Whether the dura had been incised or not the bone defect was covered with gelatin sponge soaked in thrombin.

(ix) Muscles were sewn back in position in one layer with interrupted thread sutures—i.e. right occipito-frontalis to left occipito-frontalis and left temporal muscles.

(x) The skin was sutured with interrupted thread. In the first cat the craniotomy performed differed from the above in that the hole through the skull was made with a trephine rather than a dental burr. The centre pin of the trephine had been removed as this had previously been found to cause damage to the underlying cerebral cortex.

(*d*) *Perfusion and section*

All animals were perfused through the aorta with normal saline followed by 10 % neutral formal-saline. After perfusion the brains were removed and placed in 10 % neutral formal-saline for 3 to 4 weeks.

20μ frozen sections were taken and stained by the Nauta-Gygax technique (1954). Sections were taken as follows:

Rabbits. (i) The left hemispheres of each pair of animals were sectioned and stained in pairs. The part of each hemisphere sectioned included the area of cortex under the bone defects.

(ii) Sections were taken of the right anterior cortex from the animal in which the dura had been left intact. These sections were used as controls.

Cat 1. (i) Sections taken from the cortex under the bone defect. (ii) Sections taken from the right frontal cortex and used as control.

Cats 2 *and* 3. (i) Sections taken from the cortex under the anterior and posterior defects.

(ii) Sections taken from the right frontal cortex and used as controls.

The two groups of sections taken from each animal were divided into batches. The sections in each batch were stained at the same time and in the same solutions.

RESULTS

(*a*) *Rabbits*

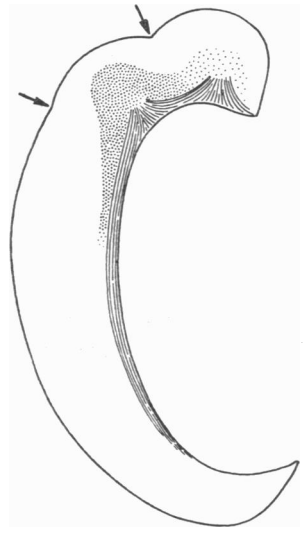
In those rabbits in which the dura had been left intact the brain appeared normal macroscopically. There was no discoloration or sign of compression and after the brain had been perfused and removed it was not possible to see which area of cortex had been underlying the bone defect.

In those rabbits in which the dura had been incised the dura had retracted to the bone edges in all the animals and the brain had herniated, to a small extent, through the dural and bone defects. When the brain had been perfused and removed a small 'hillock' was seen on its surface, with well-defined edges, clearly showing the extent of the dural and bone defects. The surface of each hillock was smooth and no haematomata were seen on any part of the herniated areas of cortex. Thus, apart from the raised area the brain appeared normal.

Size of the bone defects

These were approximately 1 cm. in diameter in all the rabbits but varied between 0·8 and 1·2 cm.

Striking signs of degeneration were seen in all the animals that had undergone craniotomy with incision of the dura, other parts of the cortex and the controls being free of degeneration (Pl. 1). The most marked degeneration was seen in the deepest parts of the cortex, but in the area under the central parts of the defect the degenerating fibres could be traced nearer to the surface. In two sections of one animal it could be traced right up to the surface. In these two sections degeneration could also be seen in the tangential fibres of layer one. As each section included the whole dorso-ventral extent of the hemisphere, cortex well away from the defect was included. In all sections this was clear of degenerating fibres (see Text-fig. 3).



Text-fig. 3. Drawing showing the extent of the degenerating fibres in a transverse section of rabbits brain. The arrows demarcate the extent of the herniation. (Drawn from a section.)

The distribution of degenerating fibres is not an indication of the actual number present. It is more difficult to stain the smaller superficial fibres with this technique and the apparent small number stained does not necessarily mean that few fibres were degenerating.

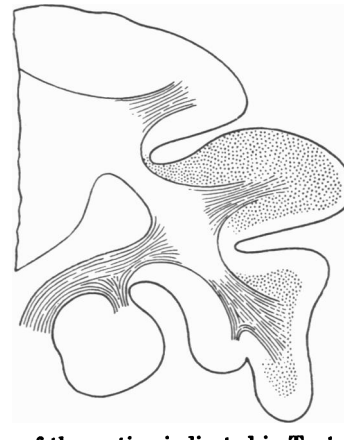
In the animals in which the dura was left intact there was either very little degeneration to be seen or none at all. Of the four animals examined three showed no degeneration and in one a small number of degenerating fibres was visible in the cortex under the defect.

(*b*) *Cats*

In all three animals the brains appeared normal. No herniation had occurred through the dural defects and after the brains had been perfused and removed it was not possible to tell which had been the exposed areas of cortex.

In *Cat* 1 the bone defect was large (4 cm. × 2·4 cm.) and after perfusing the brain it was found that the dura had not retracted right to the bone edges as in all the other animals used. It had only partially retracted and exposed an area of cortex 2·1cm. × 1·6 cm. (Text-fig. 2). Sections were taken through the exposed area of cortex as shown in this illustration and degenerating fibres were found in great number in the area of cortex left exposed by the retracting dura (Text-fig. 4). The cortex which had been covered by dura, even though not covered by bone, was free of degeneration.

The fibre degeneration was seen through the entire thickness of the cortex, including the tangential fibres in layer one and the picture resembled that seen in the cortex following a lesion in the underlying medullary tissue (Pl. 1, figs. 1, 2).



Text-fig. 4. Cat 1. Drawing of the section indicated in Text-fig. 2 by the line *AB*. Dotted area shows the extent of the degeneration.

Cats 2 *and* 3.

Size of bone defects.

Cat 2 { *Anterior* 0·6 cm. × 0·5 cm. Dura intact.
Posterior 0·4 cm. × 0·5 cm. Dura incised.

Cat 3 { *Anterior* 0·6 cm. × 0·4 cm. Dura incised.
Posterior 0·4 cm. × 0·3 cm. Dura intact.

In both these animals the cortex under the incised dura showed degenerating fibres (Pl. 1, figs. 5, 6). In cat 2, however, its full extent could not be determined because of failure of the stain in one batch of sections. It appeared to be minimal in amount and extent. This was confirmed in cat 3. In the cortex under the craniotomy where the dura was left intact no degeneration was seen in Cat 2 but a small number of degenerating fibres were seen in cat 3.

DISCUSSION

The original suspicion that a simple craniotomy and incision of the dura will give rise to degeneration in the underlying cortex has been verified. Large cranial defects in the region of 1–3 cm. in diameter including incision of the dura result in heavy degeneration. If lesions are made in the brain through such a defect the degeneration resulting from the craniotomy will confuse the picture. However, if

the bone defect and subsequent dural incision is small—in the region of half a centimetre in diameter—the resulting degeneration is minimal. It may be possible to use a simple craniotomy of over 1 cm. diameter and with incision of the dura to produce degeneration in a small area of cortex.

As it is the intention of this paper only to record the observation made, no attempt has been made to trace the exact cause and mechanism of production of the degeneration, but certain conclusions can be drawn from the known facts. When the dura was incised during craniotomy the pia was left exposed to air for about 30–45 sec before the dural flaps were placed back in position and the bone defect covered with a gelatin sponge soaked in thrombin. In these exposed areas of cortex degeneration could be demonstrated. However, in cat 1 the dura had not retracted completely to the bone edge so that the dural defect was less than the bone defect. Degeneration could only be seen in the cortex left exposed by the retracting dura. In the cortex still covered by the dura no degeneration could be seen. It seems therefore that the dura protected the cortex from whatever it was that caused the degeneration even when the dura in a neighbouring area has been damaged.

The factor causing the degeneration must be found either in the technique of the craniotomy or in the post operative period.

Damage during the craniotomy might be the cause of the degeneration. This is the main reason why a detailed description of the routine used has been given. However up to the point at which the dura was opened the procedure in all animals was the same and yet it was only in those which subsequently had the dura incised that degeneration regularly occurred. This exonerates from blame all the steps before this stage, including the use of rongeurs for enlarging the bone defect. The use of this instrument with its thick beaks almost certainly resulted in some pressure being applied to the cortex but degeneration did not necessarily result from this. Similarly, the use of the dural hook to anchor the dura before its incision almost certainly resulted in no harm to the cortex even though several attempts have to be made to 'catch' the dura. It seems, therefore, that the cause of degeneration must be sought in the post-operative period when some factor was acting on the unprotected area of cortex.

In no animal or section examined was any necrosis of brain tissue seen. There was no mass destruction of tissue and so no direct interference with nerve fibres. This would indicate that any mechanical pressure applied to the cortex was not severe and certainly not sufficient of itself, to cause fibre degeneration. That no pressure was in fact exerted can be seen from the fact that herniation of the rabbit brains occurred when the opposite effect would be expected if a pressure had been applied to the cortex. For degeneration to occur in the depths of the cortex as seen in the rabbits it is probable therefore that the factor responsible acted on the pial vessels, not on the cortex itself and produced a vascular spasm. This spasm resulted in ischaemia of the underlying cortex of sufficient severity to cause the degeneration seen, but insufficient to cause necrosis.

Shortly after opening the dura the author has often seen spasm of the pial vessels, without any stimulation being directly applied to them. Echlin in 1942 showed that constriction of the pial arteries of the cat occurred after electrical or mechanical

stimulation. Following this he was also able to show that a focal cerebral ischaemia resulted and that the spasm and resulting ischaemia remained localized to the area stimulated. The mechanical stimulation used by Echlin was stretching or stroking the vessel wall and it seems that the type of stimulation to which the vessels in the exposed areas of pia following the craniotomies were exposed could have been similar. Further from Echlin's experiments it can be argued that a vascular spasm was set up which was localized in extent and gave rise to a local area of ischaemia.

Holmes, Highet & Seddon (1944), in their studies of peripheral nerve changes in Volkmann's contracture, showed that it is possible to have a degree of anoxia sufficient to cause Wallerian degeneration in a nerve without necrosis. There is no reason to suppose, therefore, that a degree of anoxia may not be brought about in the cortex sufficient to cause fibre degeneration but insufficient to cause necrosis.

Apart from the mechanical factors causing a vascular spasm there is also the effect of gelatin sponge and thrombin on the cortex to be considered. Gelatin sponge soaked in thrombin was always applied to the bone defects before the operation was completed and in those animals in which the pia was exposed these substances would be in direct contact with it. As a result they may themselves cause a vascular spasm similar to that described above or have a direct action on the cortex.

Whatever the factor may be which causes this degeneration a large bone and dural defect will give rise to degeneration in the underlying cortex of such quantity that it may be difficult or impossible to differentiate it from that caused by a subsequent lesion in or under the cortex. On the other hand, a small bone and dural defect gives rise to minimal degeneration and if the dura is left intact there may be no degeneration at all.

SUMMARY

1. Experimental craniotomy in rabbits and cats with incision of the dura will result in fibre degeneration in the underlying cortex.

2. Small bone and dural defects, in the region of 0·5 cm. in diameter, will result in minimal degeneration.

3. Large bone and dural defects (over 1 cm. in diameter) will result in profuse degeneration.

4. Experimental craniotomy leaving the dura intact does not necessarily result in fibre degeneration.

I wish to thank Prof. J. Z. Young for his continuous support and help during these experiments and in the subsequent written account. Also Dr D. Sholl for his encouragement and suggestions. In addition I would like to thank Mr Armstrong for the photomicrographs, Mr Lee for the drawings and Miss Shira for technical assistance.

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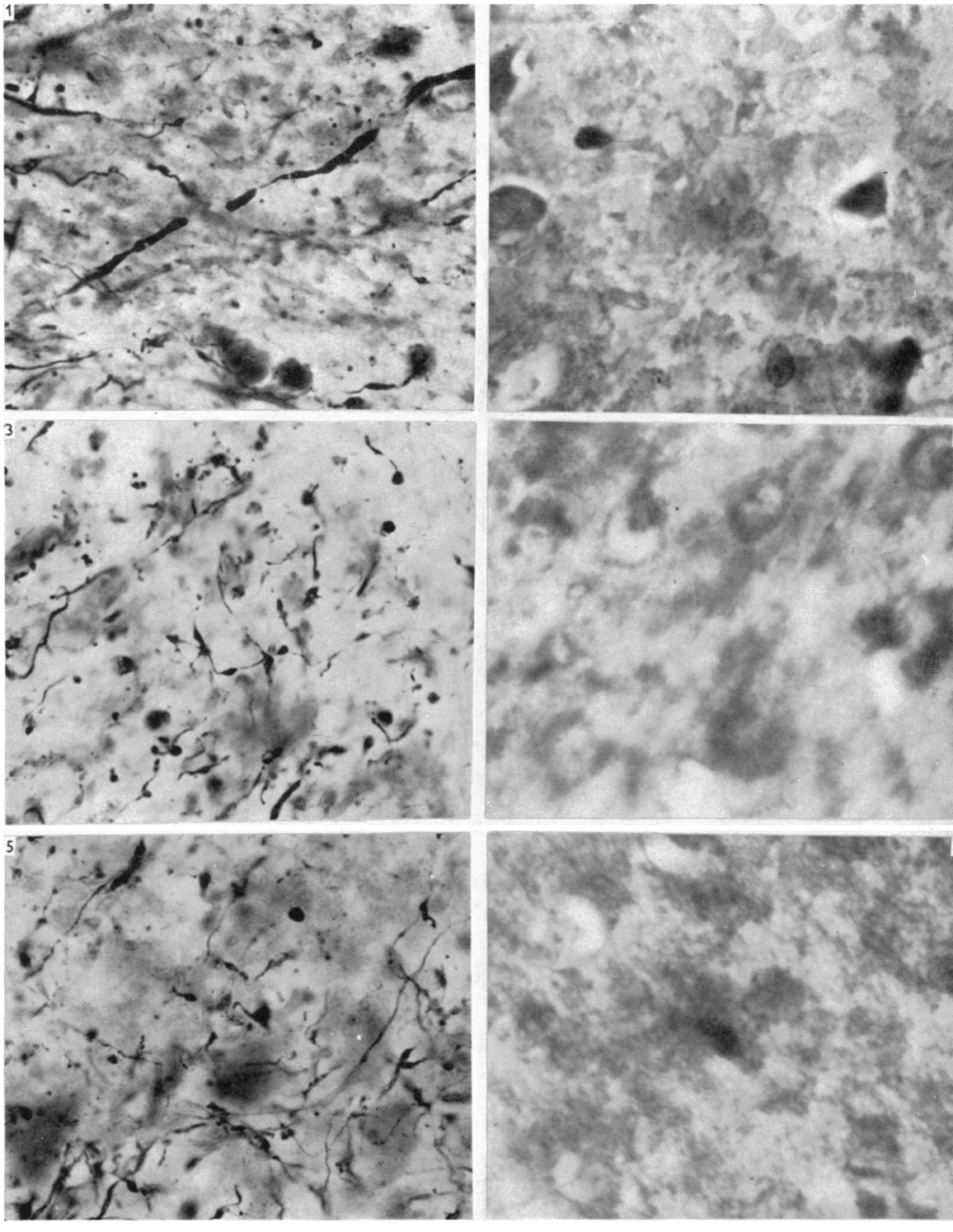

HARRIS—FIBRE DEGENERATION FOLLOWING CRANIOTOMY

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EXPLANATION OF PLATE

(All $\times 1100$.)

Figs. 1, 2. Cat 1. Fig. 1. The section shows a large degenerating fibre in the cortex underlying the dural defect. Fig. 2. Control section from the right frontal region.

Figs. 3, 4. Rabbit 1. Fig. 3. Degenerating fibres and terminals in the exposed cortex. Fig. 4. This is the same section as Fig. 3 but shows an area of cortex which had not been exposed.

Figs. 5, 6. Cat 2. Fig. 5. A section showing degenerating fibres and terminals in the exposed cortex. Fig. 6. Control from the right frontal region.