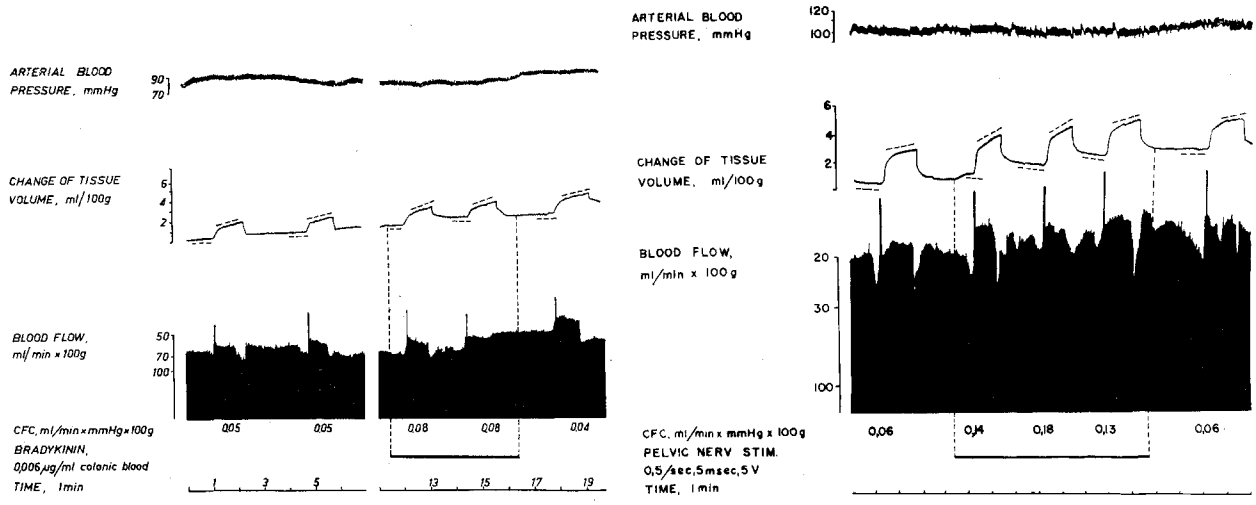


Fig. 2. The effect of subthreshold doses of bradykinin (left panel) and subthreshold stimulation of the pelvic nerves (right panel) on colonic blood flow, tissue volume and the capillary filtration coefficient (CFC). Note the almost identical responses.

comitantly a sustained and powerful motor contraction (left panel), an effect which is in many respects similar to that produced by efferent electrical stimulation of the pelvic nerves (right panel). Close intraarterial infusion of bradykinin in low doses (0.006 µg/ml) decreased vascular resistance only moderately, while the capillary filtration coefficient (CFC) increased considerably. As is shown in Figure 2 (left panel), a marked increase in CFC occurred following infusion of bradykinin in doses that did not affect blood flow at all. When the pelvic nerves were stimulated at high rates, the motor response interfered with the tissue volume recordings and made CFC determinations impossible. On the other hand, pelvic nerve stimulation at a low rate which did not affeet motility or blood flow resistance nevertheless increased CFC to a considerable extent, Figure 2 (right panel).

*Discussion.* Specific vasodilator fibres were previously assumed to be widely distributed throughout the gastrointestinal tract. In recent years this concept has changed, however, and it has been suggested that neurogenous vasodilatation, which occurs only in certain restricted parts of the gastrointestinal tract, i.e., the salivary gland, the pancreas and probably the stomach, is partly or mainly caused by the release of a stable vasodilator material, a plasmakinin [2–5]. The present results indicate that a similar mechanism might be involved, even in the regulation of colon blood flow and secretion.

The vasodilatation and the concomitant motor response following pelvic nerve stimulation are largely atropine-resistant. This coupled response is closely mimicked by infusion of bradykinin. Following infusion of subthreshold doses of bradykinin as well as after pelvic nerve stimulation at a frequency that did not affect motility or resting blood flow, CFC increased considerably. The magnificant increase in CFC which occurred despite unchanged blood flow might therefore be due to increased capillary permeability. CFC often reached figures comparable to those commonly recorded when the vascular bed is brought to maximal dilatation by an unspecific vasodilator drug.

*Zusammenfassung.* Indiz, dass Plasma-Kinin sowohl in den Regulationsmechanismus der Kolon-Motilität als auch der Blutströmung eingreift.

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## A Quantitative Investigation of the Response to Injury of the Central Nervous System of Rats Treated with ACTH and Triiodothyronine

Although interruption of a tract in the mammalian central nervous system (CNS) is not usually followed by any functional regeneration, histological signs of axonal growth and/or indications of some return of function have been claimed following the administration of the thyroid hormones triiodothyronine (T3) and tetraiodothyronine (T4), [1,2] and adrenal corticoids [3,4] or substances which cause their release, such as ACTH [1,5] or the bacterial polysaccharide 'Pyromen' [3,6–9].

Most workers consider that circulating corticoids stimulate the phagocytic activity of macrophages, depress the cellular and fluid phases of inflammation and decrease the formation of connective tissue at the site of a wound in the CNS and thereby facilitate regeneration by providing an environment through which axons grow more easily. On the other hand thyroid hormones may promote regeneration by increasing protein synthesis in central neurons [1].

This paper reports the findings of a quantitative study on the effects of ACTH and T3 on the glial response within the corpus callosum following surgical incision.

*Materials and methods.* Adult male Wistar rats aged 40 days post partum were used. 30 animals were allocated to each of the following 4 treatment groups: 1. normal saline; 2. ACTH (Synthecin Depot CIBA); 3. T3 (Glaxo Freeze Dried preparation); 4. ACTH and T3 together. Within each group 5 animals were allocated for study at 1, 2, 5, 10, 50 and 100 days after cutting the corpus callosum. Injections were given 6 h before making the lesion and at 24 h intervals thereafter. The total number of injections received by each animal surviving for a period of 1, 2, 5, 10, 50 or 100 days were 2, 3, 6, 7,7 or 7 respectively. The doses given (per 100 g body weight) were as follows: 0.75 ml normal saline; 10 μg ACTH; 3 μg T3; 10 μg ACTH + 3 μg T3 (see FERTIG et al[1] for rationale of dosages). The entire corpus callosum was cut stereotaxically along a saggittal plane 2 mm from the midline.

The glial reaction occurring in the corpus callosum 1, 2, 5 and 10 days after making the lesion was measured counting the number of cells in 5 sections from each animal, occupying a grid 75 μm × 75 μm placed 50, 150, 250, 500 and 1000 μm from the boundary of the wound in sections stained with cresyl violet. As well as estimating total density, the cell population was differentiated into seven sub-populations, namely: light oligodendroglia, medium oligodendroglia, dark oligodendroglia, astrocytes, microglia and endothelial cells according to their nuclear characteristics[10–14] and 'cytoplasmic cells' according to both the configuration of chromatin and the presence of a stainable cytoplasm (a group of cells probably analogous to 'brain macrophages').

The functional tests for regeneration of axons consisted of eliciting an interhemispheric response (IHR) in 2 groups of 5 animals surviving for 50 and 100 days after making the lesion. The IHR is mostly eliminated by cutting this tract except for a characteristic low amplitude residual response[15]. Qualitative histological examination of silver stained sections from the brains of these animals were also carried out.

The activity of the ACTH and T3 were tested by measuring the release of corticosterone using a fluorimetric technique[16] and the uptake of $I^{131}$ sodium iodide in the thyroid glands respectively. Control animals received injections of normal saline.

*Results.* It was found that none of the treatments with hormones caused any change in the time course or magnitude of the reaction of any of the cell types when compared with the reactions in control animals. Figure 1, shows the reactions of the cell population as a whole and demonstrates this finding clearly. Most individual cell

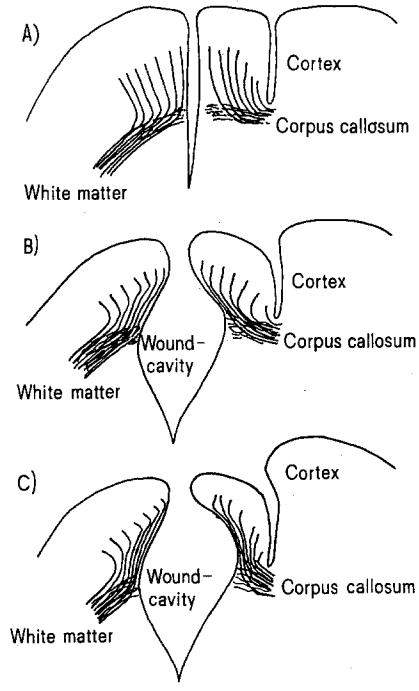


Fig. 3. Proposed explanation through A to C. for the formation of the tract of axons seen to lie along the edges of the wound in animals sacrificed 50 and 100 days after operation.

Fig. 2. Photomicrograph of a coronal section (7 μm thick) of the brain of a rat showing the site of the lesion on the 50th post-operative day. Note the cavitation of the wound and the tract (T) of fibres which lines the cavity (Glees-Marsland × 16). S.F., Sagittal fissure; W.M., White matter; C. C., Corpus callossum; the dotted line marks the line of the incision.

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types in the corpus callosum reacted to injury in a characteristically similar manner; initially their numbers dropped near the site of the lesion to values below those recorded at a distance but soon recovered and by 10 days the number near the lesion was consistently greater than the number at a distance. The one exception to this pattern of response was the reaction of 'cytoplasmic cells'. On the first post-operative day 'cytoplasmic cells' were seen in larger numbers near the edge of the wound than at a distance and this pattern persisted throughout the 10 day period of study.

The electrophysiological tests for regeneration carried out at 50 and 100 days failed to elicit any response which was clearly indicative of the growth of axons across the lesion. Histological examination of specimens revealed that regeneration had not occurred because of the presence of a large cavity between the cut ends of the tract. In a number of cases this cavity was lined by a tract of axons (Figure 2). It was considered that the tract was created by shrinkage of the damaged cortex rather than regrowth of axons along the edge of the wound. This proposition is explained in Figure 3. The ACTH and T3 assay procedures showed that in both cases the hormones were physiologically active.

*Discussion.* In the light of these results, it seems unlikely that ACTH and T3 induce regeneration in the CNS by way of altering the glial reaction or the number of 'cytoplasmic cells' that collect at the site of injury. The validity of these conclusions is supported by the fact that the preparations of hormones used in these experiments were shown to be physiologically active at the dosages used. This finding substantiates the work of CAVANAGH and JOSEPH[17] and challenges the accepted ideas about the mode of action of ACTH in promoting regrowth of axons[13,14]; strongly suggesting that an alternative explanation for the ability of these substances to induce regeneration must be sought.

FERTIG et al[1] showed that both T3 and ACTH can promote regeneration in the mammalian CNS. However it was not possible to demonstrate regeneration in the present experiments simply because the leakage of CSF from the ventricle into the incision produced a cavity which could not be bridged by axons.

*Résumé.* Une étude quantitative des effets de ACTH et T3 sur la réaction des cellules gliales dans le corpus callosum, après incision, a montré que ces 2 hormones n'ont aucun effet sur cette réaction. Ainsi, on ne peut plus soutenir l'idée généralement acceptée que ces hormones provoquent une régénération partielle de l'axone central du système nerveux, en modifiant la cicatrice gliale.

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[18] Acknowledgments. The authors are indebted to Mr. R. MORRIS at the Women's Hospital, Birmingham, for the assay of corticosterone and to Mrs. S. BUCKLEY for preparing the many slides for histological examination.

## Catfish and Electric Fields

Since PARKER and VAN HEUSEN[1] discovered the sensitivity of the brown bullhead, *Ictalurus nebulosus* LeS., to electric currents less than a microampere, the lack of attention to this subject in the next period was followed by a rather explosive increase in interest when DIJKGRAAF[2] again tackled the problem of the electroreceptive properties of these fish. It was found that receptors of the ampullary type, the 'small pit organs' (SPO), were the electroreceptors involved[2–6]. The current density threshold of these SPO's proved to be as low as $10^{-11}$ A/mm$^2$ in water with a specific resistivity of 20 $\Omega$.m. The frequency response ranged from DC to about 25 Hz[3–7]. Further several types of natural electric fields were detected. Some of these fields were produced by living organisms, other were of unknown origin but nevertheless unmistakably a real property of the ponds inhabited by catfish[8]. The strengths and frequency components of these fields corresponded with the sensitivity and frequency response of the SPO's. The aim of the following experiments was to investigate the significance of these fields for *Ictalurus*.

The observations of PARKER and VAN HEUSEN[1] and those of Dijkgraaf[2] suggest that catfish might use the

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Table I. Number of responses of fish fed with *Xenopus* larvae to 2 simultaneously offered dummies of which one (X~) generated an electric field

| response/prey | X~ | Xo |
|---|---|---|
| Swallowing | 39 | 6 |
| Interest | 15 | 17 |
| No reaction | 0 | 31 |
| Flight | 0 | 0 |

Table II. Number of responses of fish fed with meat to 2 simultaneously offered dummies of wich one (X~) generated an electric field

| response/prey | X~ | Xo |
|---|---|---|
| Swallowing | 4 | 3 |
| Interest | 4 | 1 |
| No reaction | 13 | 19 |
| Flight | 3 | 1 |