

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 JOSEPH¹⁷ 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.

FERRIG et al¹ 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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¹⁷ J. B. CAVANAGH and J. JOSEPH, *Guy's Hospital Rep.* 107, 144 (1958).

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Catfish and Electric Fields

Since PARKER and VAN HEUSEN¹ 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 DIJKGRAAF² 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 involved³⁻⁶. The current density threshold of these SPO's proved to be as low as 10⁻¹¹ A/mm² in water with a specific resistivity of 20 Ω.m. The frequency response ranged from DC to about 25 Hz³⁻⁷. 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 catfish⁸. 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 HEUSEN¹ and those of Dijkgraaf² suggest that catfish might use the

¹ G. H. PARKER and A. P. VAN HEUSEN, *Am. J. Physiol.* 44, 405 (1917).

² S. DIJKGRAAF, *Experientia* 24, 187 (1968).

³ A. ROTH, *Z. vergl. Physiol.* 61, 196 (1968).

⁴ A. ROTH, *Z. vergl. Physiol.* 65, 368 (1969).

⁵ A. ROTH, *Z. vergl. Physiol.* 75, 303 (1971).

⁶ A. ROTH, *J. comp. Physiol.* 79, 113 (1972).

⁷ R. C. PETERS and R. J. A. BUWALDA, *J. comp. Physiol.* 79, 29 (1972).

⁸ R. C. PETERS and F. BRETSCHNEIDER, *J. comp. Physiol.* 81, 345 (1972).

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 which one (X~) generated an electric field

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

bioelectric fields among other things for prey detection. On the other hand, the hydroelectric fields could be of significance in orientation.

To test the first supposition we investigated how catfish reacted to an artificial plastic prey with imitated electric field. For this purpose 4 catfish were fed daily with 4 larvae of *Xenopus laevis*, the clawed toad. Two other catfish were fed daily with 4 pieces of meat. After 1 week 2 plastic dummies were simultaneously introduced in the fish tank during feeding. One of these dummies generated an artificial electric field that corresponded with the natural electric field of a *Xenopus* larva. These natural electric fields, which showed a strong dipole character (mouth + with respect to gill slits), were earlier recorded on magnetic tape and could be reproduced by feeding the taped signal via an isolation unit and a voltage-to-current-converter to 2 silver thread electrodes fixed at those sites of the plastic dummies where mouth and gill slits were supposed to be. The electric field so reproduced corresponded sufficiently well to the original field of the real *Xenopus* larva. The responses of the catfish to each of these plastic larvae with (X ~) and without (Xo) electric field were protocolled as 1. *Swallowing*, when the fish after having approached the dummy to about 5 cm jerked its mouth heavily in the direction of the prey and tried to devour it; 2. *Interest*, when the fish nibbled quietly at the imitated prey; 3. *No reaction*, when it neither swallowed nor nibbled; 4. *Flight*, when the fish increased its swimming speed in the direction of the bottom, after having reached the vicinity of the dummy. The reactions of fish fed with *Xenopus* are represented in Table I; those of fish fed with meat in Table II.

The chi-square test applied to the material of Table I gave a significance smaller than $\frac{1}{2}\%$ ($X^2 = 55$, $n = 3$) for differences between responses to X ~ and Xo, i.e. electric and non-electric dummies. Catfish fed with meat showed not that great difference. For these animals the

chi-square test gave no significant differences between responses to X ~ and Xo ($X^2 = 4.0$, $n = 3$, $p > 5\%$). No statistics are needed to see that the 'swallowing'-reactions of these fish to X ~ are less frequent than those of fish fed with *Xenopus* larvae. These results show clearly that *Ictalurus* can detect such dummies - if it recognizes them as food - by means of their imitated bioelectric fields. This is a strong indication for the use of electric fields in prey detection.

To test the second hypothesis, orientation in electric fields, catfish were placed in different electric stimulus situations, i.e. electric fields of different forms, dimensions, strengths and durations. As the results are rather incomplete yet, we will mention only the most conspicuous traits in the spontaneous behaviour of the fish. In DC-fields with strengths corresponding with the natural hydroelectric fields, *Ictalurus* proved to orientate itself parallel with the field lines. Further the fish mostly dwelled in those areas where current density was lowest.

Both kinds of experiments mentioned above indicate the importance of natural bioelectric and hydroelectric fields to the electro-sensitive catfish. Other experiments are in progress.

Zusammenfassung. Verhaltensversuche, bei denen die Reaktionen des Zwergwelses (*Ictalurus nebulosus* Le.) auf künstlich wiedergegebene pseudo-bioelektrische und -hydroelektrische Felder registriert wurden, ergaben, dass *Ictalurus* beim Beutefang die von der Beute hervorgebrachten elektrischen Felder benutzen kann und dass in hydroelektrischen Feldern spontan Orientierungsverhalten auftritt.

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Interaction Between β -Adrenergic Stimulant and Phosphodiesterase Inhibiting Drugs on the Bronchial Muscle

Recent reports show that bronchodilator effects can be achieved by adenylylase stimulation, phosphodiesterase inhibition and even by direct injection of 3'5'AMP^{1,2}. We therefore considered it would be of interest, both from a theoretical and a practical point of view, to investigate the types of interaction existing between salbutamol, a selective, long-acting β -stimulant agent³⁻⁵, theophylline and dibutyryl-3'5'AMP, a lipophilic derivative of the cyclic nucleotide.

Assuming that salbutamol acted through adenylylase stimulation, synergism could be expected between this drug and theophylline, known to inhibit phosphodiesterases, or dibutyryl-3'5'AMP which is not a substrate for these enzymes⁶ and even inhibits them at concentrations as low as 100 μM ⁷.

Experiments were carried out on urethane-anaesthetized guinea-pigs, according to the slightly modified² method of KONZETT and ROSSLER⁸, and on guinea-pig tracheal chain, set up according to AKASU⁹. In both experimental conditions, histamine was chosen as the bronchoconstrictor agent. Its dose/effect curves were determined before and in the presence of the 3 drugs given at different dosage.

The ratio between histamine equiactive doses before and after treatment was calculated; this value $\times 100$, referred

to as % responsiveness, was inversely related to drug dosage and allowed us to calculate ID₅₀ or IC₅₀ (i.e., drug doses or concentrations able to halve the responsiveness of the preparations to the agonist). The results are summarized in Tables I and II. The potency of salbutamol was many times greater than that of theophylline and dibutyryl-3'5'AMP, but a definite potency ratio could not be calculated because of the different slopes of the dose/effect curves.

¹ Y. VULLIEMOZ, M. VEROSKY, G. G. NAHAS and L. TRINER, *Pharmacologist* 73, 256 (1971).

² A. BERTELLI, B. BIANCHI and L. BEANI, *J. Pharm. Pharmacol.*, 25, 60 (1973).

³ R. T. BRITTAIN, J. B. FARMER, D. JACK, L. E. MARTIN and W. T. SIMPSON, *Nature*, Lond. 219, 862 (1968).

⁴ D. HARTLEY, D. JACK, L. H. C. LUNTS and A. C. RITCHIE, *Nature*, Lond. 219, 861 (1968).

⁵ P. L. KAMBUROFF and F. J. PRIM, *Br. J. Dis. Chest*, 64, 46 (1968).

⁶ C. A. MENHAM, K. D. HEPP and O. WIELAND, *Eur. J. Biochem.* 8, 435 (1969).

⁷ A. LUCACCHINI, V. MONTALI, M. RANIERI and C. A. ROSSI, *Boll. Soc. Ital. Biol. sper.* 48, 17 (1972).

⁸ H. KONZETT and R. ROSSLER, *Arch. exp. Path. Pharmacol.* 795, 71 (1940).

⁹ A. AKASU, *Archs int. Pharmacodyn.* 722, 201 (1959).