

It is evident that histamine slightly decreases after feeding for 1 to 2 h, and rises again, at the 5th h, towards fasting values.

The conclusions drawn from the above results are that HDA of the stomach undergoes rapid increases in response to refeeding, and that the return to basal values requires several hours.

The mechanism determining the rapid enzymic induction is unknown. It may be supposed that the increase of free histamine or else reduction of its bound fraction are the triggers of induction. In fact, the concentration of total gastric histamine is reduced 1 h after refeeding. Probably the distinction of gastric histamine pool in free and bound amine at different times of fasting and feeding may furnish an answer to the above hypothesis.

Riassunto. L'autore descrive le variazioni dell'attività istidinica decarbossilasica nello stomaco di ratto in funzione del ritmo digestivo. L'attività enzimatica già alla 1^a-2^a ora di rialimentazione è molto superiore a quella dello stomaco in condizioni di digiuno. Contemporaneamente all'aumento dell'attività enzimatica si manifesta riduzione della quantità della istamina gastrica. Si prospetta l'ipotesi che la liberazione di tale ammina sia responsabile dell'incremento dell'attività enzimatica osservata.

A. CASTELLUCCI

*Istituto Farmacobiologico Malesci, Firenze (Italy),
December 4, 1964.*

Nervous Activity of the Frog's Epiphysis Cerebri in Relation to Illumination

Maintained activity in the absence of an external stimulus is a common feature of sense organs. While in the invertebrate lateral eye the impulse frequency is reported to rise with the level of illumination¹, the discharge rate of retinal ganglion cells of the cat changes with illumination, depending on whether the on-region or the off-region of the receptive field is dominant^{2,3}. In the frog's optic nerve there are, among many others, units continuously active, even under bright light; their activity is inversely proportional to the light intensity and increases to a maximum in darkness⁴. Light sensitivity of individual neurons of the epiphyseal stalk (pineal organ) of the frog's diencephalon has recently been studied. In contrast to what has been found in the vertebrate lateral eye, the action of light on the frog's diencephalon is only of one type, namely causing inhibition of the spontaneous discharge⁵. At cessation of the light stimulus, this is followed either by a return of the spontaneous discharge (low stimulus intensities), by an off-discharge (moderate stimuli), or by a persisting inhibition of the spontaneous discharge (strong stimuli) which may last for many seconds⁶.

In the present experiments, the impulse activity of single elements of the frog's epiphyseal stalk has been recorded by means of microelectrodes under steady lighting conditions. The experiment started with the measurement of the absolute threshold in preparations which had been dark-adapted for at least 2 h⁷. Then the diencephalon was exposed to constant lights of several intensities from zero to the highest obtainable. After some minutes (usually 5) of light adaptation to each intensity, the spontaneous discharge was recorded and its frequency was measured. Figure 1 illustrates the electrical activity of a single unit of the frog's pineal stalk during darkness and in response to steady illumination of several intensities. During darkness and at a low level of illumination, the frequency of impulses is high. It decreases to about 50% if the illumination is increased to $3.2 \cdot 10^{-2}$ lm/m². At 7.9 lm/m² no impulses can be seen. At the end of illumination of this intensity, impulse activity suddenly reappears (Figure 1, lowermost record). For several units of the epiphyseal stalk investigated in this way, there are individual differences of the absolute frequency of the maintained

activity in the dark-adapted state, ranging from 4 to 10 per sec. However, the relative change of frequency with rising illumination is about the same for all units investigated (Figure 2). At low levels of light adaptation, 10^{-8} to 10^{-4} lm/m², a small (4 to 12%) rise of frequency, as compared to the steady discharge in the dark, can be

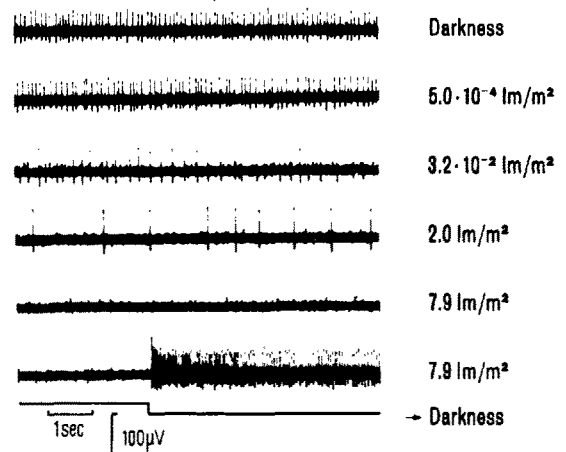


Fig. 1. Microelectrode recording, by means of a steel needle electrolytically sharpened and insulated except at the tip, of a single excitable unit, probably ganglion cell, of the epiphyseal stalk of *Rana esculenta* in the dark (upper record) and at different levels of illumination (intensities as given). The effect of sudden termination of the light stimulus is shown in the lowermost record. Note the strong change of size of the individual spike at different frequencies of discharge⁸.

- ¹ H. K. HARTLINE and C. H. GRAHAM, *J. cell. comp. Physiol.* 7, 277 (1932).
- ² S. W. KUFFLER, R. FITZHUGH, and H. B. BARLOW, *J. gen. Physiol.* 40, 683 (1957).
- ³ A. ARDUINI and L. R. PINNEA, *Arch. ital. biol.* 100, 425 (1962).
- ⁴ H. R. MATURANA, J. Y. LETTVIN, W. S. McCULLOCH, and W. H. PITTS, *J. gen. Physiol.* 43, Suppl. 2, 129 (1960).
- ⁵ E. DOTZ and M. JACOBSON, *J. Neurophysiol.* 26, 752 (1963).
- ⁶ Y. MORITA, *Pflügers Arch. ges. Physiol.* 279, R2 (1964).
- ⁷ E. DOTZ and Y. MORITA, *Vision Res.* 4, 413 (1964).

seen. At higher intensities the relative decline of frequency is almost the same for all units investigated. No impulse activity has been found with light adaptation of more than 10 lm/m^2 .

The range of illumination over which changes of impulse activity of the epiphyseal stalk occur seems to be confined to the scotopic level. However, the illumination given above refers to the surface of the exposed dience-

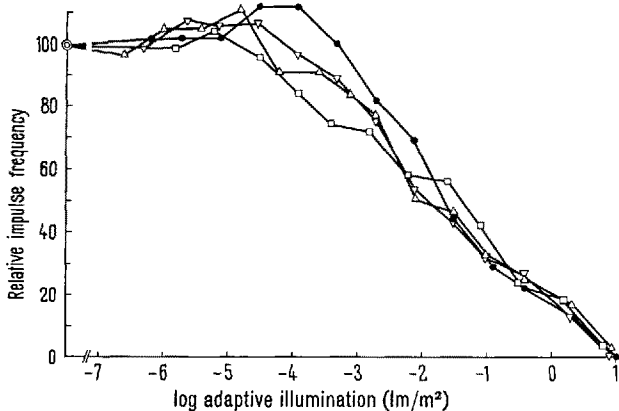


Fig. 2. Plot of the steady discharge (relative values) of single photosensitive elements of the frog's epiphysis cerebri at different levels of light adaptation. Measurements proceeding from dark to light adaptation in steps of 0.6 log units. Values after 2 h dark adaptation equal to 100%. Four different elements depicted by different symbols.

phalon after removal of the skin and the skull. After allowance is made for the loss of light absorbed by the tissues of the head, the above values should be shifted by about 3 log units towards higher intensities⁵. Thus complete inhibition of the nervous discharge of the pineal organ in situ does occur under natural lighting conditions above 1000 lm/m^2 , the absolute threshold being of the order of 0.01 lm/m^2 , i.e. quite common lighting conditions. Recently, similar values have been found for the darkening reaction of frog tadpoles deprived of their lateral eyes⁸.

Zusammenfassung. Die proximale Anlage des lichtempfindlichen Pinealorgans adulter Anuren zeigt eine Daueraktivität, die durch Belichtung gehemmt wird. Die mit Hilfe von Stahlmikroelektroden bestimmte absolute Schwelle einzelner Neurone des Organs liegt zwischen 10^{-5} und 10^{-6} lm/m^2 . Bei Belichtung vermindert sich die Impulsfrequenz der Daueraktivität linear mit dem Logarithmus der Beleuchtungsstärke. Der Halbwert der Entladungsfrequenz liegt bei 10^{-2} lm/m^2 . Oberhalb 10 lm/m^2 ist keine Impulsaktivität zu beobachten.

Y. MORITA and E. DODT

William G. Kerckhoff-Herzforschungsinstitut der Max-Planck-Gesellschaft, Bad Nauheim (West Germany), December 18, 1964.

⁸ H. BOGENSCHÜTZ, Pflügers Arch. ges. Physiol. 281, 18 (1964).

Acute Toxicity and Elimination of Phenol Injected into Fish (*Carassius auratus* L.)

According to MAICKEL et al.¹ the ability to conjugate phenols (phenolphthaleins, 8-hydroxyquinoline, α -naphthol or *p*-nitrophenol) with either glucuronic or sulphuric acid seems to be completely lacking in fish (goldfish, perch²). Doses of these phenols as low as 0.5 mg/kg are often fatal; fish placed in solutions of 10 ppm of phenols absorbed enough of the phenols through the gills to be toxic in 4–8 h, whereas frogs were found to excrete 90–95% of a 5 mg dose of phenols as conjugated compounds within 48 h after administration. KUHN and KOECKE³, however, observed that concentrations of phenol (hydroxybenzene) up to 1:50000 were tolerated by goldfish without untoward effects: in the presence of higher concentrations the gills act mainly as point of entry of the poison, undergoing minor damage, and the true toxic effects are produced on other organs. In terrestrial vertebrates (frog, mouse, rat, guinea-pig, and rabbit) the MLD (minimal lethal dose) of phenol s.c. is reported to be 300–550 mg/kg⁵.

For our experiments, healthy well-acclimatized goldfish (*Carassius auratus* L.), weighing 10 to 15 g, were kept in running fresh water, temperature 16–18°C. A 5% solution of phenol (hydroxybenzene) in water was used; the injections were administered in the muscular masses of the tail; a gentle pressure was held at the injection point for a short time.

To determine the acute toxicity, 50 animals in groups of five were injected i.m. with different doses of phenol and observed for 4 days. The MLD of phenol was found to be 230 mg/kg. The toxic effects noted were excitation, followed by depression, loss of locomotor coordination, and eventually convulsions and death.

Another 12 animals were injected i.m. with a standard dose of 200 mg/kg of phenol and immediately placed each into a separate jar containing a volume of fresh water 20 times the weight of the animal. Control fishes, also 12 in number, were administered saline for fish⁶ and held in a similar manner. Every 30 min, for the first 4 h, a small sample of the water was taken from each jar. Free phenols were directly determined with GIBB'S reagent⁷ colorimetrically. Total (free + conjugated) phenols were deter-

¹ R. P. MAICKEL, W. R. JONDORF, and B. B. BRODIE, Fed. Proc. 17, 390 (1958).

² The capability of some marine fishes to conjugate aminobenzoic acid isomers with glucuronic acid has been observed by HUANG and COLLINS³.

³ K. C. HUANG and S. F. COLLINS, J. cell. comp. Physiol. 60, 49 (1962).

⁴ O. KUHN and H. U. KOECKE, Z. Zellforsch. 43, 611 (1956).

⁵ W. S. SPECTOR, Handbook of Toxicology (W. B. Saunders Co., Philadelphia 1955), vol. I.

⁶ J. Z. YOUNG, Publ. Staz. Zool. Napoli 12, 425 (1932).

⁷ H. D. GIBBS, J. biol. Chem. 72, 649 (1927).