the reserpine administration. It has been shown[7] that 20 h after treatment with iproniazid, the HT content of the brain is not greatly affected by reserpine. The demonstration that brain monoamine oxidase inhibition by iproniazid proceeds in step with reduction in reserpine hypothermia supports the view that reduced destruction of brain HT is the factor diminishing the hypothermic action of reserpine after iproniazid.

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Zusammenfassung

Durch Vorbehandlung mit Iproniazid wird die hypothermische Wirkung von Reserpin bei Mäusen abgeschwächt. Dieser Effekt geht mit der Monoaminoxydase-Hemmung parallel.

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Variations in Encephalic and Intestinal Serotonin After Electrical Shock[1]

The increasing amount of research carried out in recent years on the relations between drugs active in schizophrenic forms (Reserpine and Chlorpromazine) and serotonin (5 HT)[2] led us to undertake a series of experiments on the variations of encephalic 5 HT after electrical and cardiazolic shock.

We employed rats of an average weight of 150 g (supplied by the firm C. Erba of Milan), to which cardiazol was administered intraperitoneally at the dose of 80 mg/kg, or on which electroshock of 0·2 s, 125 V and 130 mA was carried out. At 10 min, 1 h, 2 h and 24 h after this electric treatment, or after the first appearance of convulsions in rats treated with cardiazol, the animals were killed by decapitation and their brains and large intestine removed.

Two methods, spectrophotometric and biological, were used for 5 HT determination. For the spectrophotometric method, the serotonin was extracted according to BOGDANSKI *et al.*[3], and assayed at 275 mμ according to UDENFRIEND *et al.*[4]; for the biological method, we employed the isolated rat colon in atropinized, calcium-free Ringer, according to the suggestions of DALGLIESH *et al.*[5].

The results obtained are shown in two tables.

Our values show that, very soon after electroshock or cardiazolic shock, there is an increase in cerebral 5 HT and a decrease in intestinal 5 HT. The variations obtained by employing the two methods of assay, are qualitatively similar but quantitatively very different. It should be remarked, however, that whereas the spectrophotometric data concerning cerebral 5 HT of control animals are in satisfactory agreement with those quoted in the literature[6], those obtained by biological method are distinctly lower.

Our data on the physiological 5 HT content of intestine agree with those in the literature.

The very marked increase of 5 HT in the brain, as shown by the biological test which we used after electro- and cardiazol-shock, might also depend upon the release of an active substance which may potentially give the serotonin effect, or from the lack of inhibition due to decreased presence of an inhibiting factor present in the normal extracts, for instance noradrenaline. It is necessary to point out, moreover, that serum adrenaline is increased and not decreased after electroshock[7].

As to the mechanism which causes the rapid increase of cerebral 5 HT and the rapid decrease of intestinal 5 HT after electrical and cardiazol shock, we can merely suggest as possible hypothesis, a variation of enzymatic activities involved in 5 HT synthesis, or breakdown or release of free 5 HT from complexes that may conceal its presence.

The decrease of 5 HT in the intestine may indicate its mobilization, which might also be significant with regard to the increase of 5 HT in the brain, bearing in mind other experiments showing increased cerebral permeability after cardiazol or electroshock[8].

[1] Paper partially communicated at the XX. Congress of Physiology, Bruxelles, July 30 – August 4, 1956.

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Table I

Brain 5 HT concentration (spectrophotometric method)

Treatment	Time after treatment	Number of animals	Number of assays	Cerebral 5 HT γ/g ± S.E.	Range
–	–	64	10	0·97 ± 0·04	0·75 – 1·3
Electroshock . . .	10 min	13	4	3·48 ± 0·22	3·17 – 4·0
Electroshock . . .	1 h	13	4	2·96 ± 0·21	2·5 – 3·5
Electroshock . . .	2 h	13	4	1·72 ± 0·09	1·5 – 1·9
Electroshock . . .	24 h	15	5	1·03 ± 0·07	0·85 – 1·4

Other assays show a decrease in intestinal 5 HT 10 min after electroshock (from the normal values of 2·5 γ/g down to values of 1·2 γ/g). These values go back to normal after only 2 h.

Table II

Brain and large intestine 5 HT concentrations (biological method).

Treatment	Time after treatment	Number of animals	Number of determinations	Encephalic Serotonine ng/g ± S.E.	Range	Intestinal Serotonine ng/g ± S.E.	Range
–	–	27	9	13 ± 4	6– 48	2300 ± 300	1200–3600
Electroshock . . .	10 min	27	9	360 ± 7	90–720	920 ± 100	480–1400
Electroshock . . .	1 h	22	7	160 ± 40	48–300	1530 ± 300	960–3000
Electroshock . . .	2 h	22	7	47 ± 10	12– 72	1780 ± 470	1080–3600
Electroshock . . .	24 h	22	7	13 ± 3	4– 36	2370 ± 300	1740–3600

Some assays were carried out on the test of rat's isolated uterus. Also in this test, 10 min after electroshock, an increase in cerebral serotonin can be observed. Also after cardiazol (80 mg/kg intraperitoneally), the variations in encephalic and intestinal serotonin are similar.

We also wish to point out the difference between our results and those obtained after reserpine administration, when a fall in brain 5 HT concentration (and not a marked raise, as in our experiments) parallels the fall of intestine 5 HT concentration.

Addendum: Further determinations, with spectrophotometric method, show after electroshock a second increase in brain 5 HT starting from the 36th hour to the 72nd hour. In the same time intestinal levels of 5 HT do not change.

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Institute of Pharmacology, University of Milano (Italy), March 14, 1957.

Riassunto

Si dimostra che dopo uno shock convulsivo elettrico o cardiazolico il contenuto in serotonina aumenta in maniera molto rilevante nell'encefalo e si abbassa nell'intestino crasso.

L'aumento encefalico e la diminuzione intestinale, che raggiungono gradi molto cospicui già 10 min dopo il trattamento convulsivante si attenuano poi nei tempi successivi: intensamente diminuiti dopo 1 h, non sono più rilevabili dopo 24 h.

Effects of Short Chain Fatty Acid Anions upon Cortical Blood Flow and EEG in Cats

It has recently been reported by White and Samson[1] and by Samson and Dahl[2] that buffered fatty acid anion solutions, injected intravenously in rabbits, produce slow waves in the EEG in combination with behavioural signs of sleep. Furthermore, it has been demonstrated that fatty acids to some extent may participate in the normal cerebral metabolism in man[3].

Investigating the influence of various metabolites upon the EEG and the cortical blood flow in the cat, recorded with a new method[4], we have injected small doses of butyric (1 *M*) and octanoic (0·5 *M*) acid solutions (buffered with NaOH) as well as a solution of oleic acid (dissolved in 10% human albumine)[5]. Heparinized preparations were used, either lightly anaesthetized (Nembutal) or unanaesthetized (*encéphale* or *cerveau isolé*). The EEG, the blood pressure and the cortical blood flow were recorded continuously during the experiments.

No effects were obtained by the oleic acid solution. Octanoic anions had the same effect as butyric anions.

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[5] The solutions were kindly prepared by B. Borgström, M. D., Department of Biochemistry, University of Lund.

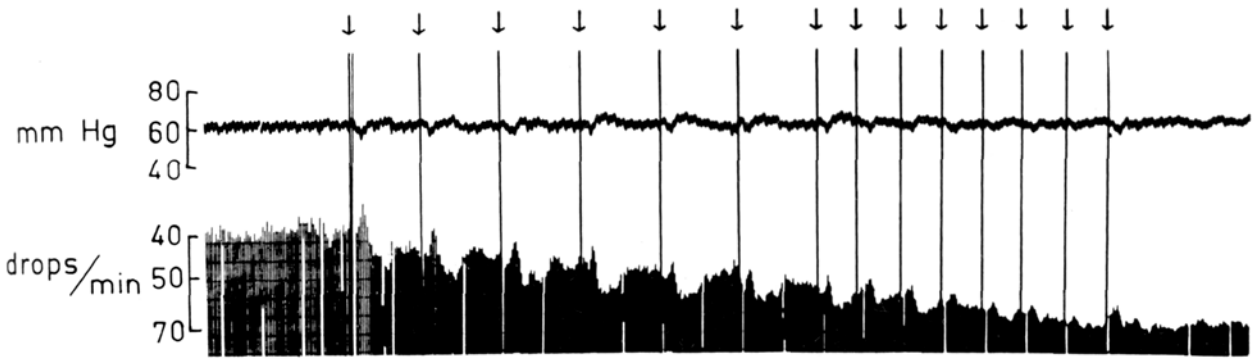

Fig. 1. – Cat. *Cerveau isolé* preparation. Cervical sympathetic nerves sectioned. Records of *blood pressure* (recorded by damped electromanometer in the brachial artery) and *cortical blood flow* in rostral parts of the brain. The flow record consists of dense vertical lines. The height of each line is proportional to the interval between blood drops from the cannulated superior sagittal sinus. Decreasing height of vertical lines therefore means increasing flow. Record interrupted every 30 s. Arrows indicate intravenous injections of 1 ml of 1 *M* buffered butyric acid solution. Note increase of cortical blood flow in spite of constant blood pressure.