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Rate of Displacement of Oxytomic Substances from Dyencephalon to Tuber Cinereum in Hypophysectomized Rats. (22474)

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We reported(1) an increase in concentration of oxytomic substances in the tuber of hypophysectomized rats killed 5 to 14 days after hypophysectomy. The oxytomic activity, determined by its effect on uterus *in vitro*, was approximately 8 times higher in the tuber of hypophysectomized animals than in nonhypophysectomized controls.

In the present work we have attempted to determine the rate at which this change takes place by determining the oxytomic activity of tuber extracts obtained from hypophysectomized animals killed half an hour after hypophysectomy.

Method. Fifteen experimental sets of animals were used, each one of them included the following groups: 1) nonhypophysectomized animals; 2) animals killed half an hour after hypophysectomy; 3) animals hypophysectomized after death. Hypophysectomy was performed through the base of the skull in animals anesthetized with avertin by intraperitoneal injection, the anesthesia lasting 20 minutes. All animals were anesthetized and killed in a gas chamber (death in about 3 minutes) when the effects of anesthesia had disappeared. The sets included animals of the

same sex, weight, and age, each group containing 4 animals, with a total of 59 nonhypophysectomized and 67 in each one of the other groups. Separate extracts were prepared immediately after the animals were killed using equivalent amounts of tissue from the tuber. Tissue from 4 animals belonging to the same group was ground with micronized quartz sand and 0.5 ml of water (acidified to pH 3) per 200 g of rat weight was added. The extract was centrifuged at 2000 rpm for 15 minutes. The oxytomic activity was determined on a uterus of a rat in diestrus immersed in Tyrode solution prepared according to Gaddum with the addition of 2 mg of atropine per liter(2). Previously neutralized extracts were added to the bath in volumes ranging from 0.1 to 0.5 ml. The oxytomic activity of the unknowns was obtained by proper dilution and comparison with a standard solution of commercial oxytocin ("Pituitrol") containing 10 u. per milliliter.

Results. A higher oxytomic activity of the tuber region was found in animals hypophysectomized and then killed than in animals hypophysectomized after death. Only in 4

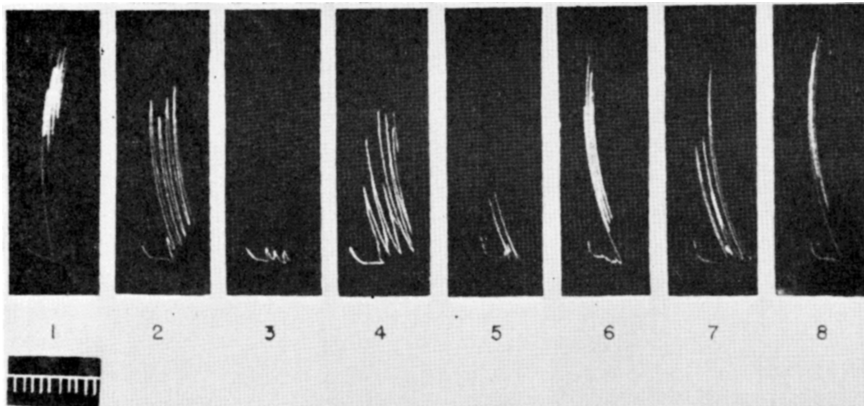


FIG. 1. Contraction of isolated uterus immersed in Tyrode solution. Additions: 1—1 μ oxytocin. 2—.2 ml extract of tuber from rats killed half hour after hypophysectomy. 3—.2 ml extract of tuber from rats hypophysectomized after death. 4—.4 ml, same as 3. 5—.1 ml, same as 2. 6—.6 ml, same as 2. 7—.6 ml, same as 3. 8—1 μ oxytocin.

animals no difference was observed in relation to those killed prior to hypophysectomy. The oxytomic activity of the tubers of animals hypophysectomized and then killed was about twice as high as those of animals hypophysectomized after death. No difference was found between the activity of the tubers of animals killed before hypophysectomy as compared to nonhypophysectomized animals, with the exception of 4 sets, in which the oxytomic activity was slightly higher in the latter.

Discussion. The increase of the oxytomic potency observed in the tuber extracts of hypophysectomized rats shows the rapidity of the change in concentration of the active principles of this hypothalamic region. Such an increase may be explained as an accumulation of active material which cannot continue in its way to the neurohypophysis, the latter representing the discharge area. This observation appears to be in agreement with previous findings showing rapid changes in the sectioned pituitary stalk(3,4) or in the median eminence (5) after application of painful stimuli.

On the other hand Rothballer(6) has reported significant changes in the distribution of the neurosecretory material of the diencephalon 4 to 6 minutes after application of a

painful stimulus.

Even when painful manipulations are avoided, it is possible that the changes observed in the concentration of oxytomic substances are due to the stress preceding the extraction of the encephalon rather than to the extirpation of the hypophysis.

The preceding results support the hypothesis that the active principles of the neurohypophysis are produced in the hypothalamus and are rapidly mobilized to the discharge area.

Summary. Extracts of tuber cinereum from 67 hypophysectomized rats obtained half an hour after the operation, showed an oxytomic potency twice as high as that observed in tuber extracts of 67 animals hypophysectomized after being killed.

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