Effect of Ablation of Neocortex on Ability of Pituitary to Secrete Thyrotropin in the Rat.* (23013)

MONTE A. GREER† AND HERBERT F. SHULL. (Introduced by R. L. Swank)
Radioisotope Service, Vet. Admin. Hospital, Long Beach, Calif. and Department of Medicine, UCLA School of Medicine.

It has been shown that lesions in the anterior hypothalamus will interfere with secretion of thyrotropin by the pituitary(1-4). Since it has not yet been ascertained whether the hypothalamus exerts a primary role in controlling thyrotropin secretion or merely transmits influences from higher centers, the present investigation was undertaken. Originally, it was planned to study thalamic preparations, but it was not possible to keep such animals alive more than one week in spite of forced-feeding and daily antibiotics. Therefore the operation was limited to removal of the neocortex. Such animals had a reasonable survival and permitted evaluation of the goitrogenic response to propylthiouracil administration. The size of the goiter produced was considered an index of the ability of such animals to secrete thyrotropin in response to maximal stimulus.

Materials and methods. Female Holtzman rats of the same age, weighing approximately 180-200 g were used as both control and experimental subjects. Removal of the neocortex was accomplished by exposing dorsum of skull through a longitudinal incision, scraping away the galea, and coagulating the underlying vascular tissue by application of electrocautery to the skull. A dental drill was then used to perforate the skull in several places along the border of muscle insertions and the piece of bone was removed with the aid of small bone cutters. This exposed most of the dorsum of the brain with very little bleeding. The neocortex was then removed by suction through a fine glass pipette under direct vision. The ablated cortical tissue was replaced by small pieces of oxycellulose and the skin sutured over the operative site without replacement of the dorsum of the skull. Postoperative care included intramuscular penicillin for the first few days and intraperitoneal isotonic saline until the animals began drinking spontaneously. Pelleted and powdered purina checkers were supplied *ad lib.* In 2 groups, one week of postoperative recovery was allowed and in one group 5 weeks. One ml of propylthiouracil suspension in 10% acacia containing 30 mg/ml was then injected subcutaneously once daily at rotated sites. Control animals received only the propylthiouracil injections. All animals were killed 11 days after beginning propylthiouracil treatment and thyroids, adrenals, uteri and ovaries weighed on a 200 mg torsion balance. The skin and mandible were removed from the skulls of the decorticate animals. After a few days fixation in formalin, the brains were then examined to determine the extent of cortical ablation.

Results. The autopsy data are summarized in Table I. No great difference was found between the goitrogenic response of the control and operated animals nor did the other endocrine organs examined show striking deviation of the operated from control animals. Although gross inspection of the brains of the operated animals revealed that ablation of the neocortex was not always quite complete, no correlation existed between deficiency of cortical tissue and size of the thyroid or other organs examined. It is possible that the slightly smaller thyroid weights of the operated animals reflect their inferior nutritional status.

This study failed to demonstrate any significant loss of hypophyseal function after removal of the neocortex in the rat. Previous studies by Davis(5) indicated that removal of the neocortex in this species did not interfere with mating, pregnancy or parturition. Since lesions of the hypothalamus can lead to such profound alterations in pituitary func-

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† Present address: Dept. of Medicine, Univ. of Oregon Medical School, Portland.

TABLE I. Body and Organ Weights of Decorticate Rats Treated with Propylthiouracil.*

Group	No. animals	Initial body wt (g)	Final body wt (g)	Thyroid (mg)	Ovaries (mg)	Adrenals (mg)	Uterus (mg)
I	6	198 ± 4.8†	208 ± 5.2	15.1 ± .6	42.3 ± 5.8	63.2 ± 2.2	271.1 ± 27.8
II	5	207 ± 4.6	198 ± 7	40.5 ± 1.5	48.7 ± 6.2	60.6 ± 2.9	290.7 ± 32.8
III	4	196 ± 3.9	164 ±10	29.2 ± 1.0	35.8 ± 2.7	59.8 ± 3.3	269.3 ± 13.7
IV	4	201 ± 4.1	162 ± 9.4	32.2 ± 1.2	38.3 ± 2.9	58.5 ± 4.1	271.1 ± 18.2
V	3	199 ± 3.2	162 ± 4.0	31.3 ± 2.4	37.2 ± 3.2	53.3 ± 3.0	251.9 ± 15.1

* Group I = Untreated controls; II = propylthiouracil-treated controls; III & IV = decorticate rats allowed one wk for post-operative recovery; V = decorticate rats allowed 5 wk for post-operative recovery. Groups II through V inj. with propylthiouracil suspension for 10 days and killed on 11th day.

† All figures given as mean ± stand. error.

tion, it appears that, whatever extra-hypothalamic nervous pathways may be concerned in modifying hypothalamic activity, none of these are mediated primarily by the neocortex.

Summary. Removal of the neocortex in female rats did not greatly affect the goitrogenic response to propylthiouracil administration nor the weights of the adrenals, ovaries or uteri.

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In vivo Synthesis of Ascorbic Acid by the Alloxan Diabetic Rat. (23014)

J. V. STRAUMFJORD, JR.* AND E. S. WEST

Department of Biochemistry, University of Oregon Medical School.

The capacity of the albino rat to synthesize ascorbic acid has been known for many years, but only recently has the mechanism of synthesis been partially clarified. King and associates(1) reported that certain compounds accelerate synthesis and excretion of ascorbic acid. One of these compounds, Chloretone, has been used extensively in the study of precursors and mechanism of ascorbic acid synthesis in the rat. Chloretone is capable of increasing urinary excretion from a basal rate of 0.3 mg to 50 mg/24 hours. The evidence that glucose is a precursor for ascorbic acid in the rat is conclusive. Jackel, Mosbach, Burns and King(2) injected uniformly labeled C^{14} glucose into Chloretone treated rats and found 0.3% conversion into ascorbic acid. Degradation studies indicated that ascorbic acid was also labeled uniformly. This work suggested that glucose is the precursor and that the entire molecule is used. Horowitz, Doerschuk and King(3) injected D-glucose-1-C^{14} into Chloretone stimulated rats and found approximately 56% of the total activity in carbon 6 of the excreted ascorbic acid, the position expected according to theory. Horowitz and King(4) similarly showed conversion of glucose-6-C^{14} to ascorbic acid-1-C^{14}. More recently Burns and Mosbach(5) have shown that the normal rat as well as Chloretone-treated animal converts D-glucose-1-C^{14} to ascorbic acid-6-C^{14}.

The purpose of this study was to ascertain whether or not the synthesis of ascorbic acid by Chloretone-stimulated rats is affected by the diabetic state in which the primary meta-

* Present address: Department of Surgery, State University of Iowa, Iowa City.