Role of Pituitary in the Thyroid Hypertrophy of Pinealectomized Rats

It has been reported that pinealectomy induces thyroid hypertrophy in turtles[1], sheep[2], cats[3], mice[4] and rats[5–8]. The thyroid histological changes reported in several papers were similar, although less severe, to those induced by TSH administration[1,6–8]. On the other hand, after pinealectomy no change in thyroid weight and structure was found by others in dogs[9] and rats[10–12].

The administration of pineal extracts induced histological signs of thyroid involution in rats[6,7,13]. The administration of melatonin inhibited the thyroid hypertrophy in rats treated with methylthiouracil[14], in rats with a chronic low iodine diet[15] and in pinealectomized mice[4]. The administration of high doses of melatonin for 2 weeks in rats did not change the thyroid weight but induced histological signs of thyroid hyperfunction[16].

Pinealectomy was performed in several groups of female rats using the technique of PAZO[4]. The animals were killed 7, 14, 21, 28, 35, 42 and 49 days after the operation and the sham-operated controls 7 and 49 days after the sham-operation. The groups were selected so as to have similar body weights when autopsy was performed. At the end of the experiment, the animals were killed with ether and the thyroid, thymus, adrenals and ovaries were carefully dissected and weighed. The thyroids were fixed in Bouin's solution and prepared for histological study with hematoxylin-eosin.

The mean and standard error of the weights of the organs are shown in the Figure. There was a transitory increase in the ovarian weight 2 and 3 weeks after surgery. After 4 weeks had elapsed, there was a significant weight decrease of both organs. The increase in adrenal weight was significant only in the second week. The most consistent endocrine gland weight change was the increase in thyroid weight which was significant during the 7 weeks the experiment lasted.

The thyroid histological changes associated with the thyroid weight increase were not very great. These data made us doubt the role of the pituitary in the thyroid weight increase after pinealectomy and the following experiment was devised in order to decide this point.

In experiment 2, four groups of animals were studied: (1) hypophysectomized-pinealectomized, (2) hypophysectomized, (3) pinealectomized and (4) controls. Pinealectomy was performed 10 days and hypophysectomy 7 days before the autopsy. All 4 groups of animals were autopsied on the same day. The animals were killed with ether and the thyroid, thymus, adrenals and ovaries were dissected and weighed. The thyroids were fixed in Bouin's solution and prepared for histological study with hematoxylin-eosin.

The mean and standard error of the weights of the organs, and the probabilities calculated using Student's *t*-test from the table of FISCHER and YATES, are presented in the Table. In the control rats pinealectomy produced a significant increase in the weight of thyroids and adrenals, but there was no change in the weight of ovaries and thymus. In the hypophysectomized rats, pinealectomy induced a significant increase in the weight of thyroid and ovaries, and a non-significant increase in adrenal weight, there being no change in thymus weight.

Pinealectomy did not produce marked histological changes in the thyroid of the non-hypophysectomized rats, but the thyroids of pinealectomized-hypophysecto-

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Effects of pinealectomy in hypophysectomized female rats

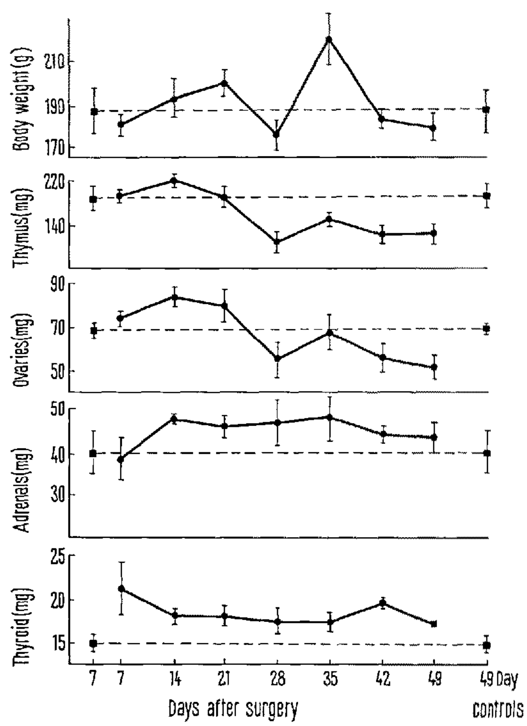
	Hypophysectomized			Non-hypophysectomized		
	Pinealectomized	Non-pinealectomized	*P*	Pinealectomized	Non-pinealectomized	*P*
Time interval (days)						
After pinealectomy	10	–		10	–	
After hypophysectomy	7	7		–	–	
Animals						
No.	15	10		16	11	
Weight (g)	87.4 ± 5.1	79.4 ± 4.1	n.s.	101.0 ± 6.8	99.9 ± 6.2	n.s.
Organ weights (mg)						
Thyroid	6.1 ± 0.3	4.3 ± 1.7	< 0.001	8.2 ± 0.6	5.6 ± 0.5	< 0.01
Adrenals	24.8 ± 1.7	20.3 ± 1.7	< 0.10	35.3 ± 2.2	27.8 ± 1.4	< 0.01
Ovary	33.2 ± 1.6	24.6 ± 3.1	< 0.05	44.6 ± 3.7	44.5 ± 3.1	n.s.
Thymus	70.6 ± 3.1	68.5 ± 4.3	n.s.	225.3 ± 10.1	226.4 ± 10.0	n.s.

mized rats were less atrophic than those of hypophysectomized rats.

It is at present accepted that the pineal gland influences the function of gonads[17,18]. Ovarian and testicular weight increase after pinealectomy are not always found and are related to the time interval after the operation: it develops shortly after pinealectomy and has a tendency to disappear after several weeks[17]. Ovarian and testicular weight increase is found with few or no alterations in its histological structure in animals whose pineal is removed[18].

Similar features were found in the thyroid of our pinealectomized rats. The thyroid weight increase was found very soon after the operation and disappeared after several weeks. There were few histological modifications in the thyroids of which weight was increased.

The removal of the pituitary did not prevent the thyroid or ovarian weight increase after pinealectomy. This suggests a direct effect of the pineal gland upon the size of these organs[19].



Effects of pinealectomy on the weight of the endocrine glands in rats.

Zusammenfassung. Epiphysektomie bei verschiedenen Gruppen weiblicher Ratten ergab Zunahme des Schilddrüsengewichtes. Diese war postoperativ in der ersten Woche besonders stark und perennierte während 7 Wochen der Experimentdauer. Entsprechende Gewichtszunahme der Schilddrüse resultiert auch nach Epiphysektomie bei hypophysenlosen Tieren.

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Cholesterol Metabolism in the Myelin of Rat Brain

Studies of DAVISON et al.[1] and DAVISON and WAJDA[2] using labeled cholesterol in developing animals demonstrated the metabolic stability of cholesterol in brain white matter. Since the white matter is rich in myelin, the results suggested that once cholesterol is incorporated in the myelin membrane it is retained without apparent turnover. In a recent study on rat brain myelin, CUZNER et al.[3] suggested that the myelin lipids continue to turnover at the same rate throughout the life span of the animal. More recently SMITH[4], and SMITH and ENG[5], have demonstrated the incorporation of labeled acetate and glucose into myelin cholesterol of adult rat brain.

Myelin cholesterol accounts for about 70% of the total cholesterol in the adult rat brain[6], and is generally considered metabolically stable[1]; almost all of it is incorporated into the myelin during the early period of active myelination.

In the present investigation the uptake of glucose carbon into cholesterol and total lipids of brain myelin was studied beyond the period of active myelination. Since no blood brain barrier exists for glucose, it was hoped that injection of glucose through the i.p. route would serve as an efficient precursor if any cholesterogenesis continued in the CNS myelin beyond the period of active myelination.

Six-week- and 6-month-old female rats of the Sprague-Dawley strain (Charles River Laboratories, Wilmington, Mass.), weighing 135–145 and 335–365 g respectively, were used in these studies. The animals were given an i.p. injection of 4.8 μc U-^{14}C glucose/100 g body weight and killed after different intervals of time over a period of 200 days. The animals had free access to water and Purina Laboratory Chow prior to and after receiving the labeled substrate. The animals were anesthetized and decapitated. The brain was removed and washed in saline, blotted on filter paper and weighed. Myelin was isolated from the brain by a slight modification of the method of ADAMS et al.[7]. Only the crude mitochondrial fraction as isolated by KHAN and WILSON[8] was used for the separa-

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