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Effect of Thyroidectomy on the *in vitro* Utilization of Glucose by Hypophysis and Hypothalamus in the Rat[1]

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Abstract. The *in vitro* utilization of 1-^{14}C- and 6-^{14}C-glucose was studied in the neuroendocrine structures of the hypophysis and hypothalamus 2 months after thyroidectomy in rats fed a low iodine diet. At this time, their PBI was markedly decreased and TSH levels were increased. Elevated levels of 6-^{14}C-glucose uptake and its conversion to $^{14}CO_2$ and ^{14}C-lactate were obtained in the posterior hypothalamus from the thyroidectomized rats compared to control animals. The formation of $^{14}CO_2$ from 1-^{14}C-glucose was increased in both the median and posterior hypothalamus of the thyroidectomized animals. No differences were found between thyroidectomized rats and controls in the uptake of glucose and formation of $^{14}CO_2$ and ^{14}C-lactate in the hypophysis and in the anterior hypothalamus. The effects of thyroidectomy on glucose metabolism are discussed in terms of the functions of the neuroanatomical structures in the hypothalamus and hypophysis of the rat.

Many close relationships among thyroidal, hypophyseal and hypothalamic functions are well-established [15]. Efforts to establish the metabolic situation of the hypophysis under conditions of altered thyroid status have shown, for example, that thyroidectomy produces an increase in both carbohydrate utilization [12, 14] and protein synthesis [8, 10, 13, 16, 17] in the pituitary and that administration of thryoid hormone suppresses these effects. We became interested in the relationship between the hypothalamus and thyroid status, but were unable to find studies on the metabolism of the hypothalamus in thyroidectomized animals. Therefore, we examined the *in vitro* utilization of 1-^{14}C- and 6-^{14}C-glucose by different regions of the hypothalamus from thyroidectomized rats.

[1] Part of this study was carried out at the Departamento de Endocrinologia Experimental, Instituto G. Marañón, CSIC. Madrid.

Materials and Methods

50–60 g Wistar female rats were surgically thyroidectomized. 2 days later, an intraperitoneal injection of 50 μCi ^{131}I-NaI was administered to destroy any remaining thyroid gland. Age- and sex-matched intact animals were used as controls. Thyroidectomized animals were fed *ad libitum* with a low iodine diet containing 0.05–0.09 μg iodine/g diet [5]. The controls were fed the low iodine diet supplemented with 1.7 μg KIO_3/g diet. All animals drank distilled water *ad libitum.* 50–60 days after thyroidectomy, rats were killed by decapitation. Blood was collected from the neck into heparinized beakers. After centrifugation, PBI [2] and TSH [6] were evaluated in the plasma. Hypophysis and hypothalamus were removed immediately from the head and weighed. Each hypothalamus was dissected into its anterior, median and posterior parts. Tissues were incubated in 0.25 ml of Krebs-Ringer bicarbonate buffer (pH 7.4) containing 1 μCi 1-^{14}C-glucose or 6-^{14}C-glucose (1 mg/ml). After 60 min incubation at 37°C and shaking (100 cpm), the media was processed for the determination of labelled glucose, CO_2 and lactate as previously described [3].

Results

Table I presents the data obtained for the plasma PBI and TSH, and body, pituitary and hypothalamus weights in the intact controls and thyroidectomized rats 2 months after removal of the thyroid gland. Plasma PBI was significantly lower in the thyroidectomized rats than in the controls while plasma TSH was elevated after thyroidectomy. Growth ceased soon after thyroidectomy and at the time of decapitation the thyroidectomized rats weighed significantly less than the controls. The absolute weight of the hypophysis and hypothalamus did not differ between the thyroidectomized and control groups, but when expressed in terms of body weight, the relative weight of the hypophysis and hypothalamus in the thyroidectomized rats was significantly greater than in the controls.

Table II presents the data obtained for glucose metabolism in the hypophysis and hypothalamus in intact and thyroidectomized rats. The uptake of 1-^{14}C-glucose and 6-^{14}C-glucose and their conversion to $^{14}CO_2$ and ^{14}C-lactate in the hypophysis and the anterior hypothalamus was essentially the same in thyroidectomized and control animals. In the medium hypothalamus, however, the formation of $^{14}CO_2$ from 1-^{14}C-glucose was higher in the thyroidectomized rats than in the controls. The formation of $^{14}CO_2$

Table I. Effect of thyroidectomy in the female rat (mean ± SEM)

	Plasma PBI[1] µg/ml	Plasma TSH µg/ml	Body weight g	Pituitary weight mg	Pituitary weight mg/100g body weight	Hypothalamus weight mg	Hypothalamus weight mg/100g body weight
Controls	5.7 ±0.3 (13)	14 (13)	183±5 (13)	10.5±0.4(15)	5.7±0.2(16)	46.9±2.3 (16)	25.5±1.3 (16)
Thyroidectomized	0.28±0.02 (11)*	1,080 (11)	99±3 (19)*	8.4±0.3(14)	9.3±0.4(14)*	39.7±2.7 (14)	44.2±3.4 (14)*

Number of rats/group in parentheses. * $p<0.001$ compared to controls. [1] PBI = Protein-bound iodine.

Table II. Effect of thyroidectomy on the *in vitro* utilization of (1-^{14}C) and (6-^{14}C) glucose by whole hypophysis and regions of the hypothalamus from female rats (means ± SEM)[1]

	Uptake of 1-^{14}C-glucose	Formation of $^{14}CO_2$	Formation of ^{14}C-lactate	Uptake of 6-^{14}C-glucose	Formation of $^{14}CO_2$	Formation of ^{14}C-lactate
Hypophysis						
Controls	13.3±0.3 (5)	0.80±0.09 (6)	6.9±0.6 (6)	12.6±0.9 (8)	0.67±0.14 (9)	7.6±0.7 (7)
Thyroidectomized	12.5±1.0 (8)	0.79±0.08 (8)	6.9±0.6 (8)	12.4±0.7 (7)	0.52±0.08 (8)	6.7±0.6 (7)
Anterior Hypothalamus						
Controls	24.7±2.4 (7)	0.88±0.12 (8)	19.4±2.7 (8)	24.8±2.6 (8)	0.76±0.20 (8)	16.9±1.8 (7)
Thyroidectomized	30.1±2.1 (8)	1.05±0.10 (8)	20.4±1.1 (7)	30.5±1.8 (7)	1.02±0.22 (8)	21.0±1.4 (8)
Median Hypothalamus						
Controls	23.4±2.3 (6)	0.66±0.06 (8)	17.1±1.7 (8)	23.6±1.2 (7)	0.68±0.14 (8)	16.6±1.2 (6)
Thyroidectomized	25.6±1.8 (8)	0.98±0.05 (8)*	18.9±1.5 (8)	26.6±1.4 (7)	1.19±0.20 (8)	18.6±1.5 (8)
Posterior Hypothalamus						
Controls	24.1±1.3 (7)	1.14±0.07 (8)	16.8±1.2 (7)	23.7±1.9 (8)	1.05±0.21 (8)	15.1±1.7 (7)
Thyroidectomized	26.0±1.4 (7)	1.55±0.16 (8)*	18.2±1.0 (7)	30.6±1.9 (7)*	1.88±0.33 (8)*	21.1±1.2 (8)*

Number of rats/group in parentheses. * $p<0.05$ compared to controls.
[1] The data are expressed as the percentage of initial radioactivity in the incubation medium/10 mg tissue.

from 6-^{14}C-glucose also tended to be higher in the medium hypothalamus of thyroidectomized rats than in controls, but the difference was not statistically significant. In the posterior hypothalamus, the formation of $^{14}CO_2$ from 1-^{14}C-glucose and the uptake of 6-^{14}C-glucose and its conversion to $^{14}CO_2$ and ^{14}C-lactate were significantly enhanced in the thyroidectomized animals.

Discussion

An intense degree of hypothyroidism was present in our thyroidectomized rats, as shown by their early ceasation of growth, low plasma PBI level and high TSH values. Despite this, glucose utilization in the hypophysis of the thyroidectomized animals failed to differ from the level observed in the intact control animals. Our results are in apparent contradiction with those of MATSUZAKI [12] who found an augmented utilization of glucose by the hypophysis of thyroidectomized rats. The different results could be explained by the fact that our study was carried out 2 months after thyroidectomy while MATSUZAKI used animals 2 weeks after thyroidectomy. It is known that opposite metabolic changes are present in the hypophysis of thyroidectomized rats such as an increase in the synthesis of TSH and prolactin [8, 18], a reduction in that of growth hormone [8] and degeneration of non-TSH-trophic cells [7]. The possibility exists that these compensatory opposite changes are balanced after prolonged time of thyroidectomy to normalize the previously augmented glucose metabolism.

We have seen here that glucose metabolism in the anterior hypothalamus does not differ between the thyroidectomized rats and the controls. This hypothalamic area includes the preoptic area and the suprachiasmatic nucleus, [4, 15], where few TRH-secreting cells seems to be located [4, 5].

The increased production of CO_2 from glucose in the median hypothalamus from the thyroidectomized rats might be related to the role of this region in the secretion of TRH: the median hypothalamus includes the paraventricular nucleus and the nerve fibres that go through the median eminence where most TRH-secreting cells are located [1, 9, 11, 15]. The high TSH levels in the plasma of the thyroidectomized rats suggests that the TRH-secretion in these animals was elevated. Perhaps the augmented metabolic activity in the median hypothalamus of the thyroidectomized rats reflects an enhanced activity of neuroendocrine structures for the production and secretion of TRH.

The augmentation of glucose utilization observed in the posterior hypothalamus from the thyroidectomized animals was unexpected. This area contains the mammillothalamic tract and the interpeduncular nucleus [4, 15] where no TRH-secreting cells nor areas giving positive TSH responses following electrical stimulation are located [9, 15]. Based on our findings, however, the posterior hypothalamus appears to play a role in the neuroendocrine physiology of the thyroidectomized animals. The relative contribution of the cell types in the posterior hypothalamus on glucose utilization in the presence and absence of the thyroid gland remains to be investigated in order to clarify the functions of this region under conditions of altered thyroid status.

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