

Effect of *l*- and *d*-Thyroxine on the Supraoptic Neurosecretory Ganglion Cells of the Rat

The relationship between thyroid function and hypothalamic neurosecretion is still obscure. Indeed, there is a difference of opinion about the changes in the hypothalamo-hypophysial neurosecretory system following thyroidectomy. SHIBUSAWA *et al.*¹ showed that the ablation of the thyroid gland causes depletion of neurosecretory material in the neurosecretory ganglion cells, whereas some authors^{2,3} claim that it causes an increase in the amount of neurosecretory material. Moreover, it is reported⁴ that a reduction of the nuclear volume of these ganglion cells occurs after thyroidectomy.

The present study, in which especially histoquantitative methods were employed, has been undertaken with the purpose of throwing some light on this problem.

Material and Methods. 24 male albino rats weighing 210–254 g were used. They were fed a standard pellet diet of constant composition *ad libitum*. The drugs used in the experiments, Na-*l*-thyroxine ('Thyroxine', Orion) and Na-*d*-thyroxine ('Dethyron', Pharmacia), were given orally in the ground standard pellet diet at a concentration of 0.01%. The rats were divided into three groups. Each group consisted of 8 rats: one group received *l*-thyroxine, one *d*-thyroxine and one served as a control. During the test period the body weight decreased in the *l*-thyroxine group 15% on the average, and in the *d*-thyroxine group 6%; in the control group the weight increased 4%. The rats treated with *l*-thyroxine showed 'clinical' signs of hyperthyroidism, e.g. increased consumption of water was observed. Similar but weaker signs could be encountered also in the rats treated with *d*-thyroxine. All the animals were killed by rapid decapitation after three weeks. The brains were embedded in paraffin after fixation in 10% formalin. The sections (7 μ) were stained with a haematoxylin-eosin and aldehyde-fuchsin stain. The nuclear area of 250 ganglion cells of the supraoptic nucleus was measured in each animal. Six thousand cells were measured in all. The nuclear areas were determined planimetrically from camera lucida drawings magnified 2500 times.

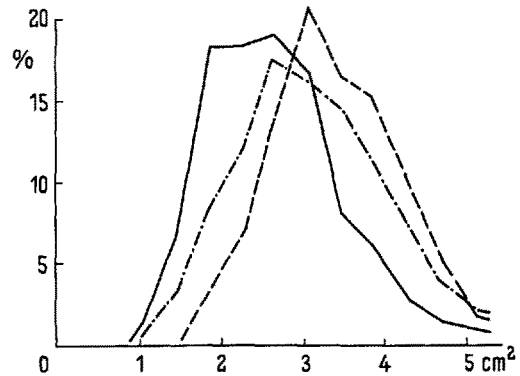
Results and Discussion. The amount of neurosecretory material in the supraoptic ganglion cells was estimated visually. The changes were so slight and so variable that little can be concluded from these observations.

On the other hand, marked changes in the nuclear areas of these ganglion cells were found. The mean nuclear areas in various groups were: the control group 2.66 cm², *d*-thyroxine group 3.09 cm² and *l*-thyroxine group 3.39 cm². The areas are expressed as cm² on the camera lucida drawings magnified 2500 times. The distribution of nuclear areas is presented in the Figure.

The nuclear volume is generally related to the synthesis of secretion. An increase of the nuclear volume is attributed to an increase of secretion. This is also true of the neurosecretory ganglion cells⁴. The present results thus suggest that the thyroxine isomeres produce an increase in the activity of the neurosecretory ganglion cells in the supraoptic nucleus. The effect of *d*-thyroxine, though very evident, is not as strong as that of *l*-thyroxine.

The assumption that this effect of thyroxine isomeres is a simple manifestation of the hypermetabolism is open to question. The dose of *d*-thyroxine used in this experiment was great enough to produce the hypermetabolic effect. According to earlier studies⁵, a 50% rise occurs in consumption of oxygen of the rat when our dose is used. Yet the changes in the activity of the neurosecretory

ganglion cells might also be due to the changes in the water balance of the body in hyperthyroidism. In fact, rats with hyperthyroidism have a tendency to polyuria which clearly points to the diuretic effect of thyroxine. The activation of neurosecretion, or in other words the elevated secretion of antidiuretic principle, may be a compensatory phenomenon to this polyuria⁶.



Distribution of nuclear areas of the supraoptic ganglion cells. — control rats, - - - - rats treated with *d*-thyroxine, and - · - · - rats treated with *l*-thyroxine. The areas are expressed as cm² on the camera lucida drawings magnified 2500 \times .

Zusammenfassung. Mittels grosser Dosen von *l*- und *d*-Thyroxin erhielt man keine deutlichen Veränderungen in der Menge und Verteilung von neurosekretorischem Material in den Zellen des Nucleus supraopticus bei der männlichen Ratte. Das Volumen der Kerne dieser Zellen nahm dagegen zu, besonders bei mit *l*-Thyroxin behandelten Ratten. Diese Veränderungen sprechen für eine vermehrte neurosekretorische Aktivität dieser Zellen.

S. TALANTI,
M. VIRANKO, and A. EISALO

Department of Anatomy and Embryology, College of Veterinary Medicine, Helsinki (Finland), October 21, 1963.

- 1 K. SHIBUSAWA, S. SAITO, K. NISHI, T. YAMAMOTO, C. ABE, and K. TOMIZAWA, *Endocr. Jap.* 3, 138 (1956).
- 2 N. SHIOZAKI, *Endocr. Jap.* 3, 242 (1956).
- 3 D. H. FORD, *Acta anat.* (Basel) 40, 13 (1960).
- 4 S. MATSUI and FR. ENGELHARDT, in *Moderne Entwicklungen auf dem Gestagengebiet* (Springer Verlag, Berlin 1960), p. 343.
- 5 G. S. BOYD and M. F. OLIVER, *Brit. med. Bull.* 16, 138 (1960).
- 6 This investigation was supported by a grant from Sigrid Jusélius Foundation, Helsinki. The authors wish also to express appreciation to Pharmacia Company, Sweden for generous supplies of Na-*d*-thyroxine used in this study, and to Miss S. NURMINEN for technical assistance.