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Thyroid Functional Status and Tonin Activity in Rat Submandibular Glands

Tonin is a hydrolytic enzyme which acts directly upon angiotensinogen and angiotensin I to yield angiotensin II. The studies performed to clarify the mechanism controlling tonin activity have shown that the synthesis and release of this enzyme by the submandibular glands is closely related to β -adrenergic receptors (3). It has been demonstrated recently that in hyperthyroidism plasma renin activity (PRA) increases while in hypothyroidism PRA depends both on the age of the animal and on the method used to induce hypothyroidism.

When hypothyroidism is induced pharmacologically in adult rats PRA decreases while in surgically induced hypothyroidism in young animals PRA remains unchanged (5). The aim of this work is to study the effects that hypo and hyperthyroidism exert on tonin activity in submandibular glands of adult rats.

Three experimental groups of animals with surgically-induced hypothyroidism were used (all three groups were sacrificed on day 70 after birth): a) Thyroidectomized one week after birth; injected with 100 μ Ci of 131 I 24 h after birth and fed with a low iodine diet starting 3 weeks after birth and continued until sacrifice. This group was used as control of hypothyroidism, b) treated as group

(a) and injected daily with 0.5 μ g of L-triiodothyronine/100 g b.w. from day 58 onward (12 injections) and c) treated as group (a) and injected daily with 3 mg KI/100 g.b.w. from day 63 onward (7 injections). Hypothyroidism was induced pharmacologically in a group of animals by daily injection of 0.5 μ g of propylthiouracil (PTU)/ 100 g b.w. from day 58 until sacrifice on day 70 (12 injections). The euthyroid controls were injected with phosphate buffered solution following the same protocols. Immediately after sacrifice the SMG were removed and extracted with acetone (2). Tonin activity was determined by a kinetic method which measures the fluorescence of the his-leu dipeptide released after the incubation of the glandular extracts in the presence of Ileu⁵-angiotensin I (1). Results were expressed as μ mol of his-leu per gram of tissue.

Figure 1 shows the changes in tonin activity observed in the different experimental groups studied. In hyperthyroid animals an increase in tonin activity was observed ($p < 0.005$) while in both surgically—and pharmacologically—induced hypothyroidism this activity decreased ($p < 0.05$ in both cases).

Although a slight increase in tonin activity was observed in iodide- and L-

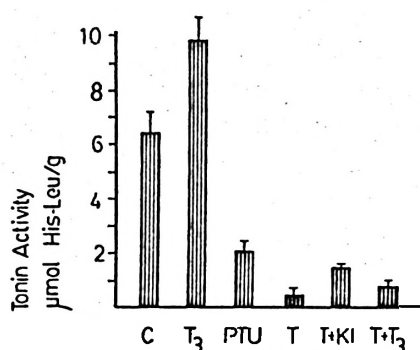


Fig. 1. Tonin activity in euthyroidism (C), hyperthyroidism (T_3), hypothyroidism (PTU), thyroidectomized rats (T) and thyroidectomized treated with potassium iodide ($T \times KI$) and with T_3 ($T \times T_3$).

triiodothyronine-treated in thyroidectomized animals when compared with untreated thyroidectomized rats ($p < 0.005$ and $p < 0.05$, respectively) no restoration to control levels appeared.

Tonin synthesis and release appear to be directly related with β -adrenergic receptor activity. This could explain the increase in tonin activity observed in hyperthyroidism, which is probably secondary to an increase of the number of β -adrenergic receptors induced by hyperthyroidism. This effect is very similar to that observed in the same situation for renal renin (4) and SMG renin (7).

The decrease of tonin activity found in both surgically—and pharmacologically—induced hypothyroidism could be explained in a similar manner. These results do not fully agree with those obtained by other authors (6) who do not find significant variations of tonin activity in hypothyroidism. These differences may be due to the distinct protocols used by the various authors (thyroidectomy performed one week prior to sacrifice) and the one used in this work.

It can be concluded that the influence of the thyroid state upon tonin activity seems to be mediated by the β -adrenergic receptor system. The increase in

tonin activity observed in normal animals may be due to an increase of β -adrenergic receptors.

However, hypothyroidism induced in early stages of life may impair the normal maturation of β -adrenergic receptors in SMG and this fact prevents a latter response to L-triiodothyronine or KI treatment.

Key words: Submandibular glands, Tonin activity.

Palabras clave: Glándula submaxilar, Actividad de tonina.

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