The Effect of Thyroid Hormones on Rat Pineal Indoleamine Metabolism *in vitro*

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Summary

The effect of TSH, triiodothyronine (T₃) and thyroxine (T₄) on basic and noradrenaline (NA)-induced indoleamine metabolism was investigated in rat pineal culture based on the observation that, under the experimental system used, melatonin is formed from its amino acid precursor tryptophan. When added to the culture medium, alone or in the presence of NA, TSH in dosages of 5 and 20 mU had no significant effect on pineal tryptophan metabolism. T₄ at 2.5 μg increased the melatonin concentration and, in the presence of NA 10⁻⁴M, also induced an increase in N-acetylserotonin (NAS). T₃, already at a dosage as low as 0.25 μg enhanced the melatonin concentration, while 2.5 μg produced significant increases in concentrations of all pineal indoleamines measured. The latter dosage of T₃ also enhanced the NA-stimulated NAS. On adding larger quantities of T₄ or T₃ to the medium none of the changes encountered with the lower dosages could be seen. The results obtained may suggest a direct positive feedback between the thyroid and pineal glands.

Key words: Pineal, indoleamines, thyroid hormones, TSH, N-acetylserotonin, *in vitro.*

Introduction

Substantial evidence of a feedback mechanism between the pineal and other endocrine glands has been accruing during recent years (Cardinali, 1974). A mainly modulatory effect of the pineal on the peripheral glands and hypothalamus-pituitary axis has been demonstrated; conversely, the pineal has been found to be influenced by the hormones of the peripheral glands. Pineal-gonadal interaction has been thoroughly investigated. The activity of hydroxyindole-O-
methyl-transferase (HIOMT) (Wurtman et al., 1965) and N-acetyltransferase (Nir and Hirschmann, 1977)—enzymes involved in the synthesis of melatonin, the major pineal indoleamine—correlates with the stages of the rat oestrous cycle, indicating a reciprocal relationship between oestrogen output and pineal melatonin synthesis. Administration of gonadal hormones, testosterone, oestradiol and progesterone were found to affect pineal melatonin (Cardinali et al., 1975 a) and protein synthesis in rats (Nir et al., 1970). It was shown that the pineal gland, embodying sex steroid receptors in its pinealocytes, can serve as a target organ for the three mentioned sex hormones under the control of noradrenaline via β-adrenergic receptors (Cardinali et al., 1975 a, b).

Regarding the interrelationship between the pineal and pituitary, the data are conflicting. Pineal melatonin production was found to be unaffected by LH and FSH (Weiss and Costa, 1968; Urry et al., 1972; Smith et al., 1975) and ACTH (Weiss and Costa, 1968). In a recent in vitro experiment, however, Cardinali et al. (1976) found that FSH, LH and prolactin have a direct stimulatory effect on the synthesis of melatonin by increasing HIOMT activity.

Information on the interrelationship between the pineal gland and the pituitary-thyroid axis is sparse. While most reports indicate that the pineal hormones bring about a decrease in thyroid metabolism and hormone production (Cardinali, 1974) there are some data to the contrary, suggesting stimulatory effects (Nir et al., 1977). Thyroxine appears to increase basic metabolic activity (Milcu et al., 1968 a, b; Tasca et al., 1971) and enhance serotonin conversion (Csaba and Bernád, 1972) in cultured pineal glands. TRH was found to inhibit noradrenaline-induced cAMP synthesis (Tsang and Martin, 1976) but no information is available on the effect of TSH and thyroid hormones on pineal indoleamine producing capacity. In the study reported here, the effect of TSH, triiodothyronine (T3) and thyroxine (T4) on basic and noradrenaline-induced indoleamine metabolism was investigated in rat pineal culture based on the observation that, under the experimental system used, melatonin is formed from its amino acid precursor tryptophan (Shein et al., 1967; Wurtman et al., 1968).

Materials and Methods

Pineal glands were collected from male rats of the Hebrew University's "Sabra" strain weighing 180—200 g each. The glands were sliced in half and placed two at a time in Wassermann tubes containing 0.5 ml nutrient medium (Shein et al., 1967), and d-l14C-tryptophan (New England Nuclear) 0.5 µg in a 10⁻⁴ M solution, to which the test substances (noradrenaline HCl