Short Communication

Stimulation of β-Adrenergic Receptors in the Pineal Gland Increases the Noradrenaline Stores of Its Sympathetic Nerves

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Summary. The administration of isoproterenol decreases the level of serotonin in the rat pineal gland and at the same time it increases pineal noradrenaline. These effects depend on the stimulation of a β-adrenergic receptor because they are blocked by pretreatment of the animals with propranolol; this drug by itself does not modify either serotonin or noradrenaline levels in the pineal. The elevation of noradrenaline produced by isoproterenol is selective for the pineal because it is not observed in the salivary gland innervated by postganglionic adrenergic fibers from the same origin as pineal nerves. Pineal serotonin is stored in equilibrium in two compartments, i.e., the parenchymal cells and the adrenergic nerves and thus is most probably reduced in both sites. Since noradrenaline and serotonin are detected in pineal nerve vesicles and may coexist in them, the diminution of intravesicular serotonin, by making more storage sites available, probably determines the selective increase of pineal noradrenaline. A similar modification in the ratio of intravesicular amines as a result of the physiological stimulation of pineal β-adrenergic receptors by the adrenergic neurotransmitter may explain some of the changes observed in the content of pineal amines.

Key words: Noradrenaline — Serotonin — Pineal Gland — Amine Storage.

The indole metabolism in the pineal is controlled by noradrenaline released from the postganglionic sympathetic fibers innervating the gland. The circadian variations in neurotransmitter release appear to be responsible for the 24 hr rhythm of indole metabolism in the pineal (ref. see Axelrod, 1974; Klein, 1974). However, the content of noradrenaline in the pineal increases during the night when it is presumed to be released and when its turnover rate is greatly accelerated, while pineal noradrenaline diminishes at the end of the light period when its turnover is the lowest (Wurtman and Axelrod, 1966; Brownstein and Axelrod, 1974). We thought that this puzzling situation might be explained by

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the particular mechanism of noradrenaline storage in pineal adrenergic nerves.

The pineal gland of the rat contains large amounts of serotonin which is stored both in the parenchymal cells and in the nerve fibers innervating the gland. Although these postganglionic sympathetic nerves contain noradrenaline, they have the capacity to incorporate the serotonin synthesized in the pinealocytes (Pellegrino de Iraldi et al., 1963; Owman, 1964; Neff et al., 1969). Cytochemical observations, subcellular distribution studies and pharmacological experiments indicate that noradrenaline and serotonin share common storage sites in the vesicles of pineal adrenergic nerves (Jaim-Etcheverry and Zieher, 1971, 1973, 1974). For example, the pharmacological depletion of neuronal serotonin produces a marked and selective rise in pineal noradrenaline (Jaim-Etcheverry and Zieher, 1971) while the depletion of noradrenaline increases neuronal serotonin (Zweig and Axelrod, 1969).

The serotonin content of the pineal is controlled by β-adrenergic receptors of the pinealocytes (Klein et al., 1973; Brownstein et al., 1973). During the night, when sympathetic activity increases, noradrenaline is released from the nerves and these receptors are activated. This enhances the activity of the enzyme serotonin-N-acetyltransferase and consequently the concentration of serotonin decreases due to an acceleration of its conversion to N-acetylserotonin (Axelrod, 1974; Brownstein et al., 1973; Klein et al., 1973).

Since parenchymal and neuronal serotonin are in equilibrium (Neff et al., 1969), the depletion of total pineal serotonin produced by the activation of postsynaptic β-adrenergic receptors during the night most probably affects the content of serotonin of the nerve fibers as well. In this case, and in accordance with the proposed coexistence of amines in pineal nerve vesicles, the noradrenaline content of the gland should be expected to increase as a result of the enhanced availability of vesicular storage sites.

With the aim of demonstrating that this mechanism of amine coexistence responds to physiological changes, the activation of the β-adrenergic receptors which normally takes place at night, was mimicked by the injection of isoproterenol during the day. The content of endogenous amines was determined in the gland under these experimental conditions.

Methods

Female Wistar rats of 150—200 g were kept under diurnal lighting with the lights on from 07.30 hr to 19.30 hr for at least a week before the experiments. Drugs were dissolved in saline and injected subcutaneously; dosages of drugs refer to salts. (±)-Isoproterenol HCl (Sigma Chemical Co.) was injected at 07.25 hrs