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Dopaminergic Influences on Prolactin Synthesis and Release from Rat Anterior Pituitary Cultures

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Dopaminergic influences on prolactin release from lactotrophs have been studied using the rat anterior pituitary cell culture. The prolactin inhibiting activity of hypothalamic extracts was examined in relation to dopamine.

Dopamine inhibited prolactin secretion from the rat anterior pituitary cell culture in a dose dependent fashion. The median effective dose was 2 x 10^{-7} M and the maximal inhibition (70–90 % of the control value) was shown by 10^{-5} M dopamine. Further increase in dopamine concentration did not result in any further inhibition of prolactin secretion.

Dopamine antagonists such as haloperidol and (+)butaclamol could inhibit the effect of dopamine on prolactin release. A Schild plot from the relationship between dopamine and (+)butaclamol in prolactin release in the anterior pituitary cell culture showed that pA_2 value of (+)butaclamol is 8.9 with a slope of 1.00.

High concentrations of haloperidol or (+) butaclamol (both above 10^{-5}M) caused a marked inhibition in prolactin release initially, followed by some irreversible cytotoxicity on the anterior pituitary cells. The major damage seems to be on the plasma membrane which was verified by light, scanning and transmission electron microscopy. Neither the inhibitory nor the cytotoxic effect by these drugs seems to be mediated through a dopaminergic mechanism.

Hypothalamic and cortical extracts also inhibited prolactin release in the rat anterior pituitary cell culture in a dose-dependent fashion. The maximal concentration of cortical extracts which did not affect the release of prolactin from the rat anterior pituitary cell culture was 0.5 hypothalamic weight equivalents. On the other hand, hypothalamic extracts of 0.5 hypothalamic equivalents showed about 40 % inhibition of prolactin release. The effect of the hypothalamic extracts was completely blocked by either 2 x 10^{-6}M haloperidol or 10^{-6}M(+) butaclamol, concentrations which could also reverse all the inhibitory effect of 10^{-6}M dopamine.

Addition of hypothalamic extracts to 10^{-7}M dopamine did not enhance the inhibitory effect of dopamine, but rather reduced the effect of dopamine. However, the total inhibitory effect of the combination of hypothalamic extracts and dopamine was completely reversed by 2 x 10^{-7}M haloperidol.

It is concluded that all the prolactin in-

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can be accounted for by dopaminergic activity, hibiting activity of hypothalamic extracts but not necessarily by dopamine alone. Other catecholamines such as norepinephrine and epinephrine also may be involved. All these catecholamines seem to exert their prolactin inhibiting activity by acting on the dopamine receptors in the rat anterior pituitary lactotrophs.

The effects of dopamine on prolactin synthesis as well as release were also studied in the rat anterior pituitary organ culture.

Dopamine suppressed the release but increased the anterior pituitary gland contents of both radioimmunoassayable and newly synthesized prolactin. The total prolactin synthesis was not affected by dopamine. These results indicate that dopamine does not directly inhibit prolactin synthesis, and the increase in prolactin contents of the anterior pituitary gland is due to the inhibition of prolactin release.

The release pattern of prolactin was studied in the rat anterior pituitary organ culture by examining the ratio of newly synthesized to total prolactin contents in both the gland and the medium. A model for prolactin dynamics was hypothesized based on experimental data. There seem to be two different types of prolactin secretory pools in the lactotrophs. The newly synthesized prolactin seems to be contained in one type of pool and is very actively secreted, while the pre-existing prolactin seems to be contained in the other type of pool and is less actively secreted. Dopamine seems to preferentially inhibit the release of the newly synthesized prolactin.