Effects of $\alpha$- and $\beta$-Adrenergic Receptor Blockade on the Isoamylases of Rat-Parotid Gland

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Summary. The in vivo activity of rat-parotid isoamylases was increased following $\alpha$-receptor block by phentolamine. Additional inhibition of the $\beta$-receptors by propranolol did not further augment the isoenzyme activities. After 21 days, the isoamylase concentrations were even lower than after $\alpha$-receptor block alone. Based upon these results, an $\alpha$-receptor mediated discharge from the duct system of already secreted gland protein and a possible role of the $\alpha$-receptors in protein secretion from the parotid gland are discussed.

Key words: Adrenergic receptor blockade — Iso-$\alpha$-amylases — Rat-parotid gland — Phentolamine — Propranolol.

Zusammenfassung. Unter $\alpha$-Blockade mit Phentolamin steigt in vivo die Isoamylasenaktivität in der Rattenparotis an. Eine zusätzliche Blockade der $\beta$-Rezeptoren mit Propranolol erhöht die Enzymaktivitäten nicht noch stärker. Nach 21 Tagen sinken die Isoamylasenkonzentrationen sogar deutlich unter die Werte bei alleiniger $\alpha$-Sympathicolyse ab. Eine über $\alpha$-Rezeptoren bewirkte Ausschwemmung bereits sezernierten Drüsenproteins aus dem Gangsystem und eine mögliche Bedeutung der $\alpha$-Rezeptoren für die glanduläre Proteinsekretion werden im Zusammenhang mit diesen Ergebnissen diskutiert.

Schlüsselwörter: Sympathicolyse — Iso-$\alpha$-Amylasen — Rattenparotis — Phentolamin — Propranolol.

The function of the adrenergic $\alpha$- and $\beta$-receptors in acinar protein secretion from the parotid gland has been elucidated, on the whole, by in vitro experiments. Stimulation of $\alpha$-receptors starts the release of $K^+$ and water [4, 5] while secretion of amylase by discharge from the zymogen granules results from the activation of $\beta$-receptors [3, 16, 17]. These results were confirmed by in vivo experiments: Pharmacological sympathectomy by guanoxane [1] and guanethidine [6] leads to conges-
tion of the secretory products in the parotid gland, increasing its protein content and amylase concentration. On the other hand, in vivo inhibition of β-receptors merely enhances the specific amylase and isoamylase activities since the protein content, particularly of the isoamylases, decreases sharply [2]. In the rat, α-amylase consists of 4 isoenzymes [7, 15] separable by electrophoresis in polyacrylamide gel [1, 2, 6, 7].

The present study attempts to differentiate between the effects of partial (α- or β-receptor) and total (α- and β-receptor) sympathetic blockade on the isoamylases of the parotid gland of the rat. We have already investigated the inhibitory action of propranolol on the adrenergic β-receptors [2]; in the experiments communicated here we used phentolamine to block the α-receptors, and a combination of phentolamine and propranolol to inhibit both adrenergic receptors of the parotid gland of the rat.

Materials and Methods

56 female rats (strain Sprague-Dawley NIH/HAN, weight between 100 and 120 g), purchased from Zentralinstitut für Versuchstierzücht, Hannover/FRG, were divided into seven groups (n = 8) and treated as shown below. Intraperitoneal injections were given at equal intervals (12 h) twice daily for the number of days indicated.

Ia (killed after 3 days): 2 × 1 mg phentolamine (Regitin®), dissolved in 2 × 1 ml Ionosteril®.
Ib (killed after 3 days): 2 × 1 mg phentolamine (Regitin®) plus 2 × 1 mg propranolol (Dociton®), dissolved in 2 × 1 ml Ionosteril®.
IIa (killed after 21 days): same as Ia.
IIb (killed after 21 days): same as Ib.
IIIa (treated for 21 days as in Ia, killed after additional 21 days without treatment.)
IIIb (treated for 21 days as in Ib, killed after additional 21 days without treatment.)
IV Control group (each 4 animals killed after 3 and 21 days, respectively): 2 × 1 ml Ionosteril®.

Throughout the experiment, the animals were kept under identical conditions (Altromin® standard diet). In group IIIa one rat died after injection.

Following death of the animals in ether narcosis, the left parotid glands were carefully dissected free, removed and weighed. They were kept frozen (−70°C) until extraction [1, 2, 6]. After determination of the protein content in the gland extracts [9] the isoamylases were separated by subjecting aliquots of 0.2 µg protein from each sample to electrophoresis in starch-containing polyacrylamide gel [1, 2, 6]. The experimental procedures for measuring amylolytic activity [18] and protein content of the isoamylases have already been described in detail [1, 2].

Differences between experimental and control animals were assumed to be statistically significant at a level of P ≤ 1% in the Wilcoxon test of Mann and Whitney [13]. Although 4 rats of the controls (group IV) were killed after 3 days and the remaining 4 animals after 21 days, significant differences between the two groups were not detected. All 8 animals were therefore combined into one single control group.

Results

The electrophoretically separated isoamylases showed significant differences between controls and rats treated with phentolamine and propanolol plus propranolol (Table 1). The activities of the first and second (Fig. 1) and of the third and fourth isoamylases (Fig. 2) were increased after 3 and 21 days of α-receptor block; additional β-blockade enhanced the activity of all 4 isoenzymes after 3 days (Figs. 1 and 2) and again 3 weeks after termination of a 21 day drug treatment (Table 1).