Action of New β-Blocking Agents on the Submaxillary Gland of the Rat

In the submaxillary gland of the rat isoprenaline causes secretion as shown already by SELYE, VEILLEUX and CANTIN[1]. Secretory effects of adrenaline, noradrenaline and sympathetic stimulation can be greatly reduced but usually not abolished by α-blocking compounds[2,3]. These observations suggest that some β-receptors are present in the gland. The responses persisting after α-blockers can be further diminished but not completely annulled by pronethalol[3]. In the present investigation some more recent β-blockers were tested on the submaxillary gland of the rat.

The rats were anaesthetized with chloralose (80–100 mg/kg into a cannula in the femoral vein after induction with ether). Tracheal cannula was inserted, and the submaxillary ducts were exposed in the neck and cannulated using fine glass cannulae. In many experiments the chorda-lingual nerve was cut on one side 2–4 weeks prior to the acute experiment in order to sensitize the gland and thus increase the secretory responses. The experiments often lasted for as much as 8 h and pentobarbitone (20 mg/kg) was then supplied i.p. at intervals to ascertain a sufficiently deep anaesthesia. Secretory drugs (isoprenaline and adrenaline 10 μg/kg; methacholine 5 μg/kg) were injected i.v. every 5 min. The cervical sympathetic trunk was stimulated electrically during periods of 1–2 min. The following blocking agents were studied: dibenzyline, dihydroergotamine, propranolol, 1-INPEA (D(−)-1-(nitrophenyl)-2-isopropylaminoethanol hydrochloride) and metoxamine.

After dibenzyline (0.4 mg/kg) and dihydroergotamine (0.2–0.4 mg/kg) the responses to isoprenaline and methacholine were unaffected and those to adrenaline and sympathetic stimulation very much reduced. Propranolol (2 mg/kg) was found completely to abolish the secretory responses to adrenaline and sympathetic stimulation remaining after the injection of α-blockers in most glands. The effect of isoprenaline was likewise abolished, that of methacholine was not changed. The blocking action of propranolol was found to last for several hours. INPEA had a similar effect as propranolol, but complete abolishment of the secretory responses to adrenaline or sympathetic stimulation (after α-blockers) or to isoprenaline was often difficult to achieve owing to the arousal effect of the drug in high dosage. In some glands the responses were completely suppressed by 25–50 mg INPEA/kg, but in other animals doses of this order caused arousal which was often accompanied by salivary secretion. A β-blocking action on the heart, on blood vessels and smooth muscles has been attributed to metoxamine[4]. In the present experiments no β-blocking effect of this drug could be observed. Doses as high as 10 mg/kg were tried; they caused a long-lasting slow flow of saliva.

The experiments support previous conclusions that the submaxillary gland of the rat is richly supplied with α-receptors for catecholamines and in addition with some β-receptors. They show that propranolol and INPEA are more efficient β-blocking drugs on this preparation than pronethalol[5].

Zusammenfassung. An narkotisierten Ratten wird gezeigt, dass die Submaxillarisdrüsen sowohl mit α- als auch mit β-Rezeptoren für Katecholamine versehen sind. Propranolol und 1-INPEA (D(−)-1-(p-Nitrophenyl)-2-isopropylaminoethanol hydrochloride) ergeben eine wirkungsvolle Blockade der β-Rezeptoren der Drüse.

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[5] Propranolol (Inderal) was kindly supplied by A. B. SCANMEDA, Gothenburg, and INPEA by A. B. DRACO, Lund.

Ethanol Inhibition of Audiogenic Stress Induced Cardiac Hypertrophy

Numerous investigations have presented evidence that ethanol when chronically ingested in excessive amounts is detrimental to both the socioeconomic and physiologic status of the individual[1–8].

Animal studies have investigated the interactions of ethanol with a number of the compounds (serotonin, norepinephrine, dopamine and gamma aminobutyric acid) found in the central nervous system that are postulated to play a role in its function[4–6].

Ethanol has been further demonstrated to possess some of the general capabilities (properties) of a stressor of the type outlined by SELYE 1950)[7–10]. On the other hand, ethanol in low concentration can manifest attenuative or protective actions against some types of body stress and improve certain types of mental performance[11–13].

Previous studies by the present authors had indicated that chronic 'emotional' (audiogenic) stress in the rat produced a number of biochemical, anatomical and fetal alterations[14–16]. It was also demonstrated that the ad lib ingestion of 10% ethanol by the rats during the stress periods partially blocked the biochemical responses[17]. One of the most interesting observations was the fact that although this type of stress (audiogenic) resulted in a slight decrease in body, adrenal and kidney weight, the heart showed significant hypertrophy (increase in weight). Therefore, it became of interest to attempt to inhibit these anatomic alterations, and the cardiac hypertrophy in particular, by as physiologic a means as possible. Ethanol was chosen as an adequate pharmacologic prototype compound capable of being accepted easily by the experimental animals and assimilated readily by their metabolic pathways.

Virgin female albino rats (Sprague-Dawley) were used throughout the present investigation. They were maintained on Purina Rat Chow, lettuce, bread, potato and water for 1 month before use.

The experimental animals were subjected to the auditory stress by placing them in a specially constructed, sheet metal chamber measuring 40 · 52 · 48 inches. Six