Following physostigmine subacute treatment, total ACh is the same as in the controls, but ChE activity is decreased and ChA increased almost everywhere.

The ChE reduction is obviously due to the peculiar pharmacological effects of the drug[14]. The ChA increase suggests, instead, that the subacute treatment may stimulate the cholinergic neuronal pool. Probably, the ACh increase in some synaptic areas activates non-cholinergic chains which, in turn, stimulate the cholinergic neurons. Our hypothesis agrees with the well-known desynchronizing effect of the drug[1].

The conclusions drawn from our experiments are therefore as follows: (1) The drug increases total ACh, mostly in those areas where the neurotransmitter metabolic rate is high. (2) Sub-acute treatment increases ChA activity, probably through indirect activation of the cholinergic neuronal pool.

Riassunto. L'eserina 0.2–5 mg/kg aumenta la ACh totale del cervello di cavia soprattutto nel telencefalo. Dopo trattamento sub-acuto, l'attività colinoacetilasica aumenta, forse per stimolazione mediata dei neuroni colinergici.

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Salivary Secretion of the Major Sublingual Gland of Rats

Isoprenaline, given repeatedly to rats, causes a marked enlargement of the submaxillary and parotid glands[1], while the weight increase of the sublingual gland is slight or absent[2,3]. Isoprenaline evokes a marked flow of saliva from the submaxillary gland of rats[4]. In the present investigation, the secretory responses of the rat sublingual gland to isoprenaline, as well as to some other sialagogue drugs, are studied. A continuous flow of saliva from the sublingual gland was observed at the beginning of all experiments. This continuous secretion was further studied.

Twenty-four male rats (Sprague-Dawley) weighing 255–385 g were used. The rats were anaesthetized with chloralose (100 mg/kg) intravenously after ether induction. The sublingual ducts, lateral to the submaxillary ducts, were exposed in the neck and cannulated using fine glass cannulae. The cannulae gave about 100 drops out of 1 ml of distilled water. Secretion appearing at the tip of the cannula was noted and registered on a smoked drum. The secretory responses to different doses of isoprenaline (isopropylnoradrenaline) sulphate and of the hydrochlorides of adrenaline and methacholine given intravenously were estimated. To increase the sensitivity to secretory drugs, the sublingual gland was parasympathetically denervated in 7 rats by section of the chorda-lingual nerve 3 weeks in advance. For the study of the continuous secretion, atropine sulphate and dihydroergotamine methansulphonate were given intravenously; in 5 rats the sublingual glands were sympathetically denervated by bilateral excision of the superior cervical ganglion about 2 weeks in advance.

A slow continuous flow of sticky saliva from the sublingual gland was observed. This flow of saliva was found to go on for hours at a constant rate. The rate varied, however, from one animal to another; it was calculated to correspond to about 3 μl/h (range 1–5 μl). This flow of saliva was produced by sublingual glands weighing 47 ± 2.1 mg ($n = 10$). The continuous secretion was not altered by preganglionic parasympathetic or post-ganglionic sympathetic denervation in combination with removal of the adrenals; and neither atropine 1 mg/kg nor dihydroergotamine 0.5 mg/kg abolished or changed the secretion.

The secretory responses of the sublingual gland to sialagogue drugs were always small, usually much less than 1 drop of saliva, and difficult to evaluate also because of the continuous secretion.

The rat's sublingual gland was found to be very insensitive to isoprenaline. Even after 100 μg isoprenaline/kg, no significant increase of the rate of the continuous secretion was noticed. Similarly the sensitivity to adrenaline was very low; a secretory response to adrenaline was not regularly observed, even after 20 μg/kg. Methacholine, on the other hand, evoked small but obvious secretory responses. The threshold dose of methacholine was found to be about 0.5 μg/kg. The secretory responses were augmented with increasing doses; 10 μg methacholine/kg was found to give about $^1/_3$ drop of saliva. The sensitivity of the sublingual gland to these secretory drugs was increased after parasympathetic denervation. Isoprenaline 100 μg/kg was found to elicit a small secretory response from the denervated sublingual gland while a higher dose, 1 mg/kg, evoked a long-lasting flow of saliva up to about 1 drop in $^1/_2$–$1\,^1/_2$ h. The denervated gland was still very insensitive to adrenaline, but 20 μg adrenaline/kg usually caused a small secretory response. The threshold dose of methacholine was markedly lowered, to about 0.05 μg/kg, after denervation and the secretory response to 10 μg methacholine/kg was increased by about 50%.

The sublingual gland of rats has thus been found to secrete spontaneously, like the sublingual gland of cats[5] and the submaxillary gland of rabbits[6]. When comparing the rate of this spontaneous secretion of these three salivary glands, considering the differences in gland weight, it may be noted that the flow rate is highest in cats and lowest in rabbits.

The sublingual gland of rats is very insensitive to both adrenaline and isoprenaline. A secretory response to these catecholamines is usually seen after parasympathetic denervation. Activation of the adrenergic receptors, both

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α- and β-receptors, elicits a very small secretory response from the sublingual gland but a marked response from the submaxillary gland[4,7]. The secretory response of the submaxillary gland of rats to isoprenaline is supposed to be due to activation of β-receptors. It seems likely that the salivary gland enlargement after repeated injections of isoprenaline to rats[1] is linked to activation of β-receptors. The present finding that the sublingual gland is very insensitive to isoprenaline may explain the small[2] or absent[3] enlargement of this gland after treatment with isoprenaline. The secretory responses of the sublingual gland to methacholine are similar to those of the submaxillary gland[8] when differences in the size of the glands are taken into account. A supersensitivity develops after parasympathetic denervation of the sublingual gland according to Cannon's law of denervation.

Zusammenfassung. Die Sublingualisdrüse der Ratte zeigt eine spontane Sekretion, die nach intravenöser Injektion von Adrenalin und Isoprenalin wenig vermehrt wird. Intravenöse Methacholingabe ruft eine auffallende Sekretion hervor. Die geringe Empfindlichkeit gegenüber adrenergischen Substanzen kann z.B. die geringe Drüsenvergrösserung nach Behandlung mit Isoprenalin erklären.

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Evidence for the Existence of an Outflow of Noradrenaline Nerve Fibres in the Ventral Roots of the Rat Spinal Cord

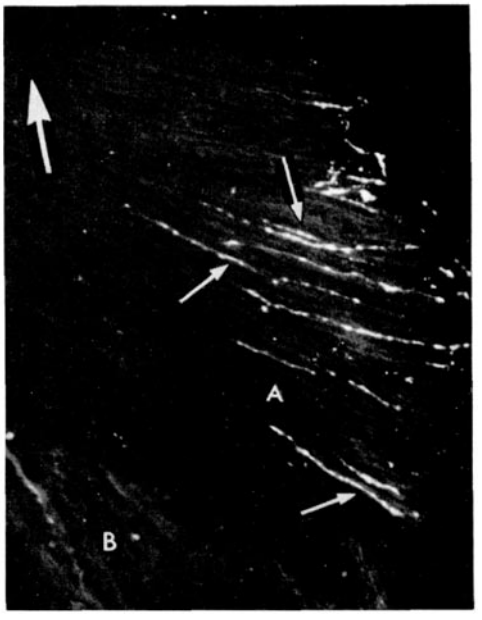
Numerous axons originating from specific noradrenaline nerve cells in the medulla oblongata descend in the lateral and anterior funiculi and terminate in the grey matter[1]. During investigation of these descending systems, observations were made which suggested that some of these descending fibres leave the spinal cord through the anterior roots. Strong evidence has now been obtained for this view.

After axotomy such large amounts of catecholamines accumulate in the proximal part of peripheral and central adrenergic fibres that their presence, distribution, and direction can readily be visualized by the histochemical fluorescence method of Falck and Hillarp[2,3]. This technique was used in the present work.

The ventral roots of several thoracic segments in the rat spinal cord were compressed bilaterally. The operated rats (Sprague-Dawley, 150 to 250 g) were divided into groups of 3 or 4 and killed 1, 2, 4, 6, or 10 days after operation. The thoracic segments with their compressed ventral roots and the spinal ganglia were dissected, freeze-dried, treated with formaldehyde gas, embedded, serially sectioned (mainly longitudinal sections), and examined as previously described[4].

In all the specimens, swollen and deformed nerve fibres with a strong specific green fluorescence were observed in the part of the ventral root immediately above the lesion. Since the histochemical criteria for the fluorescence reaction were satisfied[4], and no or only weakly green-fluorescent fibres were observed after reserpine injection (10 mg/kg, i.p., 24 h before killing), there is little doubt that these fibres contain primary catecholamines (CA).

After 1 to 2 days, an accumulation of CA was observed only immediately proximal to the lesion. After 4 to 6 days, however, the deformed CA nerve fibres could be traced from the lesion into the spinal cord (Figure). Sometimes they could even be traced up in the most ventral part of the lateral funiculus. After 10 days, the CA fibres had the



Longitudinal section from the ventral part of the spinal cord of rat 6 days after compression of the ventral roots. A number of strongly green fluorescent nerve fibres (→), due to an accumulation of CA, are seen near the exit of the ventral root (A) from the spinal cord (B). The lesion, not seen in the picture, is situated peripherally (to the right). The large arrow indicates the cranial direction. × 170.

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