mikrosomen erfolgte nach den üblichen Standardmethoden[6]. Chronisch wurden Ratten mit Thioacetamid behandelt durch Verabreichung von 0,1% Thioacetamid im Trinkwasser über eine Zeit von 6 Wochen.

Die Inkubation mit Lebermikrosomen und NADPH-regenerierendem System (Isocitrat und Isocitratdehydrogenase) wurde früher beschrieben[1]. Als Substrat wurde 1β,2β-^{3}H-Testosteron verwendet; die Substratkonzentration im Ansatz betrug 200 nMol/ml. Die Messung der Freisetzung von Tritium aus dem verwendeten Substrat erfolgte durch Bestimmung des gebildeten HTO wie früher beschrieben[1].

Ergebnisse und Diskussion. Figur a zeigt, dass in Gegenwart von NADPH ^{3}H aus 1β,2β-^{3}H-Testosteron durch mikrosomale Enzyme der Leber freigesetzt wird. Die Reaktion verläuft über 20 min linear. Die Prüfung der Kofaktorabhängigkeit dieser Reaktion (Figur b) ergibt, dass der Zusatz von NADPH für die Reaktion essentiell ist. Die Sättigungskonzentration für NADPH liegt bei 1 m*M*. Ersatz des NADPH durch NADH führt lediglich zu minimalen Umsätzen.

Aromatisierung von Testosteron durch Rattenlebermikrosomen: Einfluss einer Behandlung mit Thioacetamid

Initialgeschwindigkeit (pg Atom H/mg mikrosomales Protein/min)		
Kontrollen (unbehandelt)	168 ± 12	(n = 6)
Akute Behandlung mit Thioacetamid		
100 mg/kg	156 ± 12	(n = 4) n.s.
200 mg/kg	258 ± 67	(n = 4)[b]
300 mg/kg	234 ± 87	(n = 4)[a]
Chronische Behandlung mit Thioacetamid		
1 Woche	64 ± 5	(n = 5)[c]
3 Wochen	104 ± 17	(n = 5)[c]
6 Wochen	275 ± 35	(n = 5)[c]
2 Wochen Erholung nach chronischer Behandlung	269 ± 32	(n = 5)

Die Zahlen ($\bar{x} \pm s_x$) geben die Menge Wasserstoff an (pg Atom H/mg mikrosomales Protein/min), die aus den Positionen 1β und 2β von Testosteron bei Inkubation von 1β, 2β-^{3}H-Testosteron mit Mikrosomen und NADPH-regenerierendem System freigesetzt wird.
n.s. = kein signifikanter Unterschied gegenüber Kontrollen
[a] $0{,}05 > p > 0{,}025$; [b] $0{,}01 > p > 0{,}005$; [c] $p < 0{,}001$.

Die Tabelle zeigt den Einfluss einer akuten bzw. chronischen Vorbehandlung der Ratten mit Thioacetamid auf die mikrosomale Freisetzung von Tritium aus 1β,2β-^{3}H-Testosteron. Während eine akute Dosis von 100 mg/kg noch keine signifikante Änderung hervorruft, führt eine akute Gabe von 200 mg/kg bzw. 300 mg/kg Thioacetamid zu einer starken Steigerung der ^{3}H-Freisetzung.

Werden Ratten chronisch mit Thioacetamid behandelt (0,1% im Trinkwasser), so sieht man zunächst in den ersten 1–3 Wochen der Behandlung eine Verringerung der mikrosomalen ^{3}H-Freisetzung aus 1β,2β-^{3}H-Testosteron, der dann nach 6wöchiger Behandlung eine Steigerung der ^{3}H-Freisetzung in etwa dem Ausmasse folgt, wie sie auch bei akuter hoher Thioacetamidgabe feststellbar ist. Wird Thioacetamid in dieser Phase abgesetzt, so persistiert der Effekt über mindestens 2 Wochen.

In früheren Arbeiten[1,2] konnten wir zeigen, dass Lebermikrosomen von Thioacetamid-vergifteten Ratten eine starke Beeinträchtigung der Fähigkeit zur aromatischen Hydroxylierung von Östrogenen zeigen, was den Verhältnissen bei der menschlichen Leberzirrhose entspricht. Die hier vorgelegten Daten zeigen darüber hinaus, dass im gleichen System eine vermehrte Aromatisierung von Testosteron stattfindet.

THIJSSEN et al.[4] fanden bei Patienten mit Leberzirrhose eine gesteigerte Umwandlung von Androstendion in Östron. Sie erklärten dies mit einem primär in der geschädigten Leber verminderten Abbau von Testosteron bzw. Androstendion in Ring-A-gesättigte 17-Ketosteroide. Entsprechend stehe vermehrt Substrat für die Umwandlung in Östrogene zur Verfügung. Die vorliegenden Ergebnisse lassen ähnliche Mechanismen auch im Falle der experimentellen Leberschädigung der Ratte durch Thioacetamid vermuten.

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Lamellated Sensory Nerve Endings in Guinea-Pig Adrenals

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17 May 1976.

Summary. Lamellated sensory nerve endings were observed in the adrenal gland of guinea-pigs located at the cortico-medullary junction close to venous blood vessels. We suggest that they form the afferents of a system contributing to a local regulation of adrenal blood flow.

Lamellated sensory nerve endings are widely distributed in mammals. They show a great structural variability and are known by a variety of different names. Lamellated receptors have been described to occur both in the skin (for reviews see [1,2]) and in internal organs, such as serous and mucous membranes, heart and blood vessels, mesentery, pancreas, ureter bladder and prostate[3].

This communication deals with lamellated nerve endings located at the cortico-medullary junction in the adrenal of the guinea-pig. This observation is of particular interest in view of recent physiological evidence in favour of baroreceptors occurring in cat and rabbit adrenal glands[4].

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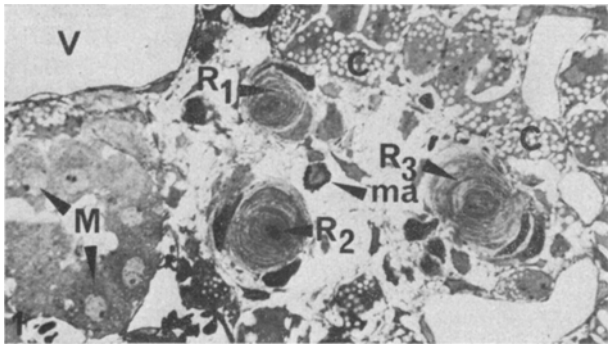

Fig. 1. Three lamellated receptors (R_{1-3}) at the cortico-medullary junction of the guinea-pig adrenal. Cortical cells (C), medullary cells (M), mast cell (ma), large venous blood vessel (V). × 560.

Newborn and adult guinea-pigs of either sex were perfused via the heart or the aorta with phosphate-buffered (0.1 *M*) 3.5% glutaraldehyde. Excised adrenals were rinsed in phosphate buffer, block-stained in aqueous uranyl acetate, post-fixed with 2% aqueous OsO_4, dehydrated in a graded series of alcohols and embedded in Araldite. Sections were mounted on naked grids, stained with uranyl acetate and lead citrate and observed in Zeiss EM 9A and Siemens 101 electron microscopes.

Figure 1 shows a group of lamellar corpuscles exhibiting the onion-like pattern typical of Pacinian, Golgi-Mazzoni or simple lamellated corpuscles[5] close to the cortico-medullary junction, and a large venous blood vessel. The size of the corpuscles was found to vary from 25 to 32 μm. They occurred either single or in small groups comprizing up to 4 corpuscles. Myelinated axons were frequently seen in the vicinity of the corpuscles.

Electron micrographs (Figure 2) revealed 2 main components, a central axon and concentrically arranged, closely packed cytoplasmic lamellae. A capsule, which is a characteristic feature of a Pacinian corpuscle and is regarded as a continuation of the perineurium of the axon[6], could not be clearly distinguished. An uninterrupted perineural sheath was also absent from myelinated nerves approaching the adrenal lamellated receptors. Within the corpuscle, the axon varied in size from 2 to 4.5 μm. It contained predominantly neurofilaments in the centre and accumulations of mitochondria in the periphery. Moreover, there were a few neurotubules and vesicles mainly located among mitochondria. The nerve fibre was surrounded by 2 opposing groups of about 10 to 25 lamellae of modified Schwann cells. The most prominent feature of these cells was an abundance of smooth plasmalemmal vesicles, some of which contained a material of medium electron density. Vesicles of similar size, with a content of medium to high electron density, were also found inside the cytoplasm intermingled with a few tubules, filaments and free ribosomes. Mitochondria and rough ER were present only in the broader lamellae. On each of the opposing sides of a corpuscle there were

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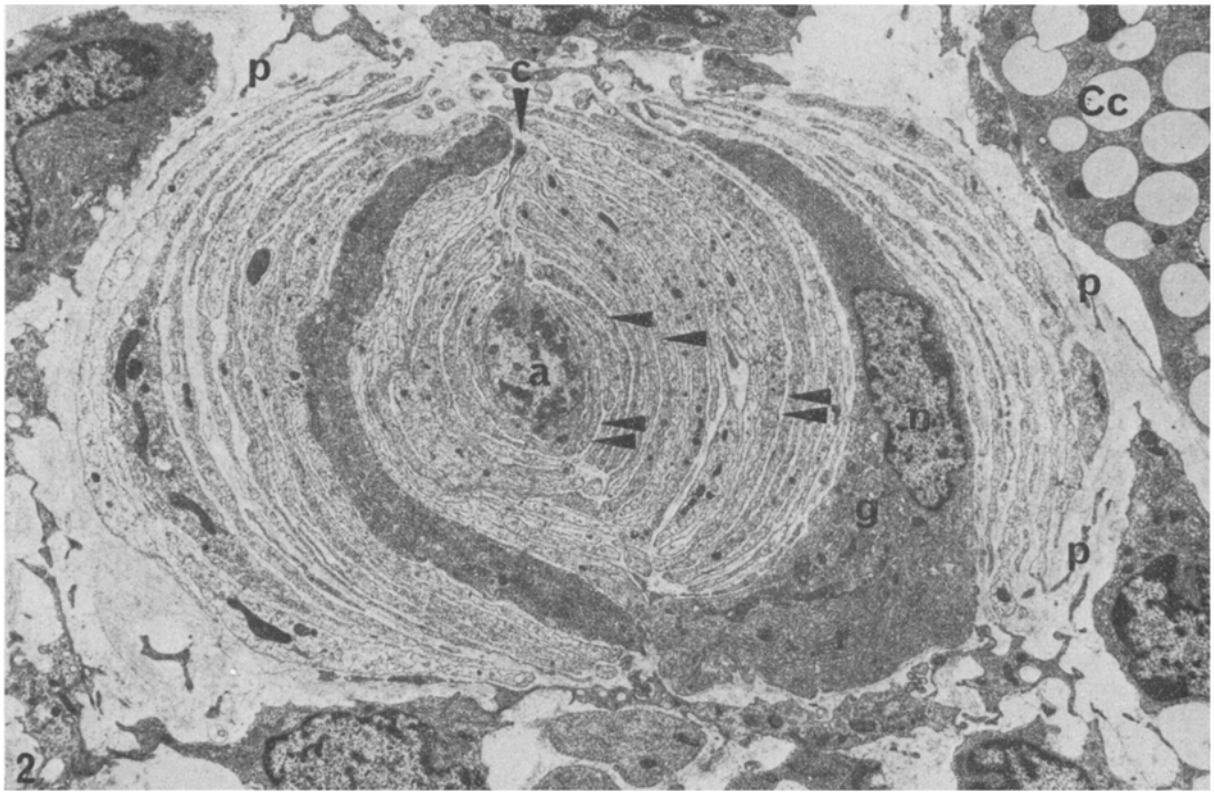

Fig. 2. Lamellated receptor in the guinea-pig adrenal. A centrally located axon containing dark mitochondria and neurofilaments is surrounded by concentrically arranged cytoplasmic lamellae (single arrows) and intercellular gaps (double arrows) forming 2 opposing groups separated by a longitudinal cleft (c). There are 2 particularly dark lamellae rich in cytoplasm, one of which contains a nucleus, Golgi area (g) and considerable amounts of rough ER. A few cells and cell processes (p), which might be part of an incomplete capsule, are present in the periphery of the lamellated receptor. Cortical cell (Cc). × 4,530.

1 or 2 particularly broad and dark lamellae, which contained the nucleus, Golgi area and great amounts of rough ER (Figure 2). The individual lamellae were separated by a gap varying in width from 33 to 540 nm. These gaps were filled with scarce microfilaments, collagen fibrils and 2 basal laminae covering the surface of the cytoplasmic lamellae. As a rule, the intercellular gaps were seen to increase in size towards the periphery of the corpuscles. The innermost lamella was contiguous to the axon and attached to it by desmosomes.

The presence of baroreceptors in rabbit and cat adrenals has been postulated on the basis of electrophysiological experiments[4]. NIIJIMA and WINTER[4] found that changes in systemic blood pressure were accompanied by changes in the firing rates of decentralized adrenal nerves. The authors concluded that these receptors could be part of a reflex system involved in the regulation of regional blood flow.

It is well agreed that Pacinian corpuscles are rapidly adapting mechanoreceptors specialized for the reception of vibration stimuli[7]. Although the corpuscles described in the present study differ from classical Pacinian corpuscles in so far as they lack a clearly identifiable perineural sheath, they are most probably mechanoreceptors as well. Hence we suggest that they form the afferents of a system contributing to a local regulation of adrenal blood flow. Adrenergic nerves, which could be interpreted as the corresponding efferents, have been observed in the walls of blood vessels in both cortex and medulla of the guinea-pig adrenal[8].

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The Central Tubuli in Distal Segments of Olfactory Cilia Lack Dynein Arms[1]

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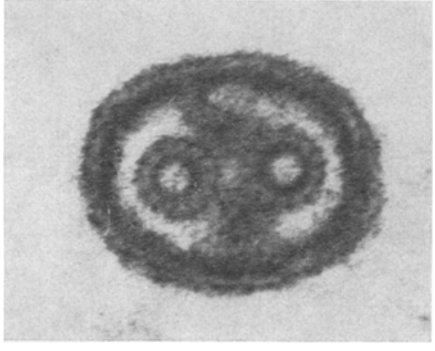
Summary. By means of the tannic acid-glutaraldehyde fixation method, the lack of dynein bridges between the central two tubuli in distal segments of mouse olfactory cilia is demonstrated. Consequently, these organelles are supposed to be unable to beat actively, in contrast to the proximal ciliary shafts.

Olfactory cilia are the terminal processes of sensory neurons in the olfactory epithelium of many animals and of man. They are suspended in a superficial thick layer of mucus and exposed directly to stimulating molecules arriving from the inspired air. Besides the olfactory vesicles, cilia are canditates for the transduction of the stimulant-receptor interaction into an electrical event, either by the action of membrane associated proteins or membrane lipids[3, 4].

Most commonly, olfactory cilia are built up by a proximal, thick shaft (diameter about 0.2 µm), and a distal, very long and thin segment, giving the cilium a total length of about 50 µm in rats[5]. With other centriole generated processes, the thick segments share the 9+2 pattern of tubuli. Towards the tip, the outer tubuli disappear and finally the central pair extends to the distal segment of the cilium[6].



Transsection of a distal segment of mouse olfactory cilium. The unit membrane is covered both on its inner and outer side by an osmiophilic layer. Note the 2 branches of osmiophilic material, which insert into the inner submembranous layer and the tubuli respectively, where their arms span 4 of the 13 protofilaments. No dynein bridges are perceivable. × 500,000.

The motility of olfactory sensory cilia is still an unsettled problem. According to the sliding filament hypothesis[7], the presence of dynein arms on tubules is an essential requirement for active movement. The present study provides evidence that distal ciliary segments in the mouse olfactory mucosa lack dynein bridges and therefore are not able to beat actively.

Methods. Nasal septae of adult and newborn Swiss mice were excised as reported previously[8], and fixed by immersion in 2.5% purified glutar aldehyde in 0.1 *M* cacodylate buffer pH 7.4. This fixative was supplemented with 4% tannic acid[9], as a mordant for tubular protomers. After postfixation in veronal acetate buffered osmium solution[10], and embedding in Epon 812 following routine techniques, thin sections were double stained in uranyl acetate and lead citrate solution[11], and examined in a Philips EM 200 electron microscope.

[1] Supported by grant Nr. 2099 from Fonds zur Förderung der wissenschaftlichen Forschung.
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