Zusammenfassend kann gesagt werden, dass viele Psychopharmaka mit zum Teil gegensätzlichen zentralen Wirkungen einen Konzentrationsanstieg der NFS im Blutplasma verursachen. Diese Zunahme der mobilen Fettsäuren kann durch eine vermehrte Freisetzung in den Fettdepots und/oder durch eine verminderte Utilisation in der Muskulatur bedingt sein. Die Wirkung von Chlorpromazin und ähnlichen Substanzen dürfte auf beiderlei Weise zustande kommen. Der mässige, nach Vorbehandlung mit einem Ganglienblocker oder bei konstant gehaltener Körpertemperatur noch feststellbare Anstieg der NFS im Plasma ist wahrscheinlich das Ergebnis einer verminderten Utilisation, während die mit der Chlorpromazin-Hypothermie einhergehende Ausschüttung der adipokinetisch wirkenden Hormone Noradrenalin und Adrenalin[10] eine vermehrte Freisetzung von Fettsäuren zur Folge hat. Dagegen scheint Corticotropin (ACTH) keine wesentliche Rolle zu spielen, denn Chlorpromazin war auch bei hypophysektomierten Tieren wirksam. Die Übereinstimmung von hier mitgeteilten experimentellen Ergebnissen mit entsprechenden Beobachtungen an Menschen[6] – auch hier war Chlorpromazin wirksam, Imipramin nicht – lässt vermuten, dass auch die übrigen untersuchten Psychopharmaka beim Menschen ähnlich auf den Fettsäurestoffwechsel wirken wie bei Ratten.

Tabelle III. Einfluss von Chlorpromazin (10 mg/kg intramuskulär) auf die nichtveresterten Fettsäuren (NFS) im Blutplasma von Ratten bei verschiedenen Umgebungstemperaturen. Mittelwerte aus n Einzelversuchen

Umgeb.-Temp.	n	NFS (μval/l) 0 h	2 h	Δ[a]	P	Δt[b]
31°C	12	291	436	+ 50%	$P < 0{,}001$	+ 0,3°C
21°C	11	283	755	+ 167%	$P \ll 0{,}001$	– 4,7°C

[a] Δ = Zunahme bzw. Abnahme der NFS im Plasma. [b] Δt = Änderung der Rectaltemperatur während 2 h Versuchsdauer.

Summary. Several neuroleptics, thymoleptics, tranquilizers, and psychoenergizers were found to elevate plasma-free fatty acid levels in the rat. Chlorpromazine and related substances probably affect both mobilization and utilization of fatty acids.

K. OPITZ

Pharmakologisches Institut der Universität Münster (Westfalen, Deutschland), 20. April 1965.

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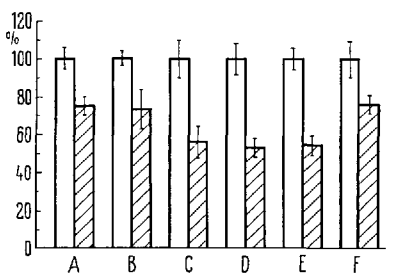
The Effect of Corticotrophine on Free Fatty Acid Content in Rat Adrenal

It has been known for some years that the adrenal glands of rats are extremely rich in lipids and that stress or administration of ACTH causes depletion of lipids, particularly of cholesterol[1,2]. There is now good evidence that cholesterol is utilized by adrenal cortex as a precursor of steroid hormones, but little specific information is available on the fate of the lipids other than cholesterol, and on the relation of adrenal fats to functional activity of the gland. In previous studies, an increase of lipase activity in adrenal glands after ACTH administration was demonstrated[3,4]; and therefore it has been deemed reasonable to study the level of free fatty acids in the adrenals under ACTH stimulation.

Adult male Wistar rats from Dobrá Voda and Lysolaje breeding stations weighing 160–180 g were used. The control groups of rats were injected with 0.2 ml of 0.9% NaCl solution and experimental groups received 2 IU of ACTH/100 g of body weight, i.p., in 0.2 ml saline solution (Corticotrophine, Léčiva, Prague). The animals of both groups were sacrificed by decapitation 10 and 30 min, 1, 2, 6, and 12 h after the injection. The adrenals were quickly removed, weighed and homogenized in ice-cooled saline solution (25 mg of fresh tissue per ml of saline solution). To 1 ml of this homogenate 5 ml of extraction mixture were added and free fatty acids (FFA) extracted and titrated according to the method of DOLE et al.[5,6].

The results of our experiments are demonstrated in the Figure. The values of FFA in the adrenals of rats treated with ACTH are expressed as a percentage of those in controls. It was found that the content of FFA in adrenal glands decreases after ACTH administration, with a maximum decrease between 1–6 h after ACTH injection.



The content of FFA in adrenal glands of rats treated with ACTH ▨ expressed as % of the control values □. Mean ± S.E. A – 10 min after ACTH injection (number of rats in control and experimental group 25, 25); B – 30 min (10, 14); C – 1 h (10, 10); D – 2 h (20, 20); E – 6 h (20, 18); F – 12 h after ACTH (18, 16). The mean value of FFA in adrenals of control animals was 4.22 ± 0.39 μEq/100 mg. The injection of saline solution has no significant effect on FFA content in the adrenals.

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It is hard to explain fully this effect of corticotrophine on FFA content, because there are only a few observations on the role of fatty acids in the biosynthesis of steroid hormones. TAMAKI[7], KUMANO[8], and ISHIHARU[9] found a close relationship between the essential fatty acid level in adrenals or in diet and the function of adrenal cortex. It was postulated that these fatty acids combine with cholesterol to form an active esterified cholesterol from which adrenocortical hormones are synthesized. It may be possible that the low values of FFA in the adrenals observed in our experiments after ACTH administration are due to increased esterification of cholesterol to more metabolically active esters. The marked cholesterol esterifying activity was demonstrated in rat adrenal homogenates[10] which maintain high levels of cholesterol esters in the adrenal glands of this species. But in the papers of PÉRON[11] and GRANT[12] it was suggested that free cholesterol was the substrate utilized for the corticoid synthesis, and loss of its esters was found as a consequence of ACTH action. Since the level of FFA in adrenal glands decreases after ACTH administration (in spite of the presence of an active lipase), it might seem reasonable to suggest that free fatty acids from cholesterol esters and triglycerides might serve as a source of fatty-acyl-CoA and acetyl-CoA from which the adrenal steroids may be synthesized[13], and ACTH probably accelerates this metabolism of fatty acids.

Zusammenfassung. Es wurde die Wirkung von ACTH auf den Gehalt unveresterter Fettsäuren in Rattennebennieren verfolgt. Nach Injektion von 2 IE ACTH per 100 g Körpergewicht (1, 2, 6 und 12 h post inj.) findet in der Nebennierenrinde keine Abnahme an freien Fettsäuren statt.

L. MACHO and M. PALKOVIČ

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Postsynaptic Inhibition Evoked from Primary Afferents in Spinal Interneurones

Several investigations have dealt with the excitatory actions evoked from different types of primary afferents in interneurones of the spinal cord[1–3]. Inhibitory effects on interneurones have been given less attention, although it has been shown that a discharge in interneurones may be evoked from one peripheral source and inhibited from another[2], and that during inhibition there is a repolarization of the membrane[3]. Such effects may be due to presynaptic inhibition at the primary afferent level, but it has now been found that in many interneurones in the spinal cord both EPSPs and IPSPs can be evoked from primary afferents.

The experiments were made on spinal cats either decorticate, unanaesthetized, or under chloralose anaesthesia. Microelectrodes (K-citrate or, in a few cases, KCl) were inserted into the dorsal horn and the intermediary region. The cells recorded from were classified as interneurones when they could not be antidromically activated from the ventral root or from either spinal half, dissected in the lower thoracic region. The effect of single volleys in ipsilateral nerves has been investigated with intracellular recording from 78 interneurones. 21 received only EPSPs (excitatory postsynaptic potential), 43 both EPSPs and IPSPs (inhibitory postsynaptic potential), while in 14 interneurones only IPSPs could be evoked. In the interneurone of the Figure there is an EPSP evoked from low threshold cutaneous afferents of the superficial peroneal nerve (SP). Superimposed on the EPSP, there is also a hyperpolarization evoked from the same nerve. The latter effect is evoked from the FRA (flexor reflex afferents = cutaneous afferents and high threshold muscle and joint afferents); there is a hyperpolarization from high threshold muscle afferents in the lower records. On recording with KCl electrodes, it was found there is a reversal during passage of a hyperpolarizing current through the recording electrode and hence that the hyperpolarization is an IPSP and not caused by removal of excitation.

IPSPs from the FRA were evoked in 22 interneurones that received monosynaptic or disynaptic EPSPs exclusively from cutaneous nerves. Volleys in the FRA also evoked IPSPs in 13 out of 22 interneurones that received monosynaptic excitation from group I muscle afferents. In some interneurones there was evidence of mixed excitatory and inhibitory effects from the FRA, either with opposite effects from different nerves or with mixed effect evoked from the same nerve. Other interneurones received IPSPs from the FRA but no EPSP from any of the nerves dissected. IPSPs are not only evoked from the FRA. Interneurones have been found that receive IPSPs from cutaneous afferents but not from high threshold muscle afferents, and in some interneurones we have observed disynaptic IPSPs evoked from group I muscle afferents.

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