Our results suggest that presence of glucocorticoids act as a rate-limiting factor for catecholamine degradation. These findings may have important clinical implications in the treatment of neuroleptic disorders caused by neurotransmitter degradation and metabolism. The possible use of glucocorticoids in the treatment of the above diseases in future could replace several synthetic MAO inhibitors widely used in clinical practice inspite of their considerable side effects.

Résumé. L'inactivation du cortex surrénal par l'hypophysectomie provoque une augmentation des activités MAO et COMT. L'administration d'ACTH ou d'hydrocortisone réduit l'augmentation des activités enzymatiques chez les foetus décapités sacrifiés à 31 jours. Chez des jeunes rats de 10 jours, surrénalectomisés à la naissance, on constate une augmentation de l'activité MAO dans le cœur et l'hypophyse. Chez le rat adulte, l'inhibition de la synthèse des glucocorticoides par la métopirone est également suivie par une augmentation rapide et hautement significative de l'activité de ces deux enzymes dans la plupart des organes.

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The Effect of the Ergoline Derivative VUFB-6683 on the Adenohypophysial Prolactin Concentration in Rats

Some ergot alkaloids, and other compounds containing an ergoline or ergolene moiety, exert an antilactation effect which can be inhibited by prolactin[1–5]. The mechanism of action of these compounds is explained by their stimulation of the secretion of the hypothalamic prolactin-inhibiting factor (PIF)[6] and inhibition of prolactin release[7]. Another compound exhibiting lactation-inhibitory activity in lactating rats and dogs is the compound VUFB-6683, D-6-methyl-8-ergolin-I-ylacet-amide tartarate[8]. Concurrent administration of prolactin protected the lactation[9]. The preparation has a low toxicity; at a single oral administration to rats, the medium lethal dose LD_{50} equals about 1 g/kg of body weight. Our study has been aimed at finding how this preparation influences the adenohypophysial prolactin level.

Material and methods. Our experiments were performed on lactating Wistar rats whose postpartum weight was 200–220 g. Each mother was caged individually together with her litter, the size of which had been reduced immediately after birth to 6 puppies. Compound VUFB-6683 was administered by gavage in daily doses of 1.4 and 10 mg/kg for 4 consecutive days, and from the 4th day postpartum on in 5 ml/kg of a 2% aqueous solution of tartaric acid. Each experimental group had its control group receiving water by gavage. Throughout the duration of the experiment, the lactation was checked by body weight gain of the presence of milk-spots. On the 5th day the mothers were killed by decapitation 10 h after removal of the offspring.

Estimation of prolactin concentration. The hypophyses were removed, the anterior pituitary lobe isolated, and, after weighing, homogenized with redistilled water in a glass homogenizer. The prolactin concentration per 1 mg of wet adenohypophysis was estimated by the standard method of polyacrylamide disc electrophoresis[10,11]. The polyacrylamide concentration was 7.5% and electrophoresis was made with a current of 3 mA per tube. After conclusion of electrophoresis, the gels were stained overnight with 1% amido black 10B, and destained electrophoretically in 7% acetic acid in a device described by PRUSÍK[12]. The optical density (OD) of the prolactin zons was meas-

[1] E. FLÜCKIGER and H. R. WAGNER, Experientia *24*, 1130 (1968).
[2] P. G. MANTLE, Proc. R. Soc. B. *170*, 423 (1968).
[3] P. V. MALUN and W. R. HAGE, Endocrinology *88*, 445 (1971).
[4] H. KARG, D. SCHAMS and V. REINHARDT, Experientia *28*, 574 (1972).
[5] C. J. SHAAR and J. A. CLEMENS, Endocrinology *90*, 285 (1972).
[6] W. WUTTKE, E. CASSELL and J. MEITES, Endocrinology *88*, 739 (1971).
[7] K. H. LU, Y. KOCH and J. MEITES, Endocrinology *89*, 229 (1971).
[8] M. SEMONSKÝ, N. KUCHARCZYK, M. BERAN, K. ŘEŽÁBEK and M. ŠEDA, Colln Czech. chem. Commun. Engl. Edn *36*, 2200 (1971).
[9] M. AUŠKOVÁ, K. ŘEŽÁBEK and M. SEMONSKÝ, Arzneimittel-Forsch., in press (1973).
[10] B. I. DAVIS, Ann. N.Y. Acad. Sci. *121*, 404 (1964).
[11] L. ORNSTEIN, Ann. N.Y. Acad. Sci. *121*, 321 (1964).
[12] Z. PRUSÍK, J. Chromat. *32*, 191 (1968).

Effect of VUFB-6683 on anterior pituitary (AP) prolactin concentration and weights in rats

Dosage of VUFB-6683	No. of rats	Prolactin concentration[a] (OD)	95% Confidence limite of means	Prolactin concentration[b] (IU)	AP weight (mg)
1 mg	14	0.42 ± 0.03	0.35–0.48	0.278[c]	6.0 ± 0.4[c]
Control	13	0.70 ± 0.03	0.64–0.76	0.459	8.4 ± 0.8
4 mg	7	0.33 ± 0.03[c]	0.27–0.39	0.279[c]	5.0 ± 0.5[c]
Control	7	0.56 ± 0.03	0.48–0.64	0.336	8.3 ± 0.2
10 mg	10	0.31 ± 0.09[c]	0.24–0.38	0.271[c]	6.7 ± 0.5[c]
Control	9	0.57 ± 0.02	0.53–0.61	0.369	8.2 ± 0.6

Mean values $\pm$ standard error are given. [c] Significant difference against control value ($p < 0.05$). [a] Prolactin concentration per 1 mg wet adenohypophysis expressed in terms of optical density and [b] in terms of international units of prolactin.

ured and integrated with the densitometer Vitatron TLD-100. A standard curve was obtained by densitometric measurement of samples containing 10–40 µg of rat prolactin (NIAMD – rat prolactin RP-1; 11 IU/mg)[13].

Results and discussion. The milk spots were completely suppressed by VUFB-6683 dosed 10 and 4 mg/kg daily, and reduced by 82% at the dosage of 1 mg/kg daily. The adenohypophysial prolactin concentrations and weights are given in the Table. It is evident that after VUFB-6683 the adenohypophysial prolactin concentration sank and the adenohypophysial weight decreased. In view of these findings, an inhibitory effect of the preparation on the prolactin synthesis in adenohypophysis can be assumed to exist.

Zusammenfassung. Mit Hilfe von D-6-Methyl-8-ergolin-I-ylacetamid-Tartarat, VUFB-6683 wurde bei säugenden Ratten das Gewicht und der Prolaktinspiegel der Adenohypophyse herabgesetzt und die Laktation gehemmt.

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A New Type of 'Node' in the Myelin Sheath of an Invertebrate Nerve Fibre

The mechanisms of impulse conduction in invertebrate nerve fibres with myelin-like sheaths and their ultrastructural correlates have not yet been cleared up. In 2 cases[1,2], nodes resembling the vertebrate nodes of Ranvier have been described in crustacean nerve fibres, but their function was not analyzed. On the other hand, certain myelinated giant fibers of shrimps, for which saltatory conduction has been claimed, lack Ranvier-like nodes. The myelin sheath is interrupted only by the emerging collaterals and these sites act probably as excitable nodes[3,4]:

In the ventral cord of earthworms, only the 3 dorsal giant fibres have myelin-like sheaths, which are also interrupted by regularly spaced collaterals on their ventral side[5]. This communication describes openings in the dorsal side of the myelin sheath of the median giant fibre of the earthworm, which have been overlooked until now.

Materials and methods. The observations were made on adult specimens of *Lumbricus terrestris*. Thin sections for light microscopy (0.5 to 1 µm thick) were obtained from Araldite-embedded ventral cords after fixation with 1% glutaraldehyde followed by 2% osmium tetroxide, both in 0.1 m phosphate or cacodylate buffer and in the cold (pH 7.4). The sections were post-stained with toluidine blue.

Results. The median giant fibre of the earthworm displays 3 ventral collaterals in all segments of the cord[5]. However, examining Araldite-embedded whole mounts of the ventral cord at low magnification, 5 regularly spaced translucent spots can be discerned in its opaque myelin sheath. After cutting off the ventral part of the cord including the ventral half of the giant fibres – and therefore the 3 ventral openings of the median giant – 2 openings are still visible in the dorsal midline of the myelin sheath of the median giant fibre. No such openings could be distinguished in the lateral giant fibres (Figure 2). These dorsal openings will be henceforth called nodes. The position of the nodes is fairly constant in all regions of the cord and in all animals examined (Figure 1). They alternate with the 2 nerve bundles which leave each segment of the cord, the side nerves 1 and the paired side nerves 2 and 3. The first node is located about midway between the side nerves 1 and 2/3, some 50 to 150 µm anterior to the median giant cell[5]. The second node is found at the end of the segment slightly closer to the preceeding side nerves 2/3 than to the side nerve 1, and at about the same level as the synchronizing bridge between the lateral giant fibres[5] (Figure 1).

The distance between consecutive nodes varies between 0.5 and 0.7 mm, depending upon the length of the corresponding segment. Generally, the internodal distance within the segment appears to be somewhat smaller than the internodal distance between consecutives segments. The nodes are of approximately circular shape and about 10 to 15 µm in diameter. The myelin lamellae are arranged around the node to envelope the protruding axoplasm concentrically (Figure 3), covering it until it reaches the fibrous capsule above the giant fibre, thus forming a funnel-like structure (Figure 4).

[1] J. H. McAlear, N. S. Milburn and G. B. Chapman, J. Ultrastruct. Res. *2*, 171 (1958).
[2] J. E. Heuser and C. F. Doggenweiler, J. Cell Biol. *30*, 381 (1966).
[3] K. Kusano, J. cell. Physiol. *68*, 361 (1966).
[4] K. Kusano and M. M. LaVail, J. comp. Neurol *142*, 481 (1971).
[5] J. Günther and J. B. Walther, Z. Morph. Ökol. Tiere *70*, 253 (1971).

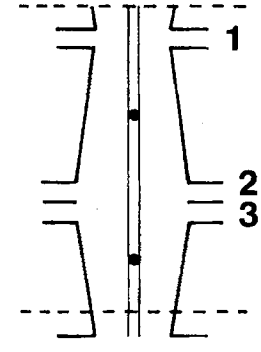

Fig. 1. Schematic drawing of a ventral cord segment showing the dosition of the dorsal nodes of the median giant fibre. Interrupted lines indicate the segmental borders of the body wall.