

Zusammenfassung. Behandlung von *Blattella germanica* im letzten Larvenstadium mit hohen Dosen von Juvenilhormon verhindert ausser der Morphogenese auch die Bildung der neuen Cuticula und die Häutung. Die Prothoracaldrüsen der entstandenen Dauerlarven sind normal; durch anschliessende Injektion von α -Ecdyson wird Cuticulasynthese induziert, die Tiere sterben jedoch in

der alten Haut. Diese Befunde unterstützen die Hypothese der antagonistischen Wirkung von Juvenilhormon und Ecdyson.

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Effect of Dopaminergic Blocking Agents on Plasma Luteinizing Hormone Releasing Hormone Activity in Hypophysectomized Rats

The releasing factor (RF) mechanisms of the hypothalamus are regulated by dopaminergic systems of the diencephalon^{1,2}. Numerous RFs are detectable in plasma after hypophysectomy³, thus providing a model for evaluating the effects of pharmacologic agents on the hypothalamic neurotransmitter/RF system. The present report describes preliminary experiments on the effect of two dopamine receptor blocking agents, pimozide and fluspirilene, on the plasma luteinizing hormone releasing hormone (LRF) activity in hypophysectomized rats.

Methods and materials. Female Sprague-Dawley (S-D) rats were hypophysectomized when 25 days old and used 60 days later. Rats (5/group) received various i.p. doses of pimozide or fluspirilene⁴ from days 85 to 91. On the following day the rats were sacrificed and plasma obtained for LRF assay. Plasma also was obtained from intact rats of the same age.

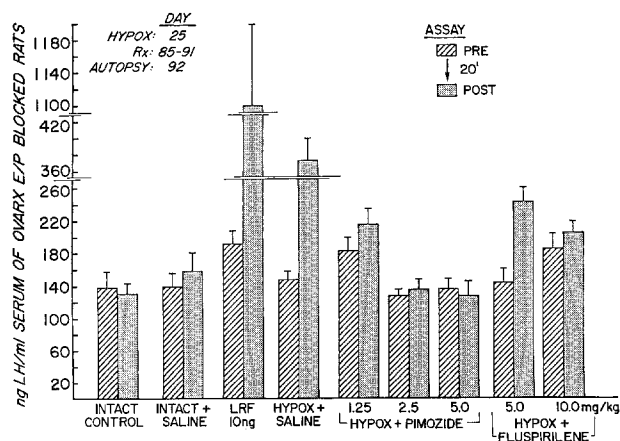
Plasma LRF activity was evaluated by measuring the quantity of LH released into the serum of adult ovariectomized S-D rats that had been treated 72 h earlier with s.c. doses of 50 μ g estradiol benzoate (E) plus 25 mg progesterone (P) (5 rats/group). A blood sample was obtained before and 20 min after i.v. injection of 1.0 ml of the donor plasma. Serum LH levels were determined by the double antibody radioimmunoassay technique of NISWENDER et al.⁵ and are expressed in terms of NIAMD-Rat LH-RP-1.

Results and discussion. The data are presented in the Figure and demonstrate that plasma derived from intact adult female rats does not possess any detectable LRF activity. The responsiveness of the ovariectomized assay rats was established by injection of 10 ng of synthetic LRF⁶, which produced a very dramatic and significant

($P \leq 0.01$) rise in serum LH. In contrast to the intact rats, plasma derived from female rats that had been hypophysectomized for 60 days and that received only saline, produced a prominent and significant increment in serum LH ($P \leq 0.01$), attesting to the presence of LRF activity. Treatment of hypophysectomized rats with pimozide or fluspirilene eliminated or reduced plasma LRF activity; the former drug demonstrated the greater potency.

Pimozide and fluspirilene are clinically effective neuroleptics^{7,8} and have been shown to be central nervous system dopamine receptor blockers⁹. Various studies support the concept that dopaminergic systems within the hypothalamus play a significant role in subserving the gonadotropin-releasing hormone (GnRH) mechanism resident in the hypophysiotropic area^{10,11}. It follows therefore, that pharmacologic agents blocking this neurotransmitter system should inhibit the hypothalamic GnRF/pituitary LH-FSH axis. The results of the present study support those of OJEDA and McCANN¹² who demonstrated that pimozide can partially inhibit the postcastration rise of plasma FSH, and show that pimozide's antagonistic action is via inhibition of hypothalamic GnRH. In addition, pimozide impedes the secretion of hypothalamic prolactin-inhibitory factor and leads to prolactin hypersecretion¹³.

Our preliminary clinical studies with pimozide are relevant to the central theme discussed herein. The drug



Effect of CNS agents on plasma LRF activity in hypophysectomized female rats.

¹ T. HÖKFELT and K. FUXE, in *Brain-Endocrine Interaction* (Eds. K. M. KNIGGE, D. E. SCOTT and A. WEINDL; S. Karger, Basel 1972) p. 181.

² S. M. McCANN, P. S. KALRA, A. O. DONOSO, W. BISHOP, H. P. G. SCHNEIDER, C. P. FAWCETT and L. KRULICH, in *Brain-Endocrine Interaction* (Eds. K. M. KNIGGE, D. E. SCOTT and A. WEINDL; S. Karger, Basel 1972), p. 224.

³ A. CORBIN, E. L. DANIELS and J. E. MILMORE, *Endocrinology* 86, 735 (1970).

⁴ Janssen Pharmaceutica, Beerse, Belgium.

⁵ G. D. NISWENDER, A. R. MIDGLEY JR., S. E. MONROE and L. E. REICHERT JR., *Proc. Soc. exp. Biol. Med.* 128, 807 (1968).

⁶ Wyeth Compound No. 16, 558.

⁷ P. JANSSEN, J. BRUGMANS, J. DONY and V. SCHUERMANS, *J. Clin. Pharmac.* 12, 26 (1972).

⁸ G. CHOUINARD, T. A. BAN, H. E. LEHMANN and J. V. ANANTH, *Curr. ther. Res.* 12, 604 (1970).

⁹ N. E. ANDEN, S. G. BUTCHER, H. CORRODI, K. FUXE and U. UNGERSTEDT, *Eur. J. Pharmac.* 11, 303 (1970).

¹⁰ R. I. WEINER, R. A. GORSKI and C. H. SAWYER, in *Brain-Endocrine Interaction* (Eds. K. M. KNIGGE, D. E. SCOTT and A. WEINDL; S. Karger, Basel 1972), p. 236.

¹¹ J. C. PORTER, I. A. KAMBERI and J. G. ONDO, in *Brain-Endocrine Interaction* (Eds. K. M. KNIGGE, D. E. SCOTT and A. WEINDL; S. Karger, Basel 1972), p. 224.

¹² S. OJEDA and S. M. McCANN, *Fedn. Proc.* 32, 227 (abstr.) (1973).

¹³ J. RAUS, Janssen Pharmaceutica, Beerse, Belgium, personal communication.

is presently being used in lipodystrophic diabetes, a disease in which the peripheral blood contains high levels of GnRH and corticotropin releasing factor activities¹⁴. In corroboration of the previous findings, the drug eliminates not only these two RF activities, but also significantly lowers plasma LH and FSH (unpublished).

In summary, the collective data demonstrate that dopaminergic components subserve hypothalamic releasing hormone mechanisms, as evidenced by their inhibition by specific antidopaminergic agents¹⁵.

dopaminergiques qui règlent les mécanismes hypothalamiques de libération hormonale.

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Résumé. Des rats femelles hypophysectomisées depuis 60 jours ont un haut niveau d'activité LRF plasmatique. Le traitement par bloqueurs des récepteurs dopaminergiques (pimozide ou fluspirilène) fait disparaître l'activité LRF plasmatique et indique que ce sont des systèmes

¹⁴ C. C. MABRY, D. R. HOLLINGSWORTH, G. V. UPTON and A. CORBIN, *J. Pediat.* 82, 625 (1973).

¹⁵ The technical assistance of J. BELL, C. CAVALCANTO, P. DOVE, K. KOCH and J. TRACY is gratefully acknowledged.

Ein Selektivsubstrat zur Isolierung von *Listeria monocytogenes*

Der kulturelle Nachweis von *Listeria monocytogenes* (*L.m.*) aus Untersuchungsmaterial, das natürlicherweise zahlreiche Bakterien enthält – wie etwa Stuhl, Vaginal- oder Rachenabstriche – erfordert die Anwendung von Selektivnährböden. Bei den bisher beschriebenen Verfahren wurden vollwertige Nährböden mit verschiedenen Hemmstoffen versetzt: Kaliumthiocyanat (LEHNERT¹, Nalidixinsäure (BEERENS und TAHON-CASTEL² oder Acridinfarbstoffe (Ralovich et al.)³ Ein synthetisches Substrat kann hingegen auch ohne Hemmstoffe schon selektive Eigenschaften besitzen. Es darf nur wenige bestimmte Nährstoffe enthalten, die gerade zum Anwachsen der gesuchten Keime erforderlich sind. Wir haben uns die Frage gestellt, ob sich die Eigenschaften des Stoffwechsels von *L.m.* ausnutzen lassen und ob solch ein synthetisches Mangelsubstrat als Grundlage eines Selektivnährmediums für den Listerienachweis besser geeignet ist.

Material und Methodik. 1. Untersuchungen über den Listerienstoffwechsel. Es wurde das Wachstumsverhalten des Stammes *L.m.* Serotyp 4b (1071/53) bei verschiedenen Aminosäurekombinationen und der Stämme *L.m.* 1/2 a (2459); 4b (1071/53) bei verschiedenen Kohlehydratkombinationen geprüft. Die Anzucht der Stämme erfolgte auf einer Blutplatte. Nach 24 h bei 37°C Bebrütung wurden glatte Kolonien auf ihre Identität geprüft und in 0,9% iger NaCl-Lösung aufgeschwemmt. Die Bakterien-suspension wurde auf einen Keimgehalt von 5×10^7 /ml eingestellt. Mit 0,05 ml dieser Bakterienaufschwemmung

¹ C. LEHNERT, *Arch. exp. VetMed.* 18, 981, 1247 (1964).

² H. BEERENS und M.M. TAHON-CASTEL, *Annls. Inst. Pasteur* 111, 90 (1966).

³ B. RALOVICH, A. FORRAY, E. MERÖ, H. MALOVICS und J. SZAZADOS, *Zentbl. Bakt. ParasitKde., 1. Abt. Orig.* 216, 88 (1971).

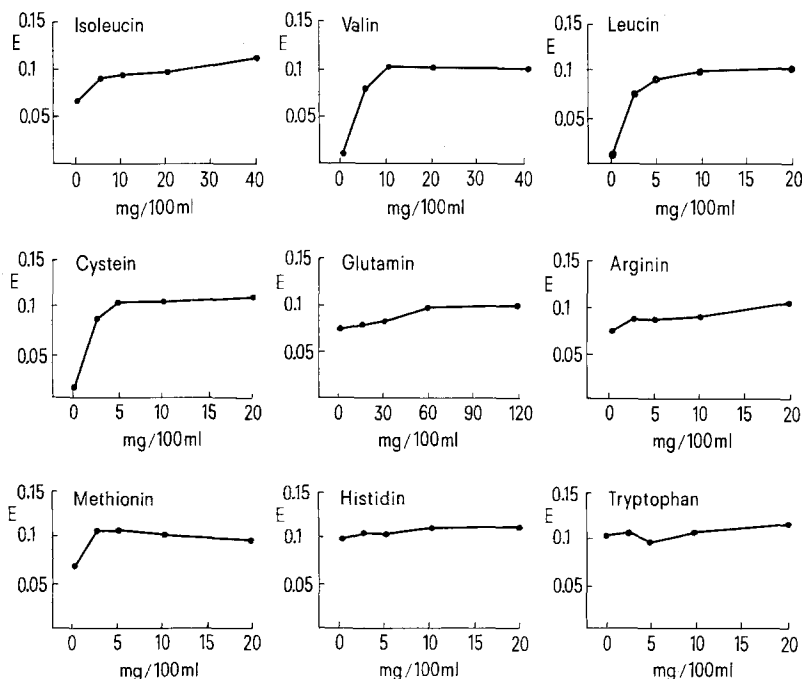


Fig. 1. Wachstum von *L.m.* Serotyp 4b (24 h) in Abhängigkeit von den Konzentrationen verschiedener Aminosäuren. E, Extinktion.