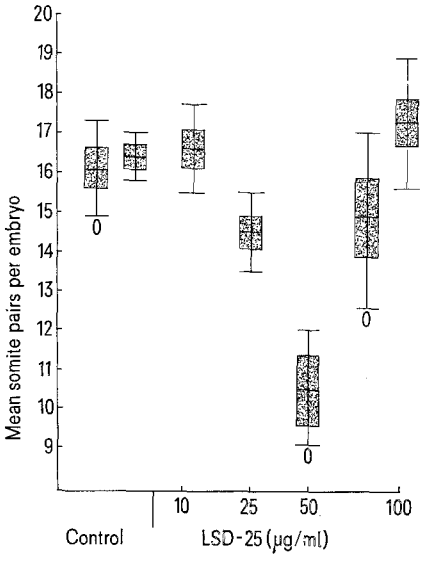


Relationships between selected doses of LSD-25 and mean number of somite pairs per embryo at 95% confidence intervals. The open circle denotes data from a previous report[6]. The mid-horizontal bar = mean; the stippled area = standard error of the mean.

*Discussion.* This study indicates that lysergic acid diethylamide disturbs the orderly formation of somites over a dose range of 25 to 50 μg, with the minimum teratogenic dose being somewhere between 10 and 25 μg. Although both 25 and 50 μg doses inhibited somite formation, no appreciable effect on the macroscopic arrangement of those somites present could be detected. Since in the chick embryo regression movements of the primitive streak play a vital role in the segmentation of the paraxial mesoderm[9], this study also suggests that the LSD over the teratogenic dose range may act to retard these cellular movements, thereby resulting in fewer somite pairs.

Ten and 100 μg dose of LSD, being non-effective in their action on somite number, give the dose-response curve a biphasic appearance. The basis for this apparently unusual effect is presently not known. However, GEBER[5] reported that another hallucinogenic drug (mescaline) produced a greater number of defects at lower concentrations than at higher concentrations.

*Résumé.* L'administration de 10 μg d'acide lysergique diéthylamide (LSD-25) aux embryons de poulet en culture n'a pas eu d'effet sur le nombre des somites. Une réduction du nombre des somites a été observée avec 25 μg de LSD, ce qui confirme notre première observation sur la tératogénie de cette drogue. Il semble exister une relation directe entre la dose de LSD et le nombre de paires des somites dans chaque embryon au niveau de 25 et 50 μg.

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[9] R. BELLAIRS, J. Embryol. exp. Morph. *11*, 697 (1963).

[10] The LSD-25 was obtained through the courtesy of the FDA-PHS Psychotomimetic Agents Advisory Committee of the US National Institute of Mental Health. Financial assistance is recognized from the Charles and Johanna Busch Memorial Fund of Rutgers University.

## Glycogenolytic Effect of Adipose Tissue Extract

ANTONIADES et al.[1] have demonstrated that an aqueous extract of adipose tissue (ATE) of rat or bovine origin produces prolonged hypoglycemia after parenteral administration to rats and mice. LENTI et al.[2] and PERRI et al.[3] have reported that ATE-induced hypoglycemia is preceded by a brief period of marked hyperglycemia. It is our finding that the administration of ATE to intact and adrenalectomized rats produces hepatic glycogenolysis accompanying the hypoglycemic effect.

*Materials and methods.* The animals used were male rats of the Sprague-Dawley strain (Laboratory Supply Co.) weighing approximately 150 g. Adrenalectomy was performed by Hormone Assay Labs, Chicago, 7 days prior to the experiments. Food was available ad libitum until 2 h prior to the experimental period. To obviate the effect of diurnal variation in endogenous carbohydrate metabolism all animals were prepared and used for study at the same daily hours. ATE of bovine origin (kindly provided by Dr. G. C. PERRI) was dissolved in saline and injected via the femoral vein; control animals were given saline alone. At the time of sacrifice the animals were anesthetized with Metofane® and bled via cardiac puncture; heparin was used as anticoagulant. The liver was quickly excised, immersed in liquid nitrogen, and stored frozen until analysis for glycogen content. Plasma glucose was determined by the glucose oxidase method[4]. Liver glycogen was isolated[5], acid hydrolyzed and determined as glucose with glucose oxidase.

*Results and discussion.* The effects of ATE on plasma glucose levels and hepatic glycogen content are summarized in the Table. Within 1 h following ATE treatment, both intact and adrenalectomized animals became hyperglycemic; subsequently this effect was reversed and hypoglycemia developed. Continuous mobilization of hepatic glycogen was seen in ATE-treated animals; this effect led to an almost complete depletion of the glycogen stores. Adrenalectomized animals were more sensitive to ATE than intact animals (effective dose 5 mg/kg vs. 75 mg/kg) and glycogenolysis and hypoglycemia occurred earlier in the adrenalectomized groups. The glycogenolytic response was apparently independent of epinephrine as evidenced by nearly total depletion of hepatic glycogen in adrenalectomized as well as intact animals.

[1] H. N. ANTONIADES, J. D. SIMON, C. A. BAILE and M. B. ETTLINGER, Endocrinology *88*, 1222 (1971).

[2] G. LENTI, A. PELLEGRINI, G. PAGANO, P. ZIZI, D. CORDA, R. CIRILLO, V. MASCIA and E. PINNA, Boll. Soc. ital. Biol. sper. *44*, 1413 (1968).

[3] G. PERRI, L. COSCIA and E. GIULIANI, Boll Soc. ital. Biol. sper. *47*, 864 (1972).

[4] L. P. CAWLEY, F. M. SPEAR and R. KENDALL, Am. J. clin. Path. *32*, 195 (1959).

[5] C. A. GOOD, H. KRAMER and M. SOMOGYI, J. biol. Chem. *100*, 485 (1933).

Effects of ATE administration on plasma glucose and hepatic glycogen levels of intact and adrenalectomized rats

| Treatment | Time (h) | Intact animals[a] | | Adrenalectomized animals[b] | |
|---|---|---|---|---|---|
| | | Plasma glucose[c] | Hepatic glycogen[d] | Plasma glucose[c] | Hepatic glycogen[d] |
| Control | 1 | 139 ± 3[e] | 48 ± 2 | 126 ± 3 | 24 ± 3 |
| ATE | 1 | 185 ± 8[f] | 40 ± 3 | 168 ± 4[f] | 14 ± 3[f] |
| Control | 2.5 | 150 ± 5 | 32 ± 2 | 143 ± 4 | 24 ± 3 |
| ATE | 2.5 | 136 ± 6 | 22 ± 4[f] | 73 ± 12[f] | 6 ± 3[f] |
| Control | 5 | 168 ± 9 | 26 ± 1 | 145 ± 4 | 20 ± 7 |
| ATE | 5 | 44 ± 11[f] | 0.1 ± 0.1[f] | 32 ± 14[f] | 1 ± 0.6[f] |

[a] 75 mg/kg. [b] 5 mg/kg. [c] mg/100 ml. [d] mg equivalents glucose/g liver tissue. [e] Mean ± S.E. 6 animals. [f] $p < 0.05$.

Hypoglycemia reflects a disturbance in one of the many physiologic, or enzymatic controls that maintain normoglycemia. We propose that ATE-induced hypoglycemia is the result in part of accelerated mobilization of hepatic glycogen stores, analogous to the hypoglycemia of endotoxicosis[6] and glucagon administration[7].

*Résumé.* L'administration i.v. d'un extrait aqueux de tissu adipeux (ATE) à des rats intacts surrénalectomisés provoque un état de glycogénolyse hépatique suivi d'hypoglycémie. La glycogénolyse semble être indépendante de l'épinéphrine. L'hypoglycémie provoquée par l'ATE résulte en partie de la mobilisation accélérée des réserves de glycogène hépatique.

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[6] J. P. Sanford, J. A. Sanford and C. Gott, J. exp. Med. *112*, 97 (1960).
[7] B. W. Siegel, N. L. Wiech and T. R. Blohm, Fedn. Proc. *32*, 311 (1973).

## Effect of Lithium and other Drugs on the Amphetamine Chlordiazepoxide Hyperactivity in Mice

The action of lithium on psychotic excitement has been shown by Cade[1] as early as 1949. Since then, its efficacity in the prevention of the manic-depressive psychosis has been well established[2,3]. Nevertheless, there are few observations on the effects of lithium on the behaviour of laboratory animals. Indeed, the action of lithium is very peculiar and cannot be compared with any reference drug; indeed, many authors think lithium acts specifically on the manic-depressive disease and cannot act out of its clinical context[4]. Nevertheless, it would be very surprizing if such a product had no effect on animals. Weisher[5], Sheard[6], Brain[7] and Eichelman et al.[8] have noted a decrease of the aggressivity in different animal species. Johnson and Wormington[9] have found that the lithium treatment decreased the rearing activity of the rat, without modifying its horizontal activity[10]. Perkinson et al.[11] have found an inhibition of the tetrabenazine depression. Moreover, some authors have studied the action of lithium on experimental agitation states, which were even called 'manic'. Matussek and Linsmayer[12] have shown that lithium decreased the rat hyperactivity, produced by the administration of desmethyl-imipramine and a reserpine-like benzoquinolizine (Ro 4.1284), but has no effect on the amphetaminic excitement. Caroll and Sharp[13] have observed that the lithium salts decreased the morphine hyperactivity in mice. Finally, lithium has been shown to decrease the hyperactivity of rats and mice, produced by the chlordiazepoxide-amphetamine association[14,15].

During this study, we attempted to reproduce this type of induced hyperactivity, and, after checking the effect of lithium, we studied other drugs under the same conditions.

*Material and methods.* The study was made with female Swiss mice (20–25 g), kept in cages of 10 animals. Treatment was the association of dexamphetamine bitartrate (5 mg/kg) and chlordiazeproxide (25 mg/kg), in solution in NaCl 0.9%. The volume injected was 0.20 ml per 20 g of body weight, the injections were made i.p. The behavioural effect was studied with a holeboard[16] 20 min after the injection. These doses and latency times were those of U'Prichard and Steinberg[15]. The control mice received the same volume of NaCl 0.9%.

[1] J. F. J. Cade, Med. J. Aust. *36*, 349 (1949).
[2] M. Schou, Encéphale *60*, 281 (1971).
[3] M. Schou and D. M. Shaw, Practitionner *210*, 105 (1973).
[4] M. Schou, Biochem. Soc. Transact. *1*, 81 (1973).
[5] M. L. Weisher, Psychopharmacologia *15*, 245 (1969).
[6] M. H. Sheard, Nature, Lond. *228*, 284 (1970).
[7] P. F. Brain, J. Endocr. *55*, 39 (1972).
[8] B. Eichelman, N. B. Thoa and J. Perez-Cruet, Pharmac. Biochem. Behav. *1*, 121 (1973).
[9] F. N. Johnson and S. Wormington, Nature New Biol. *235*, 159 (1972).
[10] F. N. Johnson, Experientia *28*, 533 (1972).
[11] E. Perkinson, R. Ruckart and J. P. da Vanzo, Proc. Soc. exp. Biol. Med. *131*, 685 (1969).
[12] N. Matussek and M. Linsmayer, Life Sci. *7*, 371 (1968).
[13] B. J. Caroll and P. T. Sharp, Science *172*, 1355 (1971).
[14] C. Cox, P. E. Harrison-Read, H. Steinberg and H. Tomkiewicz, Nature, Lond. *232*, 336 (1971).
[15] D. C. U'Prichard and H. Steinberg, Br. J. Pharmac. *44*, 349 (1972).
[16] J. R. Boissier and P. Simon, Archs int. Pharmacodyn., Thér. *147*, 372 (1964).