that the kidney is a site of formation of these metabolites. Questions as to whether the osmotic diuresis resulting from furosemide influences tubular transport of chloramphenicol metabolites by means of decreased water reabsorption, or whether Na ion has a specific effect, will require further study.

Summary. Simultaneous administration of chloramphenicol and furosemide (10 mg i.v.) decreased urinary excretion of chloramphenicol but increased the excretion of its metabolites as aryl amines and total nitro compounds. These latter increases were directly related to Na excretion.

O. SCHÜCK, J. GRAFNETTEROVÁ, V. PRÁT and E. KOTANOVÁ

Institute for Clinical and Experimental Medicine, Budějovická 800, Praha 4-Krč, (Czechoslovakia), 29 May 1975.

Dependence on Age of Methamphetamine-Produced Changes in Thermoregulation and Metabolism

It has been reported that the central stimulation which is one of the most prominent effects of amphetamines, diminishes with age[1–3]. The present experiments were performed in order to investigate whether this loss of effectiveness applies also to other actions of the amphetamines, i.e. the effect of methamphetamine on overall metabolism and thermoregulation.

Methods. Female NMRI mice aged 4–6 weeks (juvenile mice) or 20 months (old mice) were used. They were kept at 25 °C room temperature and fed ad libitum with standard diet (Herilan®) before and during the experiments. Methamphetamine (3 µg/g) was given s.c. immediately before the beginning of the experiments. Controls were treated with the same volume of saline. The animals were then placed singly into glass jars without bedding. Oxygen consumption was registered continuously by means of small spirometers, and the rectal temperature was measured at the end of the experiments as described earlier[4]. In another group of animals, 1 and 2 h after the drug administration blood glucose (according to HUGGETT and NIXON[5]), plasma non-esterified fatty acids (according to DUNCOMBE[6]) and liver glycogen (according to ESTLER and MITZNEGG[7]) were determined. For this purpose the animals were decapitated, liver samples were excised rapidly and frozen in liquid air within 10 sec. Blood was also collected from decapitated animals.

Results and discussion. As shown in the Table, juvenile mice react to methamphetamine with an increase of their oxygen consumption by almost 50 %. At the same time their body temperature rises significantly by 1.0 ± 0.3 °C over that of the control animals. These changes in overall metabolism are accompanied by a decrease of the glycogen content of the liver by ca. 60 % and a marked increase of the plasma non-esterified fatty acids. The blood glucose level remains nearly unchanged.

In contrast, in old animals liver glycogen declines only by 13 % while the blood glucose level drops by 31 mg/100 ml. Plasma non-esterified fatty acids increase even more than in the juvenile mice. For reasons discussed earlier[8], the oxygen consumption of old mice is lower than that of young animals, and it is only insignificantly raised by methamphetamine (Table). The rectal temperature of old mice treated with methamphetamine does not increase but falls significantly by 1.7 ± 0.5 °C.

These results suggest that juvenile mice treated with methamphetamine can easily mobilize their carbohydrate and lipid reserves and thus provide sufficient energy for thermogenesis and motor activity, which is increased considerably under these experimental conditions[2]. It is well known that in old animals the response of many

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Effect of methamphetamine (3 µg/g s.c.) on various metabolic parameters of old and juvenile mice

	Juvenile mice		Old mice	
	1st hour	2nd hour	1st hour	2nd hour
Oxygen consumption (Nml/g body weight/h)				
Controls (saline)	4.76 ± 0.29 (12)	4.41 ± 0.31 (12)	2.64 ± 0.20 (17)	2.43 ± 0.19 (15)
Methamphetamine	6.83 ± 0.73[a] (13)	6.51 ± 0.61[a] (14)	3.25 ± 0.37 (23)	2.75 ± 0.19 (20)
Liver glycogen (µmoles/g organ weight)				
Controls (untreated[b])	210 ± 8 (32)		206 ± 8 (32)	
Methamphetamine	82 ± 9[a] (22)	111 ± 12[a] (22)	168 ± 9[a] (22)	172 ± 8[a] (21)
Blood glucose (mg/100 ml)				
Controls (untreated)[b]	133 ± 3 (36)		134 ± 3 (36)	
Methamphetamine	135 ± 6 (23)	137 ± 5 (24)	107 ± 7[a] (23)	103 ± 7[a] (23)
Plasma non-esterified fatty acids (µeqiv/ml)				
Controls (untreated)[b]	0.49 ± 0.02 (36)		0.54 ± 0.03 (36)	
Methamphetamine	0.74 ± 0.03[a] (24)	0.71 ± 0.02[a] (24)	0.93 ± 0.03[a] (24)	0.87 ± 0.02[a] (24)

Mean values ± SEM are given, number of animals in parentheses. [a] Difference to control value significant, $p \leqslant 0.05$. [b] Untreated animals were used as controls because earlier studies have shown that injection procedure does not affect the parameters at the times given.

metabolic parameters to sympathomimetics is diminished[9-14]. In accordance with these results, the old mice were unable to mobilize as much liver glycogen as needed to meet the glucose demand and maintain their blood glucose level within a normal range. It appears that not enough substrate can be made available to enable the animals to increase their total metabolism. This, however, means that if more energy is spent for the still considerable increase of motor activity produced by methamphetamine in old mice[2], energy expenditure has to be cut down elsewhere. It seems that in this special case thermogenesis is reduced and no longer compensates for heat loss. This view is supported by the observation that the animals cannot maintain their body temperature when they are kept at an ambient temperature (e.g. 25 °C) which is below their point of thermoneutrality, but that no decline of body temperature occurs if the same experiment is carried out at a room temperature of 34 °C at which heat loss becomes very small.

The finding that in old mice plasma non-esterified fatty acids rise even higher than in juvenile mice, seems to be difficult to reconcile with our hypothesis and with reports that the lipolytic response to sympathomimetics decreases with age[9, 12-14]. One explanation for this phenomenon, which has a parallel in cold-stressed mice[8], may be that plasma levels are only the resultant from the rates of lipolysis and uptake of fatty acids by the various organs and that the oxidation of fatty acids in the citric acid cycle is dependent on the simultaneous degradation of an adequate amount of carbohydrates, which are required to provide the oxaloacetate necessary for the entry into the citric acid cycle of the two carbon fragments of fatty acids[15]. Therefore, utilization of fatty acids is necessarily also impeded when carbohydrates are lacking.

Summary. In contrast to juvenile mice, old mice treated with methamphetamine are unable to adequately mobilize their carbohydrate reserves. They cannot increase their overall metabolism and become hypothermic, while juvenile mice react with increased calorigenesis and hyperthermia.

C.-J. Estler[16]

Pharmakologisches Institut der Universität Erlangen-Nürnberg, Universitätsstrasse 22, D-852 Erlangen (German Federal Republic, BRD), 17 July 1975.

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Chemotaxis of Rabbit Macrophages in vitro: Inhibition by Drugs

The effect of several drugs on the chemotactic migration of rabbit granulocytes in vitro has been reported in a previous paper[1]. The present work deals with the effect of 15 agents on the chemotaxis of rabbit macrophages.

Materials and methods. Compounds were obtained from the following sources: hydrocortisone succinate as Solu-Cortef from Upjohn; dexamethasone and phenylbutazone from Ciba-Geigy; indomethacin, sodium salicylate and iodoacetic acid from Merck; naproxen from Syntex; vincristine from Lilly; phytohaemagglutinin P from Difco; concanavalin A from Calbiochem; cytochalasin B (phomin) from Sandoz; chloroquine as Resochin from Bayer; dipotassium ethylenediaminetetracetate (EDTA) from Fluka. The cytotoxicity of these compounds for rabbit peritoneal macrophages as judged microscopically by morphological integrity of the cell is included in the Table; it may also be seen that all concentrations tested (except one) were below toxic limits.

The Boyden chamber technique for the in vitro assessment of chemotaxis of mononuclear cells was used[2, 3]. Macrophages were derived from the peritoneal exudates of rabbits injected 4 days earlier with 50 ml of Nujol (Plough Inc., Memphis/Tenn., USA). The average composition of these exudates consisted of approximately 90% macrophages and 10% neutrophils and included a few small lymphocytes. The cells were suspended in modified Gey's solution (10 mg glucose/ml and 2% human serum albumin (HSA; Central Laboratory, Swiss Red Cross, Berne)) and standardized to 4×10^6 cells per chamber. They were mixed with the drug under study immediately before being transferred into the upper compartment of the Boyden chamber. As the incubation in the chamber lasted 5 h as compared with the 2.5 h previously used for neutrophils, preincubation of macrophages with the substance was omitted. The lower compartment contained a solution of 1% casein (according to Hammarsten, obtained from Merck AG, Darmstadt, GFR) in isotonic saline which is an excellent cytotaxin for macrophages concerning potency and reproducibility. Each drug was tested in triplicate chambers and in at least 3 experiments where exudates from different rabbits were used. Positive and negative controls were included in all tests. Normal positive chemotaxis towards casein was determined with cells to which Gey's solution instead of drug was added. For the negative controls, casein was replaced by Gey's solution containing 2% HSA. The latter controls were truly negative, as no or occasionally only one or two cells crossed the entire thickness of the filter. The following point should be stressed: only macrophages having reached the lower surface of the membrane filter were counted. The same batch of micropore filters (Sartorius Membranfilter GmbH, Göttingen, GFR) with a pore size of 12 µm was used throughout these experiments. Macrophages require a large pore size to migrate through a membrane filter about 140 µm thick[3]. The polycarbonate filters with a pore size of 5 µm (Nucleopore) used by

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