

adipocytes, and (b) the antagonist effect on metabolic peripheral actions of catecholamines (lipolytic, and calorogenic actions).

Experiments were performed *in vitro* using the following products: fenfluramine (2-ethylamino-1-(3-trifluoro-methylphenyl)propane); fenproporex (+)-1-(methyl-1-phenyl-2-ethyl amino)3-propionitrile, chlorphentermine (dimethyl-1,1-chlorophenyl-2-ethylamine).

Oxygen uptake, lipolysis (estimated as glycerol

release in incubation medium) and glucose utilization, were measured in the Warburg apparatus with Krebs Ringer bicarbonate solutions containing noradrenaline (NA) (8×10^{-5} M) or theophylline (1×10^{-5} M) or NA + theophylline + anorectic drug (1×10^{-4} to 1.4×10^{-3} M) on epididymal fat pads of 200 g Wistar rats. In man studies were conducted in epiploic (or perirenal) adipose tissue obtained during appendicectomy of 40 subjects of both sexes (17 to 72 years of age). Results are given in Table 1.

Activity of anorectic drugs (amphetamine), amfepramone and UP 507-04) on two models of obesity in animals

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The anorectic activity of three drugs (amphetamine, amfepramone and UP 507-04 (cyclopropyl-2 p-chlorophenyl-4 methyl-5 pyrrolidine succinate)) was studied on two models of experimental obesity: gold thioglucose treated mice and rats after bilateral electrolytic lesions of hypothalamic ventromedian nucleus.

The obesity, on these models, developed in two phases: dynamic and static. During the dynamic phase the rate of weight gain was very pronounced, during the static phase very poor. In plasma, total lipids, triglycerides and cholesterol levels were increased in obese rats.

Mice and rats were treated orally by drugs for 12 days during the static phase. Amphetamine (4 mg/kg in rats and mice) induced a sharp decrease of food intake and body weight without statistically significant modifications of total lipids, triglycerides and cholesterol in rats. Amfepramone (16 mg/kg) in mice had no activity on food intake and body weight. UP 507-04 (8 mg/kg in mice and 4 mg/kg in rats) decreased food intake and body weight; total lipids, triglycerides and cholesterol tended to remain at normal values in rats.

Decremental skin conductance response in mice, during iterative photostimulation; an attention-sustaining capacity model for psychopharmacological research

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As a result of repeated presentation of a stimulus to which attention is attracted, a decrement and eventual extinction of the skin conductance reaction (SCR) occurs. Delivering iterative photostimulation to mice while recording their palmar SCRs, Marcy, Quermonne & Nammathao (1976) have demonstrated that SCR extinction (i.e. habituation) is delayed by psychoanaleptics.

In this study, the same method was used. Time of extinction (in 100ths of an h) was computed against dose (mg/kg) for each drug tested. Depending on the effect obtained, the following parameters were determined: standard delaying dose, i.e. delaying SCR extinction until 125 (SDD) or standard shortening dose, i.e. speeding up SCR extinction to time 50 (SSD).

Unlike the psychoanaleptics tested, central depressants speeded up SCR extinction time. Clonazepam was more active than phenobarbitone (cf. lower SSD in Table 1) although it is definitely less active in suppressing the righting reflex. Delay of habituation obtained with amphetamines was confirmed with related compounds. Rather unexpectedly, both fenfluramine, although considered a depressant, and, above all, piracetam, although devoid of any stimulant property, also delayed SCR extinction. In fact, fenfluramine possesses some stimulant properties and piracetam improves learning

Table 1 Effect of drugs on extinction of skin conductance reaction

<i>Drugs</i>	<i>No. b</i>	<i>Dose-range Delaying effect</i>	<i>SDD (mg/kg i.p.)</i>	<i>analysis of linear regression variance</i>		
				<i>V</i>	<i>F</i>	<i>P</i>
Dexamphetamine (sulphate, sal.)	7	0.0312-8.00	0.0722 (±0.015)	347081.31	896.93	<0.001
Piracetam (sal.)	4	0.50-10.00	0.787 (±0.146)	164007.61	197.40	<0.001
Dexamphetamine (tartrate, c.m.c.)	4	1.00-5.00	1.40 (±0.111)	123764.97	525.16	<0.001
Methamphetamine (sal.)	3	2.00-3.00	2.01 (±0.040)	45212.47	211.21	<0.001
Phentermine (sal.)	3	5.00-20.00	4.84 (±0.522)	17964.87	73.48	<0.001
Fenfluramine (HCl, sal.)	4	5.00-30.00	10.06 (±1.036)	35616.91	185.43	<0.001
Benzphetamine (HCl, sal.)	3	12.50-30.00	29.17 (±1.954)	13353.17	67.81	<0.001
Ephedrine (HCl, sal.)	3	20.00-60.00	34.68 (±3.086)	15674.47	83.63	<0.001
Caffeine (+ benzoate Na, dist. water)	4	80.00-150.00	150.50 (±5.162)	12176.72	143.89	<0.001
Pyrisuccideanol (dimaleate, sal.)	4	250.00-1000.00	956.80 (±104.29)	8126.07	48.00	<0.001
<i>Speeding up effect</i>			<i>SSD (mg/kg i.p.)</i>			
Clonazepam (c.m.c.)	7	0.156-10.00	1.00 (±0.19)	20688.50	132.82	<0.001
Phenobarbital (Na, sal.)	4	10.00-35.00	22.41 (±1.76)	12524.41	88.69	<0.001

No b. = number of batches of 10 mice for the relevant experiment.

SDD, SSD = see text. Figures in brackets are confidence limits $P < 0.05$.

V = variance, *F* = variance ratio, *P* = probability.

sal. = dissolved in saline, c.m.c. = suspended in 0.5% carboxymethylcellulose water solution.

in particular conditions (Sara & David-Remacle, 1974).

Decremental SCR during monotonous solicitation may be proposed as a model for attention sustaining capacity under the effect of drugs. Results obtained show that this model is not exclusively influenced by drugs modifying general activity.

Conversely, it seems particularly sensitive to specific central effects which are not readily demonstrable otherwise.

References

- MARCY, R., QUERMONNE, M.A. & NAMMATHAO, B. (1976). Habituation to iterative photostimulation in the palmar skin conductance response of mice, its delay by psychoanaleptics. *Experientia (Basel)*, **32**, 208-209.
- SARA, S.J. & DAVID-REMACLE, M. (1974). Recovery from electroconvulsive shock-induced amnesia by exposure to the training environment: pharmacological enhancement by piracetam. *Psychopharmacologia (Berl.)*, **36**, 59-66.