adrenoceptor antagonist (Carlsson, Ablat, Brandström & Carlsson, 1972), was about 300–500-fold more potent than the cardioselective β_1-adrenoceptor antagonists, metoprolol and practolol in its ability to antagonize isoprenaline-stimulated cyclic AMP formation and [^{3}H]-propranolol binding.

In previous experiments we have demonstrated that chronic depletion of cerebral catecholamines results in an increased responsiveness of β-adrenoceptor mediated cyclic AMP formation whereas chronic isoprenaline administration induces a loss of sensitivity of this response (Nahorski & Rogers, 1975). In order to assess the possibility of an altered affinity and/or number of cerebral receptor sites in these conditions, the binding of [^{3}H]-propranolol was examined in cerebral membranes of these animals. The affinity and total number of [^{3}H]-propranolol binding sites were identical in reserpine (3 x 2.5 mg/kg) and vehicle-treated chicks. However, following isoprenaline treatment (2 x 150 μmol/kg) the loss of β-adrenoceptor responsiveness was accompanied by a significant (25–30%) apparent loss of total binding sites.

The experiments described suggest that the β-adrenoceptor in chick cerebral hemispheres resembles that found in bronchial and vascular smooth muscle (β_2) rather than that in heart (β_1). In addition evidence is presented to suggest that the loss of responsiveness of cerebral β-adrenoceptors following chronic exposure to isoprenaline is associated with a loss of available receptor binding sites.

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Peripheral effects of the amphetamine-type anorectic drugs: inhibition of catecholamine-induced lipolysis, respiration, glucose utilization in the adipose tissue of man and rat

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Some phenylethylamine derivatives are among the most important anorectic drugs which act by a central mechanism, but their peripheral metabolic actions are poorly understood.

It appears that many of the amphetamine drugs are weak agonists of the lipolysis in adipose cells but an inhibitory effect of sympathomimetically-induced lipolysis was found in the case of fenfluramine. The main body of work reported in this field has been carried out in the rat, the adipose adrenoceptor of which may well be quite different from that in man.

For this reason it seemed essential to investigate the effects of amphetamine anorectic drugs in both species (rat and man) on: (a) The adrenoceptor agonist activity for lipolysis, respiration, glucose oxidation of the

Table 1

Products	*Species*	*Lipolysis with theophylline*	*Lipolysis with theophylline + NA*	*Respiration*
Fenfluramine	Man	↓	↓	↑
	Rat	no effect	↓	no effect
Fenproporex	Man	↓	↓	↓
	Rat	↓	↓	↓
Chlorphentermine	Man	no effect	↓	↓
	Rat	↓	↓	↓

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