TABLE 1. *Changes induced by (+)-amphetamine sulphate in the self-selected circadian rhythm of the canary*

Circ. per., Duration of circadian period.

Duration of	Time of administration	Dose mg/kg	No. of experiments	Increase (mean ± standard error of mean) in hours over pre-experimental average in circadian period No. 0	1	2	3	4
Activity	AM	7·5	12	−0·13±0·25	−0·05±0·26	0·36±0·34	0·79±0·24	0·13±0·16
Activity	AM	15·0	11	−0·02±0·41	−0·79±0·33	−0·79±0·30	−0·34±0·32	−0·19±0·30
Activity	PM	7·5	12	2·60±0·93	−0·59±0·71	−0·15±0·28	−0·71±0·69	−1·22±0·72
Activity	PM	15·0	14	1·75±0·55	−0·09±0·26	−0·02±0·27	−0·34±0·25	0·23±0·31
Circ. per.	AM	7·5	12	0·06±0·07	−0·04±0·05	0·12±0·15	0·11±0·07	0·11±0·06
Circ. per.	AM	15·0	11	0·05±0·08	0·05±0·11	−0·13±0·09	−0·12±0·06	−0·17±0·13
Circ. per.	PM	7·5	12	0·41±0·16	0·05±0·14	0·20±0·12	0·05±0·14	−0·11±0·16
Circ. per.	PM	15·0	14	0·55±0·15	0·21±0·10	0·00±0·13	0·06±0·11	−0·02±0·07

was, however, a decrease in the duration of activity in the two following periods (delayed action?). The effects of amphetamine thus seem to be dependent on the timing of the drug administration and were not limited to an increased wakefulness.

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Role of catecholamines in compulsive gnawing behaviour in mice

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Apomorphine in rats induces an increased locomotor activity and compulsive gnawing, and Ernst (1967) has reported that the apomorphine-induced compulsive gnawing is not reduced by α-methyl-tyrosine. In mice even large doses of apomorphine do not induce a compulsion to gnaw. When the mice are pretreated with centrally active anticholinergics or tricyclic antidepressants, however, apomorphine also induces an intense gnaw-compulsion syndrome. Very high gnawing intensities were obtained with the tricyclic antidepressants (Pedersen, 1967).

Mice were given amitriptyline (5 or 10 mg/kg I.P.) or imipramine (20 or 40 mg/kg I.P.). Fifteen minutes later apomorphine was injected subcutaneously (10 mg/kg). The animals were placed in cages, two mice in each cage, for one hour. A cage consists of a 30 cm high box, 12×25 cm, without bottom and lid. The cages were placed on corrugated paper. If compulsion to gnaw occurred, the mice would begin to bite the paper within 5–10 min. The gnawing intensity was estimated principally as described by Ther & Schramm (1962). Five groups, each consisting of two mice, were used at each dose level.

The gnaw-compulsion syndrome was studied in mice pretreated with α-methyl-L-tyrosine (α-MT, 50 or 100 mg/kg I.P. 4 hr before test). Both doses of α-MT significantly reduced the gnawing intensities. (—)-DOPA (200 mg/kg I.P. 1 hr before testing) completely reactivated the mice pretreated with α-MT. Furthermore it was shown that pretreatment with sodium diethyldithiocarbamate (three doses of 500 mg/kg I.P., 18, 6 and 3 hr before testing) hardly affected the gnawing intensities, although the animals were markedly sedated.

The results indicate that catecholamines, probably dopamine, in mice play an important part in the mechanism, by which the gnaw-compulsion syndrome is produced by apomorphine in combination with tricyclic antidepressants.

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Effects of chlorpromazine on the metabolism of catecholamines in dog brain

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A technique was developed whereby the catecholamines and their metabolites could be estimated in the same brain sample. Using solvent extractions, these compounds were separated from a perchloric acid extract of brain into three groups, namely the acids, the amines and the amino-acids. Homovanillic acid and 3,4-dihydroxyphenylacetic acid were estimated in aliquots of the acid fraction. The amines were separated as their acetylated derivatives, using paper chromatography, eluted and estimated fluorimetrically. A new method, more sensitive than that described in the literature (Carlsson & Waldeck, 1964), was developed for the determination of methoxydopamine.

The analytical method was applied to a study of the effects of chlorpromazine (5 mg/kg and 15 mg/kg intravenously) on the catecholamine metabolism in various areas of the brains of beagle dogs. Two hours after drug administration, the following changes were observed in the caudate nucleus: the dopamine concentration was unaltered by 5 mg/kg and decreased by 15 mg/kg; the levels of homovanillic acid and 3,4-dihydroxyphenylacetic acid were increased by 5 mg/kg and unchanged by 15 mg/kg; the concentration of methoxydopamine fell after both doses of chlorpromazine. Similar changes in the levels of dopamine and its metabolites were observed in the globus pallidus. In those areas of brain containing more noradrenaline than dopamine—the hypothalamus, midbrain, thalamus and hindbrain—the concentration of noradrenaline was increased by both doses of chlorpromazine but there were generally no significant alterations in the concentrations of dopamine and its metabolites.

The main effect of chlorpromazine was considered to be a stimulation of catecholamine synthesis (Carlsson & Lindqvist, 1963). Our results could not, however, be explained entirely on the basis of increased synthesis and it was concluded that chlorpromazine exerted more than one action on the brain amines.

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Influence of drugs on catecholamine metabolism in brain as studied by ^{14}C-tyrosine

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Results from clinical and pharmacological investigations indicate that changes in the metabolism of brain monoamines exist in diseases of the central nervous system. Several of the most potent psychotropic drugs have been shown to exert specific actions on mono-