The effects of some drugs which alter the metabolism of noradrenaline in the periphery on the concentrations of the two glycols in the hypothalamus have also been investigated. After treatment with drugs which inhibit monoamine oxidase it was found that DOPEG disappeared at a rate which was at least 4 times that of MOPEG. The administration tropolone (50 mg/kg, i.p.) resulted in no change in the concentration of MOPEG although the concentration of DOPEG was doubled. Reserpine (5 mg/kg, i.p.) produced no change in the concentration of the two glycols 30 min after administration and cocaine (30 mg/kg, i.p.) or desmethylimipramine (20 mg/kg, i.p.) also did not increase the concentration of the two metabolites.

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Effect of γ-hydroxybutyric acid on dopamine metabolism in the brain

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γ-Hydroxybutyric acid occurs naturally in the mammalian brain. When administered to animals it has a depressant action on the central nervous system causing a sleep-like state. γ-Hydroxybutyric acid also causes an increase in the concentration of dopamine in the brain but does not change the concentrations of noradrenaline or 5-hydroxytryptamine (Gessa, Vargiu, Crabai, Boero, Caboni & Camba, 1966). The depression of the central nervous system and the increase in the concentration of dopamine show a close temporal correlation but little is known of the mechanism of action of γ-hydroxybutyric acid on the metabolism of dopamine.

Gessa, Crabai, Vargiu & Spano (1968) suggested that dopamine was metabolized at a normal rate in the brains of rats treated with γ-hydroxybutyric acid. These authors also found that in rats, which had been treated with reserpine to deplete the

TABLE 1. *Effect of sodium γ-hydroxybutyrate (GHB-Na) on the concentration of dopamine in the brains of mice and rats treated with reserpine and maintained at an environmental temperature of* 30–32° *C*

	Treatment	Dose (mg/kg)	Duration of treatment (h)	Dopamine concentration (μg/g)	
A. Mouse				Forebrain	
	—	—	—	0·96±0·04	(9)
	GHB-Na	1500	1·0	2·04±0·02	(6)*
	Reserpine	5	4·0	<0·03	(5)
	Reserpine+	5	4·0		
	GHB-Na	1500	1·0	<0·04	(8)
B. Rat				Caudate nucleus	
	—	—	—	6·58±0·39	(16)
	GHB-Na	1500	1·5	13·36±1·76	(6)†
	Reserpine	5	3·5	<0·07	(7)
	Reserpine+	5	3·5		
	GHB-Na	1500	1·5	<0·12	(8)
	Reserpine	5	7·0	<0·05	(10)
	Reserpine+	5	7·0		
	GHB-Na	1500	1·5	<0·07	(11)

Dopamine values are means (± S.E.M. where applicable). The number of estimations is indicated in parentheses. Difference from the control value: *, $P<0.001$; †, $P<0.005$, Student's *t* test.

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cerebral dopamine, there was still an increase in the concentration of dopamine in the brain after an injection of γ-hydroxybutyric acid. We have carried out experiments on both rats and mice to determine the effect of γ-hydroxybutyric acid on the cerebral concentrations of dopamine, and its metabolites, homovanillic acid and dihydroxyphenylacetic acid. There was a dose dependent increase in the concentration of all three substances 2 h after the injection of γ-hydroxybutyric acid. No increase in the concentration of dopamine was observed when γ-hydroxybutyric acid was administered to reserpine treated animals (Table 1). This result suggests that the action of γ-hydroxybutyric acid on the concentration of cerebral dopamine requires an unimpaired storage mechanism for dopamine.

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Central stimulant action of fenfluramine in the rat

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Fenfluramine is structurally related to amphetamine and exhibits its anorectic action. After administration to rats at anorectic doses it is almost devoid of central stimulant activity (Le Douarec, Schmitt & Laubie, 1966; Alphin, Funderburk & Ward, 1964). However, high doses produce many amphetamine-like behavioural effects (Yelnosky & Lawlor, 1970).

The effects of fenfluramine and amphetamine have been compared on confinement motor activity in rats (Tedeschi, Fowler, Cromley, Pauls, Eby & Fellows, 1964). The apparatus restricts locomotor activity by confinement of single rats in an activity chamber which is small enough to permit vertical but not horizontal movements. The vertical movements are recorded with two photoelectric cells as interruptions of either one or both light beams.

Spontaneous confinement motor activity was greater with female than male rats. In addition, female rats exhibited a greater increase in activity than male rats after orally administered DL-fenfluramine (5 mg/kg) or D-amphetamine (1 mg/kg). However, male rats were used for a further comparison of fenfluramine and amphetamine in order to avoid effects arising from changes in drug metabolizing enzyme activity which might accompany hormonal changes in the oestrus cycle.

Three dose levels of DL-amphetamine and DL-fenfluramine, injected intraperitoneally, were used for calculation of the doses of each which produced a 200% increase in the average activity count over 25 min as compared to control rats tested at the same time. The following values were obtained: DL-amphetamine sulphate, 0·6 (95% confidence limits 0·4–0·9) mg/kg; DL-fenfluramine hydrochloride, 6·1

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