in inhibiting the uptake of ^{3}H-noradrenaline and ^{3}H-5-hydroxytryptamine. Kinetic analysis indicated that the drugs in Table 1 inhibited ^{3}H-GABA uptake non-competitively.

TABLE 1. *Effect of drugs on ^{3}H-GABA uptake by cortical slices expressed as the concentration of drug which reduced the uptake by 50% (IC_{50}), and the effect of these drugs on the uptake of ^{14}C-glycine, ^{3}H-alanine, ^{3}H-5-hydroxytryptamine and ^{3}H-noradrenaline when applied to the tissue at the IC_{50} for GABA*

Compound	IC_{50} (μM) ^{3}H-GABA	% Inhibition of uptake at IC_{50} for GABA ^{14}C-Gly.	^{3}H-Ala.	^{3}H-5-HT	^{3}H-NA
p-Chloromercuriphenyl sulphonic acid (p-CS)	18	70·4	54·3	66·9	75·1
Chlorpromazine	32	47·6	40·5	92·2	89·1
Prochlorperazine	50	72·9	46·8	92·2	54·5
L-2,4-Diaminobutyric acid	66	4·9*	2·0*	13·6*	7·1*
Iprindole	78	75·0	57·6	93·9	87·4
Desmethylimipramine	100	72·5	51·8	100·0	93·0
Apomorphine	130	57·8	42·4	15·5	100·0
Diphenhydramine	370	61·8	59·2	94·0	60·0

The results are the means of four to six experiments. *=Not significantly different from controls.

These results suggest that it is unlikely that centrally acting drugs act by specifically affecting the uptake process for GABA in the brain, since the concentrations of drug required to reduce the uptake of GABA also have marked effects on the uptake of other amino-acids and on biogenic amines.

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Studies on the glycol metabolites of noradrenaline in mouse brain

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Noradrenaline can be metabolized to 1-(4-hydroxy-3-methoxyphenyl)-1,2-ethanediol (MOPEG) and 1-(3,4-dihydroxyphenyl)-1,2-ethanediol (DOPEG) in animal tissues. We have used a gas-liquid chromatographic method (Sharman, 1969) to estimate the concentrations of free MOPEG and DOPEG in the mouse brain. Both metabolites were present in the hypothalamus, part of the midbrain including the substantia nigra, olfactory tubercles, massa intermedia of the thalamus, striatum and cerebral cortex and cerebellar cortex. Although the glycol metabolites of noradrenaline could be extracted from the striatum, we have been unable to detect the presence of any free methoxylated alcohol metabolite of dopamine in this tissue. The hypothalamus was selected for further study because this tissue showed the highest concentration of MOPEG (27 ± 3 [mean $\pm$ S.E.M.] ng/g tissue).

When groups of mice were exposed to a low temperature (−5 to −15° C) the concentration of MOPEG in the hypothalamus was increased to 69 ± 6 ng/g tissue and the concentration of DOPEG rose from 31 ± 2 ng/g tissue to 58 ± 9 ng/g tissue.

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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