The sugar transport system in cerebral cortex slices appears to be regulated by local concentrations of sodium ions (Gilbert, 1966) which in turn depend upon the activity of membrane Mg-dependent Na, K-activated ATP-ase. The effects of phenobarbitone on the activities of Mg-activated ATP-ase and Mg-dependent Na, K-activated ATP-ase were therefore determined. The microsomal fraction was prepared from cerebral cortex and ATP-ase activities were determined in Tris-HCl buffer of pH 7·4 using a method similar to that of Samson & Quinn (1967). Phenobarbitone sodium (2 mM) did not significantly alter the activity of either enzyme.

It is concluded that the effect of phenobarbitone on sugar transport is probably mediated by influencing directly the apparent affinity of carrier for sugar rather than indirectly by influencing active sodium efflux from the cell.

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## Effect of centrally acting drugs on the uptake of γ-aminobutyric acid by the brain

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The brain has a specific uptake process for γ-aminobutyric acid (GABA) and this may provide an effective mechanism for terminating its inhibitory action on neurones (Iversen & Neal, 1968). Thus, it is possible that some centrally acting drugs might produce their effects by blocking the reuptake of GABA after its release from nerve endings. In the present investigation we have attempted to test this possibility by determining the effect of centrally acting drugs on the uptake of $^3$H-GABA by brain slices.

Slices of cerebral cortex (10 mg) were preincubated with the drug for 15 min at 25° C in 10 ml of medium. $^3$H-GABA ($5\times10^{-8}$ M) was added and the incubation was continued for 10 minutes. The radioactivity in the tissue was then measured by liquid scintillation spectrometry (Iversen & Neal, 1968).

Sixty-five compounds at concentrations of 0·1–1·0 mM were tested for possible inhibitory effects on the uptake of $^3$H-GABA. More than half of the drugs tested produced a significant reduction in the uptake of $^3$H-GABA by the cortex, but the only groups of centrally acting drugs in which all members consistently produced inhibition of uptake were the phenothiazines and the tricyclic antidepressants. Other compounds which had a relatively powerful inhibitory effect on uptake of $^3$H-GABA were: *p*-chloromercuriphenylsulphonate, L-2,4-diaminobutyric acid, haloperidol, apomorphine and diphenhydramine. The concentrations of some of these drugs which reduced the uptake of $^3$H-GABA by 50% ($IC_{50}$) are presented in Table 1, which also shows the effect of these drugs on the uptake by cortex of: $^3$H-alanine, $^{14}$C-glycine, $^3$H-5-hydroxytryptamine and $^3$H-noradrenaline. With the exception of L-2,4-diaminobutyric acid, all the drugs at the $IC_{50}$ for GABA, also significantly reduced the uptake of $^{14}$C-glycine and $^3$H-alanine and were often much more effective

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 | $IC_{50}$ ($\mu$M) $^3$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 ($27 \pm 3$ [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 $69 \pm 6$ ng/g tissue and the concentration of DOPEG rose from $31 \pm 2$ ng/g tissue to $58 \pm 9$ ng/g tissue.