10 mg wet weight were incubated for various times with [^{14}C]-glycine (6×10^{-7}M) in 10 ml. of oxygenated medium. The tissue was collected by rapid filtration, washed with 5 ml. of ice-cold medium and the total radioactivity was measured by liquid scintillation spectroscopy (Iversen & Neal, 1968).

There was a rapid uptake of [^{14}C]-glycine as estimated by the accumulation of radioactivity in the tissue. After incubating the slices of spinal cord for 60 min at 37° C there was a tissue : medium ratio of 30 : 1. The uptake of [^{14}C]-glycine showed saturation kinetics over a range of external glycine concentrations from 10^{-6}M to 2×10^{-4}M with an apparent *Km* for glycine $=3{\cdot}12\times10^{-5}$M and $V_{max}=$ 0·48 μ-mole/g of cord per min. The uptake of [^{14}C]-glycine was temperature-dependent, being greatly reduced at 0° and optimal at 37° C. Replacement of sodium chloride in the incubation medium by choline chloride reduced the uptake of [^{14}C]-glycine to less than 1% of the control values. Incubation of the tissue in medium containing 2,4-dinitrophenol (10^{-3}M) or with ouabain (10^{-5}M) also caused a large reduction in the uptake of [^{14}C]-glycine. Strychnine (10^{-3}M) did not affect [^{14}C]-glycine uptake but *p*-hydroxymercuribenzoate (10^{-5}M) significantly reduced the uptake of [^{14}C]-glycine into slices of spinal cord.

The results show the existence in the rat spinal cord of an efficient uptake mechanism for glycine which shows many of the characteristics of an active transport mechanism. This uptake process could act as a mechanism for terminating the inhibitory action of glycine on spinal neurones. The potentiation of the effects of glycine on motor-neurones produced by *p*-hydroxymercuribenzoate may not be due to inhibition of metabolic degradation of glycine as suggested by Curtis *et al.* (1968) but may be caused by the effect of this compound in reducing the uptake of glycine from the extracellular space.

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Subcellular distribution of endogenous and [^{3}H]-GABA in rat cerebral cortex

L. L. IVERSEN* and M. J. NEAL, *Department of Pharmacology, University of Cambridge*

We have recently described the properties of an uptake mechanism for [^{3}H]-GABA in slices of rat cerebral cortex (Iversen & Neal, 1968). The present studies were undertaken to obtain more information on the cellular location of [^{3}H]-GABA uptake in relation to the storage sites for endogenous GABA in the rat cortex, by comparing the subcellular distribution of the exogenous and endogenous amino-acid in cortical homogenates.

Slices of rat cerebral cortex were labelled by incubation with [^{3}H]-GABA and homogenized in isotonic sucrose. The subcellular distributions of endogenous GABA, [^{3}H]-GABA and glutamic decarboxylase (GAD) were studied by density gradient centrifugation. As illustrated in Fig. 1, the subcellular distributions of the labelled and endogenous amino-acid were remarkably similar, indicating that [^{3}H]-GABA is taken up into the endogenous GABA pool. About 40% of both endogenous and [^{3}H]-GABA were recovered in particles which had the characteristics of synaptosomes (equilibrium density and sensitivity to osmotic shock). In slices labelled with [^{3}H]-GABA and [^{14}C]-α-aminoisobutyric acid (AIB), significantly more [^{3}H]-GABA was recovered in synaptosomal fractions than [^{14}C]-AIB. About 80% of the enzyme GAD was also recovered in the synaptosomes which

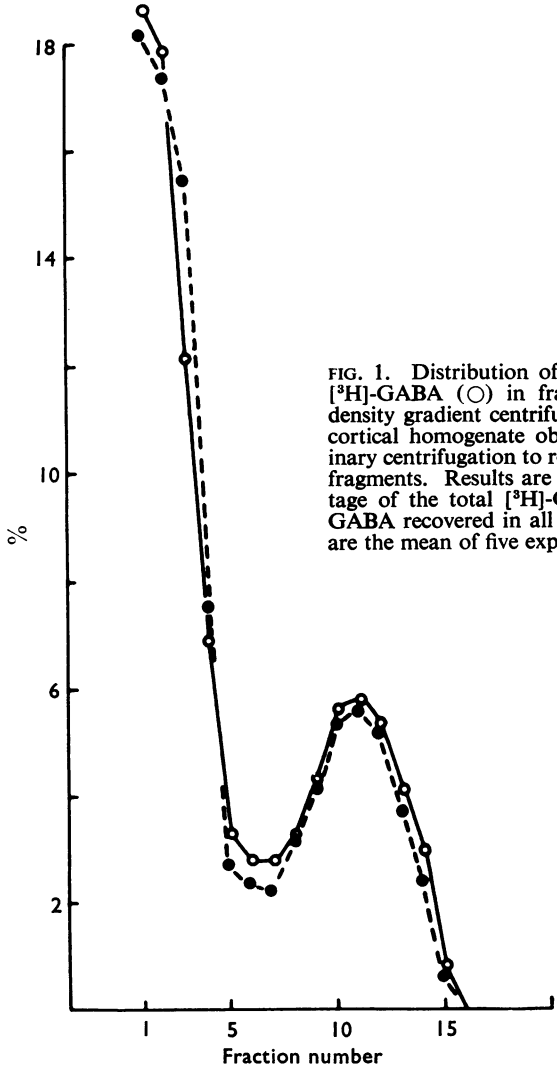

FIG. 1. Distribution of endogenous (●) and [^{3}H]-GABA (○) in fractions obtained after density gradient centrifugation of a sample of cortical homogenate obtained after a preliminary centrifugation to remove unbroken tissue fragments. Results are expressed as a percentage of the total [^{3}H]-GABA or endogenous GABA recovered in all fractions. The results are the mean of five experiments.

contained [^{3}H]-GABA and endogenous GABA. Evidence will be presented which suggests that a loss of GABA from particles occurs during subcellular fractionation procedures.

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The distribution of haloperidol in rat brain

R. J. NAYLOR* and J. E. OLLEY, *Postgraduate School of Studies in Pharmacology, University of Bradford*

Tritiated haloperidol was given intraperitoneally to male C.S.E. rats in doses having minimal (0·027 mg/kg), intermediate (0·34 mg/kg) and maximal (1·0 mg/kg) effects on locomotor activity. The animals were killed after 1 hr, preliminary experiments having shown that maximum concentration in the brain occurred at this time. The brain was dissected into the seven areas described by Glowinski & Iversen (1966) with the addition of the pineal gland, pituitary gland and cervical spinal cord.

The uptake of haloperidol in the various regions was essentially similar for all of the dose levels studied and the results for the intermediate dose are shown in Table 1. These results agree, as far as comparison is possible, with those of Janssen, Soudijn, van Wijngaarden & Dresse (1968) in the dog. Perfusion of the brain with saline before dissection did not significantly affect the results.

TABLE 1. *Uptake of haloperidol* (0·34 *mg/kg*) *into regions of the rat brain*

Area	Conc. of haloperidol μg/g of tissue	Amount of blood ml./g of tissue	Conc. of haloperidol / Amount of blood	Uptake relative to pineal gland
Pineal gland	16·55	0·1036	160	100
Striatum	0·877	0·0063	139	87
Hippocampus	0·929	0·0077	121	76
Midbrain	0·841	0·0073	115	72
Cortex	0·892	0·0080	112	70
Hypothalamus	1·311	0·0128	102	64
Spinal cord	0·639	0·0111	58	36
Cerebellum	0·886	0·0167	53	33
Medulla	0·836	0·0159	53	33
Pituitary gland	1·509	0·0744	20	13

The amount of drug available to be taken up is a function of the volume and rate of flow of blood in an area; therefore a more accurate estimate of the ability of a region to take up the drug can be made by determining the content of blood in the area using the ^{51}Cr labelled red blood cell technique (Senior, 1966). By expressing the concentration of haloperidol relative to the blood content of the area it was seen that the relatively high concentration of haloperidol in the pituitary gland may have been achieved because of its high vascularity, whereas other areas, notably the striatum, had extracted the drug more effectively from the relatively small amount passing through in the blood supply.

Pharmacologically, haloperidol is notable for its potent neuroleptic effects and its ability to influence the extrapyramidal system. Thus the general pattern of drug distribution was not surprising showing in particular the marked capacity of