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

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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

the striatum to take up the drug. The high uptake into the pineal gland, the highest in any area studied, is also worthy of notice, although this could be due to differences in the blood brain barrier in this region.

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The effects of some changes in the perfusion solution on the vasoconstrictor responses of the isolated rat mesentery preparation

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The rat isolated mesentery arterial preparation as described by McGregor (1965), perfused with Krebs solution, exhibited vasoconstrictor responses to injected noradrenaline (10 ng–500 ng) and to perimural sympathetic nerve stimulation, but did not respond to acetylcholine or isoprenaline. There was generally no response to tyramine over a wide range of doses (1 μg–1 mg); in a very small number of experiments a slight response was seen with the larger doses of tyramine.

Addition of acetylcholine ($2–20 \times 10^{-6}$ g/ml.) to the perfusate blocked the responses to perimural stimulation, an effect which was reversed by hyoscine (75×10^{-7} g/ml.), potentiated by physostigmine (1×10^{-6} g/ml.), but unchanged by hexamethonium ($0{\cdot}025–50 \times 10^{-6}$ g/ml.). Small doses of tyramine added to the perfusate enhanced adrenergic vasoconstrictor responses whilst larger doses depressed the effects of nerve stimulation. Isoprenaline (0·5–50 μg) produced inhibition of vasoconstrictor responses induced by noradrenaline (1×10^{-7} g/ml.).

Partial or total omission of calcium ions from the perfusion solution, made isotonic by the addition of sucrose, allowed the regular production of responses to tyramine. In these conditions the responses to nerve stimulation were reduced to an extent inversely related to the amount of Ca^{++} ions omitted; the responses to injected noradrenaline were not significantly altered by changes in Ca^{++} ion concentration.

The tyramine responses observed in lowered Ca^{++} ion concentrations were characterized by reduction with phentolamine and absence in rats pretreated with either 6-OH-dopamine (Thoenen & Tranzer, 1968) or reserpine (5 mg/kg subcutaneously), or after surgical denervation. The effects were blocked by cocaine (5×10^{-6} g/ml.) and were increased after pretreating the animal with nialamide (100 mg/kg intraperitoneally); in the latter case the tyramine responses were also observed during perfusion with normal Krebs solution. The omission of Mg^{++} ions from the solution induced similar responses to those of Ca^{++} ion reduction but to a lesser degree; the simultaneous omission of both ions further enhanced the magnitude of the tyramine response.

Increasing the K^+ ion concentration to twice that of normal Krebs solution enabled the demonstration of a response to tyramine.