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The effect of adrenaline on 5-hydroxyindole concentrations in the hypothalamus and thalamus of rat

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A subcutaneous injection of insulin (sufficient to induce seizures) increases the concentrations of 5-hydroxytryptamine (5-HT) and 5-hydroxyindole acetic acid (5-HIAA) in rat brain (Gordon & Meldrum, 1970) and inhibits 5-hydroxytryptophan decarboxylation in rabbit brain (Costa & Himwich, 1959).

Adrenaline is released from the adrenal medulla as a result of insulin-induced hypoglycaemia, and in the present experiments the effect of adrenaline on brain 5-HT metabolism has been observed.

Adrenaline (0.67 $\mu\text{g/g}$ subcutaneously) was administered to male Porton strain rats of 140-160 g. After intervals ranging between 30 min and 24 h, during which food and water had been withdrawn, the animals were killed by decapitation. Blood glucose and concentration of 5-hydroxyindoles in the hypothalamus and thalamus were estimated as previously described (Gordon & Meldrum, unpublished). In control experiments, adrenaline was replaced by 0.5 ml normal saline.

There was a maximal increase of 5-HT (22%) and 5-HIAA (56%) 3 h after injection. 5-HT levels returned to normal at 4 h. 5-HIAA levels were still elevated

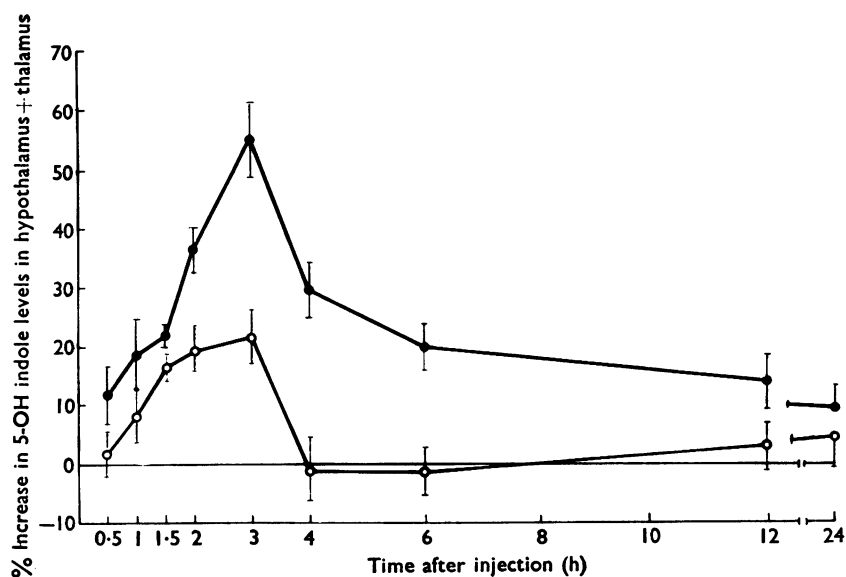


FIG. 1. Percentage increase (\pm % S.E.) in concentration of 5-HT (\circ - \circ) and 5-HIAA (\bullet - \bullet) in rat hypothalamus and thalamus after injection of 100 μg adrenaline. Number of experimental animals = 12; number of control animals = 12.

24 h after injection. The maximal increase in blood glucose levels occurred 2 h after adrenaline administration. Noradrenaline ($0.67 \mu\text{g/g}$ subcutaneously) failed to elicit any significant change in concentration of 5-HT or 5-HIAA at 3 h.

When insulin (66 i.u./kg subcutaneously) was administered to fed male rats that had undergone bilateral surgical removal of the adrenal medulla 3 weeks previously, an increase in brain 5-hydroxyindole levels, similar to that seen in non-surgically treated animals, was observed.

These results indicate (1) that adrenaline increases brain 5-HT metabolism, and (2) that the increased metabolism of 5-HT observed after insulin administration is not dependent on the secondary release of adrenaline.

I wish to thank the Wellcome Foundation for financial support.

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A comparison of the analgesia produced by morphine and the sympathomimetic drugs

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It is well established that some sympathomimetic drugs are actively analgesic in animals, but the involvement of adrenergic mechanisms in either morphine analgesia or, indeed, sympathomimetic analgesia has yet to be proved.

The effects of various drugs, known to cause changes in the amounts of nor-adrenaline and 5-hydroxytryptamine in the brain, were examined on the increase in hot-plate reaction time induced, in the mouse, by morphine sulphate (10 mg/kg) and by methylamphetamine hydrochloride (10 mg/kg). Effects of these drugs on the characteristic "stereotype" behaviour produced by methylamphetamine was also noted. The results are summarized in Table 1.

TABLE 1. *Effect of drugs on the increase in hot-plate reaction time induced by morphine sulphate, and methylamphetamine hydrochloride and on methylamphetamine "stereotype" activity*

Drug	Dose (i.p.)	Hot-plate reaction time		"Stereotype" activity methylamphetamine
		Morphine (10 mg/kg)	Methylamphetamine (10 mg/kg)	
Morphine + methylamphetamine	Various	Additive		0
Reserpine	5 mg/kg 4 h*	—	—	0 to +
Iproniazid	200 mg/kg 2 h*	0	0	0
α -methyl- <i>p</i> -tyrosine	150 mg/kg 4 h*	+	+	—
α -methyl- <i>p</i> -tyrosine + iproniazid	As above	++	++	0
5-hydroxytryptophan	75 mg/kg 10 min*	+	+	0 to +
<i>p</i> -chloro-phenylalanine	150 mg/kg twice daily for 3 days	—	—	0
5-hydroxytryptophan + <i>p</i> -chloro-phenylalanine	As above	+	+	0

—, Decrease; 0, no change; +, increase; ++, further increase. * Pretreatment.