appeared to be nonspecific, since it also often antagonized acetylcholine excitation. Bufotenin (5-hydroxy-N, N-dimethyltryptamine) and 5-methoxy-N, N-dimethyltryptamine (5-MeODMT) were more specfic in their antagonism of 5-HT.

DMT always inhibited neurones which 5-HT excited and sometimes excited neurones which 5-HT inhibited or did not affect. In decreasing order of potency, 5-MeOT, bufotenin and 5-MeODMT were able to mimic the effects of 5-HT; all were less potent than 5-HT, and appear to have some partial agonistic properties. To determine whether the 5-HT mimicking action might be due to release of 5-HT by the derivatives, 5-MeOT was applied to neurones after depletion of 5-HT stores by pretreatment with p-chlorophenylalanine or reserpine. No difference was observed in the proportion of neurones responding to 5-MeOT, indicating that 5-HT release was not involved, and that the 5-HT mimicking effects of 5-MeOT, and possibly of bufotenin and 5-MeODMT, are due to direct effects on 5-HT receptors.

These psychotomimetic drugs thus appear to be able in various ways to counteract the excitatory effects of 5-HT on brain stem neurones and this is a possible explanation of their LSD-like activities.

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Cellular localization of the uptake of 5-hydroxytryptamine in the area postrema of the rabbit after injection into a lateral ventricle

R. C. DOW, I. LASZLO* and ISOBEL RITCHIE (introduced by T. B. B. CRAWFORD)

M.R.C. Unit for Brain Metabolism, Department of Pharmacology, University of Edinburgh

The localization of the site of uptake of 5-hydroxytryptamine (5-HT) after intraventricular injection was investigated in the area postrema of the rabbit. 5-HT was injected in 100 μl of saline, or in some experiments, of artificial c.s.f., into the lateral ventricle through a guide tube inserted into the skull according to the method described by Moir & Dow (1970). Animals were killed by intravenous injection of air at different intervals after the 5-HT treatment. Noradrenaline (NA) and 5-HT were demonstrated histochemically in brain section by the method of Falck & Owman (1965) with certain modifications (Laszlo, 1972). 5-HT in brain tissue was estimated by a method using column chromatography (Eccleston, Ashcroft, Crawford & Loose, 1966).

200 μg of 5-HT after 30 min increased the background fluorescence of the area postrema to such an extent that no individual cells could be seen. 20 μg 5-HT after 30 min also produced a generalized increase in the fluorescence in the area postrema, but individual cells remained distinguishable. In summary the effect of the latter dose was: (a) an increase in the number and intensity of green fluorescent cells and of yellow fluorescent granules, (b) an increase in background fluorescence, (c) the development of green or yellow fluorescence on the dorsal surface of the area postrema, and of the rest of the brain, (d) an increase in yellow fluorescence of the ependyma of the central canal, not extending to the ventral surface of the area postrema. Treatment with pargyline (200 mg/kg I.P.) 6 h before the injection of 5-HT further increased the fluorescence in the area postrema described above. The

results of the chemical estimation also showed an increased concentration of 5-HT after treatment of the animals with the amine.

The localization of the uptake of 5-HT in the cellular population was investigated by Nissl staining after fluorescence microscopy. Glial cells identified on the basis of Nissl staining exhibited a green fluorescence after the injection of 5-HT. The results of model (droplet) experiments indicate that the colour of the formaldehyde induced fluorescence of 5-HT in a certain range of concentration is green, instead of yellow, as is usually reported. It is thus suggested that glial cells in the area postrema are capable of taking up 5-HT.

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Effect of cortisol on a central response to 5-hydroxytryptophan

SHEILA L. HANDLEY and RUTH C. MISKIN*

Department of Pharmacy, University of Aston in Birmingham, Gosta Green, Birmingham 4

It has been suggested that steroid-induced depression could be attributed to underactivity of central 5-hydroxytryptamine (5-HT) neurones, consequent on reduced 5-HT synthesis (Lapin & Oxenkrug, 1969). Cortisol activates liver tryptophan oxygenase (Thomson & Mitkuta, 1954) and hence could reduce the availability of tryptophan and/or pyridoxal phosphate (co-decarboxylase) to the brain.

Although a fall in brain 5-HT has been shown to follow a single large (5 mg/kg) dose of cortisol (Curzon & Green, 1968) no direct evidence for alteration in central tryptaminergic responsiveness has previously been obtained.

In the present experiments the 5-hydroxytryptophan (5-HTP)-head twitch response in mice (Corne, Pickering & Warner, 1963) has been used as a test of central tryptaminergic function, since the incidence of head twitches has been shown to be proportional to the amount of free 5-HT in the brain (ibid). Groups of 4 male albino mice were housed in quiet surroundings for 7 days, during which time they received the appropriate number of daily subcutaneous injections of either arachis oil (vehicle) or cortisol 75 μg/kg in arachis oil. Mice were injected with 5-HTP (180 mg/kg i.p.) 24 h after the last injection, and the number of twitches occurring in each group determined over alternate 2 min periods for up to 1 h. At least five replicates were performed for each pretreatment schedule.

The effect of cortisol depended upon the duration of pretreatment. A single dose caused a significant increase in the 5-HTP response; two daily injections had no significant effect, while 3–5 daily injections caused a progressive decline in responsiveness to 5-HTP. After five daily cortisol injections the peak 5-HTP response was only 53% of that of vehicle pretreated animals ($P<0.05$).