axis. The rates of infusion were adjusted so that the convulsive threshold was reached in about 20 min and the time course of the development of antagonism of the responses to GABA was compared with the development of convulsive activity as seen in the electrographic record of E.Co.G.

In no experiment did any clear antagonism of the effect of GABA appear before abnormal activity in the E.Co.G. became apparent. Once full seizures appeared on the E.Co.G. the pattern of firing of the cell had obviously changed and was substantially synchronized with the seizure activity. In this situation, GABA was almost completely ineffective in inhibiting cell firing, irrespective of whether bicuculline, picrotoxin or leptazol was being infused. The situation was, in fact, very similar to that found in the presence of a penicillin epileptic focus (Clarke & Hill, 1972).

In the presence of electrographic seizures, therefore, antagonism of the effect of microiontophoretically applied GABA should not be attributed solely to blockade of GABA receptors.

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The effects of methylated tryptamine derivatives on brain stem neurones

I. BRIGGS (introduced by P. B. BRADLEY)

Medical Research Council Neuropharmacology Unit, The Medical School, Birmingham B15 2TJ

Previous studies (Boakes, Bradley, Briggs & Dray, 1970) have shown that the psychotomimetic potencies of lysergic acid diethylamide (LSD 25), methysergide, and bromolysergide (BOL 148) paralleled their potencies as antagonists of the excitatory effects of 5-hydroxytryptamine (5-HT) on brain stem neurones. The effects of glutamate on neurones which 5-HT excited were also antagonized by these lysergic acid derivatives when 5-HT was blocked, but the actions of other putative transmitters were unaffected. Several methylated tryptamine derivatives possess psychotomimetic activity similar to that of LSD 25, and the effects of iontophoretic applications of four derivatives on brain stem neurones have now been investigated. The effects of these substances were complex; on some neurones the effects were similar to those of 5-HT but with a longer time course, while on others 5-HT was specifically antagonized. 5-Methoxytryptamine (5-MeOT) did not antagonize the effects of 5-HT; N, N-dimethyltryptamine (DMT) showed an antagonism that

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