These experiments on intact spinal cord tissue avoid many of the difficulties of interpretation associated with tissue slice experiments, and they demonstrate an apparently specific, and calcium dependent release of glycine and GABA when descending spinal nerve tracts are stimulated. This supports the suggestion that both glycine and GABA are synaptic transmitters in the spinal cord.

P. J. Roberts is a Medical Research Council Scholar.

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Blockade of central GABA receptors and the convulsive actions of bicuculline, picrotoxin and leptazol

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It has been shown that the depressant effects of microiontophoretically applied γ-aminobutyric acid (GABA) on feline cortical neurones can be antagonized by bicuculline or picrotoxin applied in a similar way to the same neurones (Curtis, Duggan, Felix & Johnston, 1970; Hill, Simmonds & Straughan, 1971, 1972). When given intravenously, picrotoxin and bicuculline can be shown to reduce neurally evoked inhibitions (Brooks & Asanuma, 1965; Curtis & Felix, 1971) and these observations have been used as evidence for GABA being a cortical inhibitory transmitter. Consequently, the convulsant properties of systemically administered bicuculline and picrotoxin might be largely explained by blockade of central GABA receptors with failure of neural inhibition and consequent uncontrolled discharge of excitatory pathways.

To investigate this possibility, cats were anaesthetized with nitrous oxide and halothane, paralysed with gallamine to prevent movement artifacts and artificially respired, anaesthesia being maintained throughout the experiments. Arterial acid-base balance was routinely measured and found to be within the same limits as in spontaneously breathing animals. An area of mid-suprasylvian cortex was exposed and a silver E.Co.G. electrode placed on the surface. A seven-barrelled glass micropipette containing drug solutions for iontophoresis was inserted into the same area of cortex and extracellular action potentials were recorded through one barrel. Cells were driven by continuous application of glutamate and repeated responses to GABA were obtained before, during and after a slow intravenous infusion of convulsant. In addition to infusions of bicuculline ((20 μg/min)/kg) and picrotoxin (0·15 mg), leptazol (6 mg) was also infused as a control for the other two substances, since it has been reported not to antagonize evoked inhibitions of GABA (Krnjević, Randic & Straughan, 1966) yet acts as a convulsant at a similar level in the neuro-

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

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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