The results reported in Table 1 show a statistically significant difference between the content of GABA of the cortex of the two groups of cats. No differences were found between the two hemispheres of the same cat and between the contents of glutamic acid.

These results suggest that midbrain structures influence the content of GABA of the cerebral cortex.

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The release of ^{3}H-gamma-aminobutyric acid (GABA) from rat cerebral cortex

J. F. MITCHELL, M. J. NEAL* and VASANTA SRINIVASAN, *Department of Pharmacology, University of Cambridge, England*

The status of GABA as an inhibitory transmitter in the mammalian brain remains equivocal. Although electrophysiological evidence strongly supports the suggestion that GABA is an inhibitory transmitter in the cortex (Krnjević & Schwartz, 1967), experiments performed on GABA release are less convincing. Jasper, Khan & Elliott (1966) claimed that GABA was released from the surface of the cerebral cortex and that this efflux was related to the state of activation of the brain. Efforts to reproduce these results in our laboratory have, however, been largely unsuccessful. The reason for this failure to detect appreciable changes in GABA efflux may be due to the highly efficient uptake process for GABA which is present in nervous tissue (Iversen & Neal, 1968). In order to avoid some of the difficulties of *in vivo* experiments, the release of ^{3}H-GABA from brain slices has been studied.

Slices of cerebral cortex (1 mm thick) were incubated with GABA-2,3-^{3}H (specific activity=2 c/m-mole, 0.2 μc/ml.) at 37° C in 20 ml. of oxygenated Krebs-bicarbonate Ringer containing amino-oxyacetic acid (10^{-5}M) to inhibit the metabolism of GABA. The tissue was perfused in a small vessel (volume 0.5 ml.) at a rate of 0.5 ml./min. Aliquots (0.2 ml.) of the perfusate were removed every 2 min and the radioactivity was measured by liquid scintillation counting.

The spontaneous release of ^{3}H-GABA from cerebral cortex was multiphasic with at least two major components. A rapid initial phase ($t_{\frac{1}{2}} \approx 2$ min), which presumably represented extracellular washout, was followed by a much slower release of ^{3}H-GABA ($t_{\frac{1}{2}} \approx 30$ min). Depolarization of the nerve tissue by mild electrical stimulation (rectangular pulses, 100/sec, 2 mA for 30 sec) or by Krebs medium with a high potassium concentration (40 mM) produced a striking increase in ^{3}H-GABA efflux (Fig. 1). The effect of electrical stimulation was not prevented by the absence of calcium ions in the medium. The increase in GABA efflux produced by high potassium was, however, significantly lower in the absence of calcium ($P<0.05$). The increased efflux of GABA was not a non-specific effect on the cell membrane as both these methods of stimulation failed to cause an increased release of ^{14}C-urea or ^{3}H-L-leucine from cortical slices.

The present experiments suggest that if GABA is an inhibitory transmitter in the brain it appears to use an unconventional release mechanism, because all known neurotransmitters require the presence of calcium ions for their release by electrical stimulation.

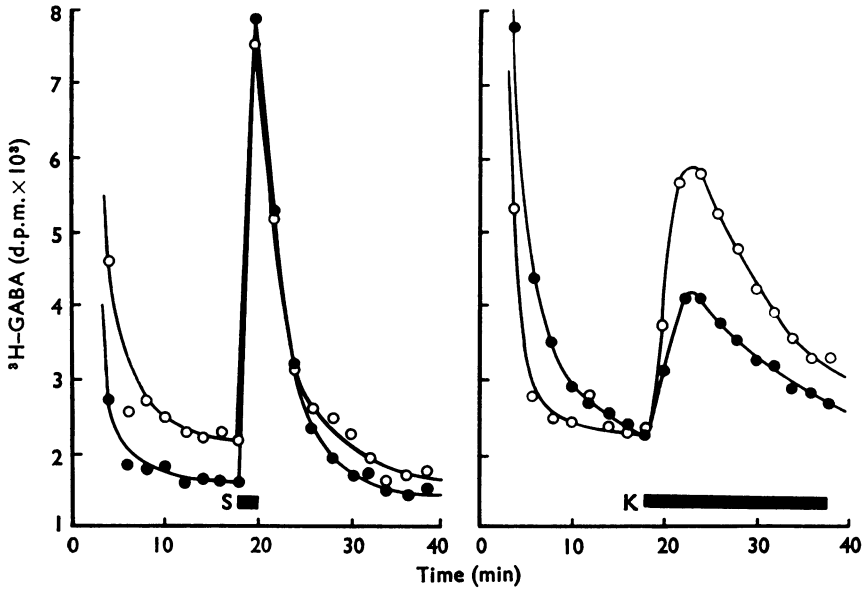

FIG. 1. Effect of electrical stimulation (S) and high potassium (K) on the efflux of ^{3}H-GABA from brain slices in normal (○) and in calcium-free (●) medium. Each point is the mean of seven results.

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5-hydroxytryptamine and 5-hydroxyindoleacetic acid in rat brain: effect of some psychotropic drugs and of electrical stimulation of various forebrain areas

E. GIACALONE and W. KOSTOWSKI*†, *Mario Negri Institute for Pharmacological Research, Milan, Italy*

In chronically implanted, unrestrained rats the following centres were stimulated: dorsal hippocampus, frontal and piriform cortex, striatum (putamen-caudatus), anterior hypothalamus and medial thalamus. 5-Hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were determined in ipsilateral and contralateral parts of forebrain as well as in the brain stem. An increase of 5-HIAA concentration was observed after stimulation but 5-HT remained unchanged or even slightly decreased. The most marked increase of 5-HIAA occurred in both parts of forebrain and to a lesser extent in brain stem after stimulation of dorsal hippocampus.

During stimulation, inhibition of motor activity, tremor, upright posture and salivation were observed. Chlorpromazine completely blocked the increase of forebrain 5-HIAA as well as the behavioural effects induced by stimulation of the dorsal hippocampus (see Table 1).