The actions of GABA on d.c. and field potential recordings from the rat cuneate nucleus

R.G. HILL*, J. HORNBY & F. ROBERTS

Department of Pharmacology, University of Bristol, University Walk, Bristol BS8 1TD

GABA is thought to be a presynaptic inhibitory transmitter in mammals largely because the GABA antagonists picrotoxin and bicuculline block presynaptic inhibition (Eccles, Schmidt & Willis, 1963; Levy, Repkin & Anderson, 1971). The present experiments are an attempt to demonstrate that exogenous GABA will enhance or mimic presynaptic inhibition, as previous attempts to do this have only been partially successful (Curtis & Ryall, 1966; Schmidt, 1971).

Experiments were performed on 20 rats prepared as described previously (Collins, Hill & Roberts, 1975). In addition, d.c. potentials were recorded from a micropipette inserted into the cuneate nucleus. The exposed dorsal surface of the medulla was continuously superfused with a Krebs bicarbonate solution to which solutions of amino acids were added. Changes in the N- and P-waves of the cuneate field potential were measured from computer averaged records.

GABA (0.01-0.5 M) in the superfusion solution reduced the size of the N-wave and increased the size of the P-wave (Figure 1). This was dose-related and approximately linear over the range 0.02-0.1 M. Microiontophoretic application of GABA (25-150 nA) produced similar changes in the field potentials. A negative d.c. shift coincided with the increase in the P-wave (Figure 1) and this was also dose-related. The GABA-evoked d.c. shift increased with depth in the medulla reaching a maximum at about the inversion point of the P-wave, and declining thereafter without inversion. This maximum coincides with the greatest density of primary afferent terminals within the cuneate and the d.c. shift may thus be a reflection of the depolarization of these terminals associated with the generation of the P-wave (Andersen, Eccles, Schmidt & Yokota, 1964). Replacement of Ca^{++} in the Krebs solution with 20 mM Mg^{++} and 0.5 mM EGTA attenuated the synaptically evoked field potential (<40% control) but did not reduce the d.c. shift suggesting that GABA may be acting directly rather than transynaptically.

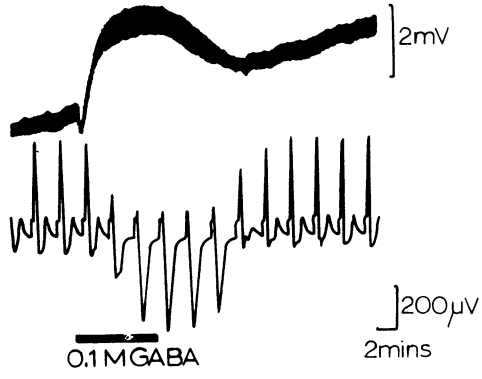

Figure 1 D.c. (upper) and computer averaged (16 sweeps) field potential records (lower) from rat cuneate nucleus in response to electrical stimulation of the ipsilateral forepaw. Application of GABA produced a negative d.c. shift accompanied by a decrease in the size of the N-wave and an increase in the P-wave. Negativity upwards in both records.

Although these results support the idea that GABA could be a presynaptic inhibitory transmitter this is not conclusive as glycine, β-alanine and taurine have been found to produce similar field potential and d.c. changes in the cuneate nucleus.

This work is supported by a grant from the M.R.C.

References

ANDERSEN, P., ECCLES, J.C., SCHMIDT, R.F. & YOKOTA, T. (1964). Depolarization of presynaptic fibres in the cuneate nucleus. *J. Neurophysiol.*, **27**, 92-106.

COLLINS, J.F., HILL, R.G. & ROBERTS, F. (1975). A study of tetramethylenedisulphotetramine (TETS) and related compounds as antagonists of presynaptic inhibition and microiontophoretically applied γ-aminobutyric acid (GABA) and glycine in the rat cuneate nucleus. *Proc. Br. Pharmacol. Soc.*, March 1975.

CURTIS, D.R. & RYALL, R.W. (1966). Pharmacological studies upon spinal presynaptic fibres. *Exp. Brain Res.*, **1**, 195-204.

ECCLES, J.C., SCHMIDT, R.F. & WILLIS, W.D. (1963). Pharmacological studies on presynaptic inhibition. *J. Physiol (Lond.)*, **168**, 500-530.

LEVY, R.A., REPKIN, A.H. & ANDERSON, E.G. (1971). The effect of bicuculline on primary afferent terminal excitability. *Brain Res.*, **32**, 261-265.

SCHMIDT, R.F. (1971). Presynaptic inhibition in the vertebrate central nervous system. *Ergebn. Physiol.*, **63**, 21-101.