References

DENT, J.G. & JOHNSON, P. (1974). *Solubilisation of mammalian tissue for scintillation counting in Liquid Scintillation Counting.* Vol. 3, eds. Crook, M.R. & Johnson, P. Heydén: London.

IVERSEN, L.L. & NEAL, M.J. (1968). The uptake of [^{3}H]GABA by slices of rat cerebral cortex. *J. Neurochem.*, **15**, 1141–1149.

LEACH, M.J., RIDDALL, D.R. & WINKLEY, C.M. (1976). Uptake of L-2,4-diamino[4-^{3}H]butyric acid into slices of rat cerebral cortex: Effect of slice size. *J. Neurochem.*, **27**, 1281–1282.

LEVI, G. & RAITERI, M. (1973). Detectability of high and low affinity uptake systems for GABA and glutamate in rat brain slices and synaptosomes. *Life Sci.*, **12**, 81–88.

RIDDALL, D.R., LEACH, M.J. & DAVISON, A.N. (1976). Neurotransmitter uptake into slices of rat cerebral cortex *in vitro:* Effect of slice size. *J. Neurochem.*, **27**, 835–839.

Prolongation of post-synaptic inhibition by barbiturates

C.N. SCHOLFIELD[1] (introduced by D.A. BROWN)

Department of Pharmacology, The School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX

When slices of guinea-pig olfactory cortex are incubated *in vitro* and the lateral olfactory tract (LOT) is stimulated the evoked excitatory post-synaptic potential (EPSP) recorded within the mono-synaptically-innervated neurones is followed by an inhibitory post-synaptic potential (IPSP). This IPSP is manifest by a large conductance increase and a small depolarization at the normally-recorded resting membrane potential of −76 mV (Scholfield, 1976). The present report concerns a unique and substantial prolongation of this IPSP by barbiturates.

Surface slices of guinea-pig olfactory cortex were maintained in a superfusing stream of Krebs solution at 25°C bubbled with 95% oxygen/5% carbon dioxide, and neurones in the prepyriform cortex were impaled with glass microelectrodes filled with K acetate as described previously (Scholfield, 1976). Extracellular surface potentials were monitored with a saline-filled microelectrode. The LOT input was stimulated at < 1 min intervals.

Sodium pentobarbitone (100 μM) increased the time to half-decay of the post-synaptic inhibitory conductance from 0.17 ± 0.04 to 1.68 ± 0.22 s (mean ± s.e. mean, 5 slices). The apparent reversal potential for the IPSP (initially −70 to −69 mV) shifted some 10 mV in the depolarizing direction during the course of the individual barbiturate-prolonged IPSP. Spikes were not generated during this prolonged depolarization.

The initial EPSP, spike potential and resting input resistance and time constant were unchanged below 200 μM pentobarbitone. At higher concentrations input resistance fell substantially, the membrane depolarized towards −60 mV and all synaptic potentials were depressed.

During a train of LOT stimuli the second EPSP is shunted by the IPSP and fails to generate a spike, but subsequently recovery normally ensues such that repetitive EPSP-spike combinations result (Scholfield, 1976). In contrast, pentobarbitone not only prevented recovery but intensified EPSP depression during repetitive LOT stimulation. This accords with previous observations made with extracellular electrodes (Scholfield & Harvey, 1975).

Effects of pentobarbitone within the range 20 μM–1 mM could be replicated by phenobarbitone (0.2–5 mM). In contrast procaine (2–10 mM) simply attenuated the spike and depressed all post-synaptic potentials. This confirms the previously-drawn (Scholfield & Harvey, 1975) distinction between the actions of barbiturates and local anaesthetics on synaptic processes in this preparation.

The present results accord with observations in other parts of the CNS *in vivo*, such as those of Nicholl, Eccles, Oshima & Rubia (1975). Since selective potentiation of the IPSP occurs at concentrations within or below the range expected during anaesthesia, such an effect may contribute to the actions of barbiturates *in vivo*.

This study was supported by a grant from the Medical Research Council.

[1] Present address: Department of Physiology, The Queens University of Belfast, 97 Lisburn Road, Belfast, BT9 7BL.

References

NICOLL, R.A., ECCLES, J.C., OSHIMA, T. & RUBIA, F. (1975). Prolongation of hippocampal inhibitory postsynaptic potentials by barbiturates. *Nature, Lond.*, **258**, 625–627.

SCHOLFIELD, C.N. (1976). A depolarizing inhibitory post-synaptic potential in mammalian brain slices. *J. Physiol., Lond.* (in press).

SCHOLFIELD, C.N. & HARVEY, J.A. (1975). Local anaesthetics and barbiturates: effects on evoked potentials in isolated mammalian cortex. *J. Pharmac. exp. Ther.*, **195**, 522–531.