citation of Renshaw cells as well as the excitations of these cells produced by NMDA, L-glutamate and L-aspartate. Here we report that in pentobarsbitone anaesthetized cats D-AA also depresses ACh-induced responses of Renshaw cells to some extent, but D-AA has little if any such action. This latter agent thus emerges as the most specific amino acid antagonist yet reported. Most importantly, D-AA blocks the DHβE-insensitive synaptic excitation of Renshaw cells evoked by dorsal root stimulation while having little or no effect on DHβE-sensitive excitation of these cells evoked by ventral root stimulation. This finding strongly suggests that synaptic excitation of Renshaw cells other than via the cholinergic motor axon collateral pathway is mediated by an excitatory amino acid. It is more likely that this amino acid is L-aspartate than L-glutamate.

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A potentiation of inhibition by various anaesthetics in the isolated olfactory cortex

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With intracellular recordings from neurones in the isolated olfactory cortex, stimulation of the presynaptic lateral olfactory tract evokes an excitatory post-synaptic potential (EPSP) generating a single action potential, followed by an inhibitory post-synaptic potential (IPSP). In this preparation, the IPSP is manifest as a long, low amplitude depolarization accompanied by a large increase in membrane conductance (Scholfield, 1976). Pentobarbitone produces a substantial increase in the duration of this IPSP (Scholfield, 1977). The present report extends this study to several other anaesthetics.

Surface slices (600 μm thick) of guinea-pig olfactory cortex were superfused with Krebs solution at 25°C. Neurones in the prepyriform cortex were impaled with K^+ acetate filled micro-electrodes connected to an amplifier with a current source and a facility for electrode resistance and capacity neutralization. Membrane resistance (R_m) was monitored during the IPSP by passing brief current pulses into the cell. Anaesthetics were added to the superfusate for 30 min periods.

The anaesthetics studied could be placed into three groups on the basis of their actions on the synaptic potentials:

1. Alphaxalone (0.2–50 μM), methohexitone (1–100 μM), chloralose (5–500 μM), pentobarbitone (0.02–1 mM) and phenobarbitone (0.1–5 mM) had the most potent actions. They all produced substantial prolongations of the IPSP at the lowest concentrations (about ten-fold increases at intermediate concentrations). The EPSP appeared to be unaffected at lower concentrations. At higher concentrations, the resting R_m was reduced and the membrane depolarised a few mV as with pentobarbitone (Scholfield, 1977). This had a secondary effect of attenuating the EPSP.
2. The general anaesthetics which had less potent actions were halothane (0.1–5.0 mM), ketamine (0.1–2 mM) and urethane (10–100 mM). At the lower concentrations they increased the duration of the IPSP by about two-fold. In spite of the modest potentiation of the IPSP, functional inhibition was markedly increased as judged by the diminished EPSPs after trains of stimuli. At intermediate concentrations, there was a depression of both the EPSP and IPSP. At the highest concentrations of halothane and ketamine, the synaptic potentials were absent and the action potentials were attenuated and increased in duration (presumably a local anaesthetic action). Halothane and urethane had no action on resting membrane potential (E_m) and R_m. Ketamine increased R_m about two-fold at 0.5–1.0 mM.

3. Lignocaine (0.02–6.0 mM) was used to assess local anaesthetic actions. Lignocaine only depressed the IPSP and the EPSP (at 0.2–0.6 mM) and depressed the action potential at 0.9–6.0 mM. E_m and R_m were anaffected.

All these general anaesthetics appear to prolong inhibition at the lower concentrations and this is likely to produce anaesthesia *in vivo*. With halothane, ketamine and urethane the depression of the EPSP probably contributes to the anaesthetic action.

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Effect of vasoactive intestinal peptide (VIP) and other neuropeptides on cAMP accumulation in brain slices

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Various peptides may act as neurotransmitters or neuromodulators in the central nervous system; these include substance P, neurotensin, vasoactive intestinal peptide (VIP), the hypothalamic releasing factors and the enkephalins and endorphins. Recent findings have demonstrated the selective distribution of such peptides in brain, their localization in nerve terminals and their release from such terminals. The postsynaptic actions of a number of neurotransmitters seem to be mediated through cAMP or cGMP (Greengard, 1976). Furthermore, several of the peptides listed above have been reported to stimulate adenylate cyclase activity (Duffy, Wong & Powell, 1975; Robberecht, Conlon & Gardner, 1976). Therefore, a number of peptides, reported to be present in relatively high concentrations in specific rat brain regions, were examined to determine their effect on cAMP and cGMP accumulation in slices of various regions of rat brain and on cell free adenylate cyclase activity in homogenates.

Substance P, luteinizing hormone releasing factor, thyrotropin releasing factor, somatostatin, neurotensin and glucagon at concentrations up to 100 μM were without effect on any of these tests in a number of brain regions. When slices (prepared according to the method of Forn, Kreuger & Greengard, 1974) from these same brain regions were incubated in the presence of VIP (0.5 μM), however, a statistically significant increase (40 to 100% over basal) in the accumulation of cAMP was observed. There were no changes in cGMP levels and no increase in cAMP was seen in cerebellar slices. A small increase in cell free adenylate cyclase activity could be demonstrated in the presence of VIP (0.5 μM). When slices were incubated in the presence of the phosphodiesterase inhibitor isobutylmethylxanthine (2 mM) a three to six fold increase in basal levels of cAMP was observed but VIP was able to elicit a further increase in cAMP, indicating that its effects on cAMP accumulation are probably due to activation of adenylate cyclase. The increase in cAMP in tissue slices by VIP was diminished in media lacking calcium or media containing high calcium concentrations (4.0 mM). When tissue slices were incubated in the presence of VIP and the antagonist drugs propranolol (10 μM), phenoxybenzamine (50 μM), α-flupenthixol (1 μM), fluphenazine (50 μM) and naloxone (1 μM), no alterations in the VIP induced increase in cAMP were observed. Furthermore, when VIP was incubated in the presence of a variety of compounds which stimulate cAMP formation, dopamine (100 μM), noradrenaline (10 μM), prostaglandin E_1 (5 μM), morphine (1 μM), isoprenaline (1 μM) or adenosine (50 μM) the VIP induced increase in cAMP levels was additive to that caused by each of these agents.

These results further support a role for VIP as a neurotransmitter or neuromodulator in the central nervous system and suggests that, as in the periphery, its central actions may be mediated through an adenylate cyclase/cAMP system.

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