Table 1 The mean relative potencies ± s.e. mean are given for a series of glutamate analogues and related compounds for their excitatory effects on Retzius cells of *Hirudo medicinalis*. The results are the mean of at least five experiments. The standard dose of glutamate was normally in the range 10–100 nmol. D indicates that the compound is inactive and also desensitizes the receptors to glutamate

Agonist	*Equipotent Molar Ratio (EPMR)*	*± s.e. mean*
L-Glutamic acid	1.1	
D-Glutamic acid	25.5	2.1
(±) 4-Fluoro-glutamic acid	1.13	0.19
DL-α-Methylglutamic acid	1.3	0.14
(±)-β-Methylglutamic acid	D	
(±)-γ-Methylglutamic acid	2.38	0.76
(±)-β-Phenylglutamic acid	> 1000.0	
DL-N-Methylglutamic acid	> 1000.0	
DL-α-Aminoadipic acid	9.3	1.5
DL-α-Aminopimelic acid	D	
L-α-Aminosuberic acid	Inactive	
L-Aspartic acid	11.2	1.7
N-Methyl-DL-aspartic acid	> 1000.0	
DL-Homocysteic acid	0.25	0.04
L-Cysteine sulphuric acid	68.0	13.6
3-Aminopropylphosphonic acid	Inactive	
Quisqualic acid	0.009	0.001
Kainic acid	0.0056	0.001
Ibotenic acid	0.95	0.16

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Specific antagonism of amino acid-induced and dorsal root evoked synaptic excitation of Renshaw cells

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Evidence suggesting that acidic amino acids function as transmitters at excitatory synapses in the mammalian CNS would be considerably strengthened by the discovery of specific blocking agents for this type of putative transmitter. Agents are required which differentiate not only between amino acid and non-amino acid mediated excitation but, ideally, also between excitation mediated by L-glutamate and L-aspartate. Several agents have recently been discovered which, in addition to depressing synaptic activity, specifically block the actions of N-methyl-D-aspartate (NMDA) without reducing responses to kainate (Biscoe, Davies, Dray, Evans, Francis, Martin & Watkins, 1977). These two potent amino acid excitants have been suggested to act as selective agonists for L-aspartate and L-glutamate receptors, respectively (Johnston, Curtis, Davies & McCulloch, 1974). The NMDA-blocking agents, which include HA-966, α,ε-diaminopimelic acid (DAPA), D-α-aminoadipate (D-AA) and Mg^{2+} also depress L-aspartate-induced responses more than L-glutamate-induced responses, while exerting little or no effect on depolarizing responses to Substance P, carbachol or noradrenaline in isolated tissues. However, both HA-966 (Curtis, Johnston, Game & McCulloch, 1973) and Mg^{2+} (Davies & Watkins, 1977) depress ACh-induced ex-

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.