Two methods of stimulation were used, namely gross stimulation of the medial olfactory tract (MOT) using a bipolar silver balled electrode (0·5 ms pulses, 6 mA and 25–50 Hz), and more specific stimulation of the lateral olfactory tract (LOT) using a concentric bipolar electrode placed stereotaxically (0·2 ms pulses, 0·3 mA and 20–50 Hz). Using these parameters, stimulation for periods of 7 min (10 min collection periods) caused increases in the efflux of 'NA' (50%) and 'GABA' (40%) greater than in the preceding period. The ratio of labelled NA to labelled metabolites at rest (65–70% to 35–30%) was not significantly altered by stimulation. Metaraminol (10^{-4}M) had little effect on the resting efflux of 'NA', but significantly increased the size of the stimulation release (3 experiments, $P<0.01$ paired t-test).

Since the neurally evoked increase in the release of both 'NA' and 'GABA' was calcium-dependent and not accompanied by increase in release of the marker substances ^{3}H-inulin and ^{14}C-urea, the process appears to be specific.

Characteristically, the stimulated increases in release of both 'NA' and 'GABA' did not coincide with, but followed the period of stimulation. However, in experiments with labelled NA and lesions of the olfactory tracts caudal to the stimulating electrode, MOT stimulation induced release which coincided with the period of stimulation, and release was significantly larger than in non-isolated bulbs (5 experiments, $P<0.01$ paired t-test). These results suggest that normally some distant inhibitory influence may be responsible for delaying 'NA' release in response to tract stimulation.

In addition, the present experiments provide some evidence for a noradrenergic link in the neurally evoked release of GABA by olfactory tract stimulation. Thus the addition of cold NA (7×10^{-5}M) to the cup fluid in the presence of a high concentration of metaraminol (5×10^{-4}M) resulted in an increase in the spontaneous release of 'GABA', but not 'NA' or ^{14}C-urea. The increased release of 'GABA' which follows neural stimulation or addition of cold NA has not so far been consistently blocked by α-adrenoceptor antagonists (phentolamine 10^{-4}M; tolazoline 10^{-4}M). This is difficult to reconcile with iontophoretic studies which suggest that such antagonists should be effective (Salmoiraghi, Bloom & Costa, 1964).

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Chronic dorsal root section on free amino acid levels in the rabbit spinal cord

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Studies of the distribution of amino acids in the cat spinal cord (Graham, Shank, Werman & Aprison, 1967; Johnston, 1968) have implicated glutamate as the neurotransmitter at first sensory synapses, and aspartate and glycine as interneuronal transmitters. The effects of these amino acids applied iontophoretically are in accordance with these suggestions (Curtis & Watkins, 1960). In order to gain further information about the possible involvement of amino acids in spinal cord neurotransmission, we have studied the effect of chronic dorsal root section (DRS) on the gross levels of free amino acids in the spinal cord of the rabbit, since DRS should result in degeneration of primary afferent pathways and a reduction in associated transmitter substances.

C. C. J. and C. J. S. were M.R.C. scholars.

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The experimental procedure was as follows. Dorsal roots L6 to S2 were sectioned under halothane anaesthesia in 6 animals. In a further 4 animals (mock operated), the cord was exposed but the roots left intact. After a recovery period of 6 days, appropriate electromyograms were recorded to ensure that dorsal root pathways were functional in control animals but not in DRS animals, and that no gross cord damage had resulted from the surgical procedures. The animals were then killed by cervical fracture and the spinal cord vasculature perfused with ice-cold saline via the thoracic aorta. The deafferented cord was then removed together with an additional section from L2–L5. These were extracted separately in trichloracetic acid (10%) and analysed on a Technicon automatic amino acid analyser. Control experiments were performed to determine the reproducibility of the extraction and analysis procedures and histological studies confirmed degeneration after DRS.

Amongst the 17 amino acids studied, eleven were found to have a significantly higher concentration in the lower, as compared with the upper, section of the cord of mock operated control animals. Such a distribution is compatible with the greater proportion of grey matter in the lower part of the cord where substances with a neurotransmitter role would have a relatively higher concentration. However, only two amino acids, aspartate and cystathionine, were significantly ($P<0.05$) reduced (48% and 51% respectively) by DRS. Although glutamate and GABA levels were substantially reduced (26% and 36% respectively), these changes were not significant. Glycine was little affected (+4·9%). In interpreting these results it should be noted that small changes in the concentration of a given neurotransmitter amino acid following DRS may be masked by high endogenous levels of that substance subserving some other purposes.

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A method for the induction of dependence to ethanol in mice

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If ethanol dependence is to be shown to obey normal pharmacological criteria of tolerance and dependence, then an experimental model must be available. For many years investigators have concentrated upon developing techniques for inducing ethanol preference in laboratory animals, although withdrawal signs do not appear consistently on cessation of drinking (Myers & Veale, 1971).

We have now developed a model based on the inhalation of ethanol vapour alone which consistently produces ethanol tolerance and dependence in mice.

Groups of thirty male mice (18–22 g) were exposed to increasing concentrations of ethanol in the inspired air for 7–10 days. The ethanol concentration in inspired air was measured by gas liquid chromatography using polyethylene glycol 20 m 20% with chromosorb 101 80–100 on a 9 ft glass column, and was increased from 15–25 mg/l. initially to a final level of 40–60 mg/l. after ten days. Ambient temperature was maintained at 27° C±1° C to prevent hypothermia. At intervals throughout the induction of dependence, blood and brain ethanol and acetaldehyde levels were measured (Duritz & Truitt, 1964). Brain ethanol levels were found to be closely related to blood levels, which rose gradually throughout the experiment. A representative group of thirty mice had 150±30 mg of ethanol/100 ml of blood on day 2 to 400 mg±40 mg ethanol/100 ml blood on day 10.