Chronic administration of acetaldehyde to mice: behavioural and biochemical similarities with chronic ethanol administration

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Acetaldehyde has been implicated by many workers in some of the pharmacological effects of ethanol, and recent theories ascribe an important role to acetaldehyde in ethanol dependence (Truitt & Walsh, 1971). If acetaldehyde formed from ethanol is responsible for the development of dependence on ethanol, then chronic administration of acetaldehyde alone should produce dependence of an ethanol type. Also, biochemical changes similar to those associated with ethanol dependence should be produced by acetaldehyde administration if they play some part in the production of dependence.

Griffiths, Littleton & Ortiz (1973a, b) reported that chronic administration of ethanol to mice by inhalation produces ethanol dependence, as shown by tolerance and a recognizable withdrawal syndrome, and also changes in brain catecholamine concentrations. We now report that chronic administration and withdrawal of acetaldehyde by inhalation will produce similar behavioural and biochemical changes. The methods were those described by Griffiths, Littleton & Ortiz (1973a, b).

Groups of male white mice were exposed to ethanol or acetaldehyde vapour for 10 days. Ethanol concentrations were increased from about 10 mg/l on the first day to about 25 mg/l on the last day. Acetaldehyde concentrations were increased from about 1 mg/l on the first day to about 4 mg/l on the last day of acetaldehyde administration. After 10 days' ethanol or acetaldehyde was withdrawn and behavioural changes assessed. At intervals mice were killed and blood and brain ethanol, and acetaldehyde concentrations, or brain catecholamine concentrations, were measured.

Concentrations of acetaldehyde in blood were similar in ethanol treated and acetaldehyde treated mice. Brain acetaldehyde concentrations were apparently higher in the ethanol treated group. Mice showed no increase in the rate of elimination of acetaldehyde from blood during chronic acetaldehyde administration. After withdrawal of acetaldehyde, blood and brain acetaldehyde concentrations fell to control levels within about 20 min, whereas the corresponding period for ethanol withdrawn mice was about 3 hours. The withdrawal syndromes for ethanol and acetaldehyde were similar, except that the syndrome of acetaldehyde withdrawal was shorter and more intense; and there was some degree of cross dependence. The changes in brain catecholamine concentrations, reported previously during chronic ethanol administration and withdrawal, were also shown by mice receiving acetaldehyde, although the time course of these changes during withdrawal was much shorter.

It is thought that these results suggest that acetaldehyde may play some part in the behavioural and biochemical changes associated with ethanol dependence.

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Hypothermia produced by inhibitors of catecholamine biosynthesis

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Although there is little doubt that peripheral noradrenaline (NA) turnover is increased by cold stress, there is disagreement on the extent to which central NA turnover is altered. It has been reported that brain NA depletion is more rapid after inhibition of catecholamine biosynthesis in the rat when the animals are kept in a cold environment (Gordon, Spector, Sjoerdsma & Udenfriend, 1966) and this has been adduced as evidence for an increased central NA turnover. Others (e.g., Simmonds & Iversen, 1969) have found no increase in [^{3}H]-NA elimination from