

Behavioural changes induced in mice following termination of ethanol administration

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The difficulty of assessing the efficacy of drugs in the treatment of ethanol dependence has been hindered by the lack of a suitable model. Experiments are described in which male T/O mice weighing 23-25 g receive ethanol orally or in vapour form. In the oral dosing experiment mice are on each of four successive days given intragastric injections of increased doses of ethanol (4, 5, 6 and 7 g/kg). Ethanol is administered as 40% w/v diluted with distilled water from 96% v/v.

The method used to expose the mice to ethanol vapour is similar to that described by Goldstein & Pal (1971) except that no alcohol dehydrogenase inhibitor (pyrazole) is given. Air is drawn through Perspex boxes at 2 l./minute. Ethanol (96% v/v) is metered into the air flow to give a vapour concentration of 20 mg/litre. This flow is continued for 8-14 days.

At the end of each treatment mice are grouped in fives and coloured to facilitate counting. Individual mouse head-twitch scores are recorded for periods of four minutes. Characteristic ethanol-withdrawal head-twitches are observed which reach a peak intensity about 12 h after blood ethanol concentrations fall to zero. Head-twitches were described by Corne & Pickering (1967) to occur in mice following the acute administration of hallucinogens.

'Grimaces' described by Goldstein could be induced, about 6 h after termination of ethanol vapour, by handling the mice but in our experiments there is a high incidence of this type of behaviour in control mice.

Analysis for significant differences between control and ethanol-treated animals is carried out on a quantal basis or using individual scores and the Mann-Whitney 'U' test.

REFERENCES

- CORNE, S. J. & PICKERING, R. W. (1967). A possible correlation between drug-induced hallucinations in man and a behavioural response in mice. *Psychopharmacologia (Berl.)*, **11**, 65-78.
GOLDSTEIN, D. B. & PAL, N. (1971). Alcohol dependence produced in mice by inhalation of ethanol; grading the withdrawal signs. *Science*, **172**, 288-290.

An *in vivo* method for studying release of putative neurotransmitters from the rabbit olfactory bulbs

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A modified cortical cup technique (Mitchell, 1963) has been used to study release of the putative neurotransmitters noradrenaline (NA) and γ -aminobutyrate (GABA) (Muckart, 1971).

Essentially the method involves incubating the bulbs with Krebs solution containing either radioactive (\pm)-NA (7- ^3H or methylene- ^{14}C) and marker (^{14}C -urea or ^3H -inulin), or radioactive GABA (2,3- ^3H) and ^{14}C -urea, or radioactive GABA and radioactive NA, together with appropriate additives to reduce NA and GABA breakdown (ascorbic acid 20 mg/l., EDTA 10 mg/l., amino-oxycetic acid 10^{-5}M). Following this incubation, the efflux of radioactivity is measured by liquid scintillation counting. Labelled NA and its metabolites were separated by ion-exchange chromatography in some experiments. In other experiments the total counts attributable to the original labels were measured i.e. 'NA' and 'GABA'.