from ethanol for assessment of the ethanol withdrawal syndrome.

The significant changes in several central amino acid concentrations which occur, will be described in detail elsewhere. In the context of this communication, the most interesting finding was that the concentration of tyrosine in brain showed a steady rise during ethanol administration with a time course which preceded that of the catecholamine accumulation reported previously. Since Wurtman, Larin, Mostafapour & Fernstrom (1974) have shown that brain tyrosine concentration directly influences the synthesis of catecholamines, it seems likely that the cause of catecholamine accumulation may be the increased concentration of tyrosine. The source of this increase in tyrosine is unknown but the second part of this investigation suggests that it may be a consequence of liver dysfunction induced by ethanol administration.

Liver triglyceride accumulation showed a striking similarity in time course with the intensity and duration of the withdrawal syndrome. About 6 days of ethanol administration are required before significant changes occur, the changes reach a maximum after 8 or 9 days. In female mice hepatic triglyceride accumulation is slower and these animals are correspondingly resistent to induction of dependence. This somewhat unexpected evidence that liver dysfunction may be directly related to the induction of ethanol dependence, may be linked with the changes in catecholamine metabolism discussed earlier. Preliminary experiments suggest that livers showing evidence of triglyceride accumulation have a reduced capacity for uptake of monoamine precursors.

In conclusion, we believe that liver dysfunction may influence central catecholamine metabolism by an alteration in the handling of catecholamine precursors. Such a mechanism has already been proposed (Knell, Davidson, Williams, Kantameni & Curzon, 1974) to explain changes observed in hepatic encephalopathy. We suggest that functional liver damage is not merely a secondary pathological finding associated with alcoholism but that it contributes directly to the central disease process.

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Are central cholinergic pathways involved in the habituation of exploration and distraction?

SANDRA E. FILE (introduced by M.J. NEAL)

Department of Pharmacology, The School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX

Carlton (1968) has suggested that a central muscarinic cholinergic system is essential for habituation of exploration. He exposed rats injected with scopolamine to a novel environment, but based his conclusions on their performance the following day when they were untreated. The results could be due to state-dependent learning (Overton, 1966) rather than to scopolamine preventing habituation. The purpose of the present study was to test whether muscarinic systems in the brain are involved in long-term habituation of exploration and distraction.

The effects of three muscarinic antagonists on habituation of exploration were tested in a holeboard with four holes, under which objects could be placed (File & Wardill, 1975). Exploration was measured by the frequency (head-dips/10 min) and duration of head-dipping(s). Ten minute trials were given, separated by 24 hours.

As illustrated in Figure 1, when objects were present, scopolamine hydrobromide (1 & 2 mg/kg i.p.) increased exploration in rats ($P < 0.01$) and the duration of head-dipping habituated over trials

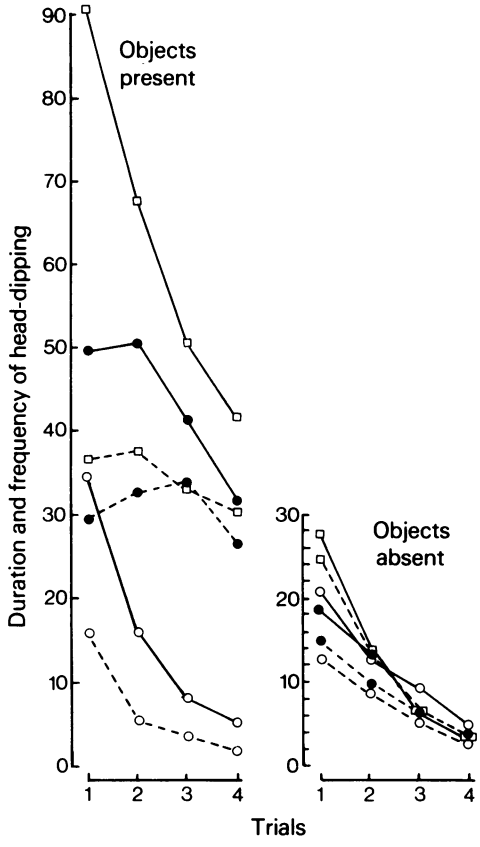

Figure 1. The frequency (- - - -) and duration (——) of head-dipping, in the presence and in the absence of objects, for rats injected with saline (○) or scopolamine, 1 mg/kg (●) or 2mg/kg (□). Each point is the mean from 10 animals. Four 10 min trials were given at intervals of 24 hours.

($P < 0.001$). The frequency of head-dipping did not habituate in the scopolamine groups. No drug effects were found when rats were tested in the absence of objects, i.e. in a simpler task. A similar pattern of results was shown by mice. Neither atropine sulphate (10 and 20 mg/kg i.p.) nor benzhexol hydrochloride (40 mg/kg i.p.) affected habituation of exploration in rats, whether this was measured by the frequency or the duration of head-dipping, and regardless of whether objects were present or absent.

The effects of muscarinic antagonists on habituation of distraction were also studied. Tones were presented to rats and their distraction and subsequent habituation to these measured by the interruption in their base-line licking. Scopolamine, methylscopolamine, atropine, methylatropine and benzhexol all failed to impair habituation.

These experiments provide no support for the suggestion that central muscarinic systems are essential for habituation of exploration or distraction.

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Effect of some phospholipids on acetylcholine output from the cerebral cortex in the rat

L. AMADUCCI, P. MANTOVANI & G. PEPEU*

Departments of Pharmacology and Neurology, University of Florence Medical School, Florence, Italy

The effect of phosphatidylserine (PS), phosphatidylethanolamine (PE) and phosphatidylcholine (PC) on acetylcholine (ACh) output from the cerebral cortex was investigated in adult Wistar rats under urethane anaesthesia according to the procedure described by Hemsworth & Neal (1968). ACh output was determined by placing a collecting cylinder filled with eserinized Ringer solution on the exposed frontoparietal cortex. Every 10 min the solution was changed and bioassayed on the dorsal muscle of the leech. The phospholipids were prepared from bovine brain and we checked their purity by thin layer chromatography. They were injected intravenously as a sonicated suspension in Tris buffer in a volume not exceeding 0.3 ml.

The spontaneous ACh output from the cerebral cortex prior to the phospholipid administration