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The effect of α-methyl-p-tyrosine, p-chlorophenylalanine, methysergide and propranolol on CO_2-induced amnesia in rats

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As there are reports that CO_2-induced anaesthesia results in amnesia (Paolini, Quartermain & Miller, 1966; Taber & Banuazizi, 1966) a study has been made of the efficacy of CO_2 as an amnesic agent in rats.

The 'step-through' passive avoidance test (Ader, Weijmen & Moleman, 1972), was used. The apparatus consists of a brightly illuminated runway attached to a darkened chamber which contains a grid floor. Three pre-training trials were found to be sufficient for the rats to enter the chamber within 1–3 s of being placed on the runway.

In the first experiment, the rats were randomly divided into 4 groups of 10. At the conclusion of the fourth trial, one group (S-CO_2) received a scrambled footshock of 0·5 mA for 3 s through the grid floor of the chamber. Immediately after this, the rats were placed in a box saturated with CO_2; they were left in the box until respiratory arrest occurred and were then revived by artificial respiration.

The second group, (S) received the footshock, but was not subjected to the CO_2 treatment.

The third group (NS-CO_2) was subjected to the CO_2 treatment alone while the control group (N) was untreated. Retention of the learned response was tested 24 h later. The latency of entry into the chamber was also recorded.

When tested for retention, group S completely avoided entering the chamber. In contrast, group S-CO_2 readily entered the chamber thereby demonstrating that CO_2 induced amnesia.

In a previous study, it was found that the behavioural changes in the S and S-CO_2 groups may be associated with alterations in the metabolism of biogenic amines in the hippocampus (Leonard & Rigter, 1973). The effect of some drugs known to inhibit the synthesis of these amines, or block their receptor sites, was therefore studied on CO_2-induced amnesia.

Pretreatment with α-methyl-p-tyrosine (300 mg/kg) and propranolol (15 mg/kg) before the retrieval trial reduced the CO_2-induced amnesia; p-chlorophenylalanine (400 mg/kg) and methysergide (5 mg/kg) were less effective. (+)-Amphetamine 2 mg/kg and physostigmine (0·5 mg/kg) had no effect on the amnesia.

From these results, it appears that the amnesic effect of CO_2 is associated with changes in brain noradrenaline metabolism; 5-hydroxytryptamine may play a subsidiary role.

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