Title : MURINE MEMORY AND HALOTHANE, ETHANOL, DIAZEPAM AND SCOPOLAMINE

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Introduction. Previous studies have shown that acute alcoholic intoxication decreased minimum alveolar concentration for halothane (MAC h.), whereas chronic alcoholism increased it both in animal models and in clinical conditions.[1,2] Work conducted on diazepam and scopolamine showed that these drugs produced temporary nonretrograde amnesia in man,[3] and scopolamine in mice only while the animals were in the learning stage.[4] We have questioned the possible relationships between memory, learning ability, and MAC h. at various stages of alcoholic intoxication and compared our findings with changes in MAC h. when alcohol was withdrawn. The effects of a single intraperitoneal injection of diazepam or scopolamine were studied for their effects on memory and learning ability.

Methods. MAC h. was tested by the tail clamping method on 12 normal male albino mice. Another 24 mice had 15% alcohol in water (weight for weight) substituted for their normal water supply for 60 days. After that period, they were divided into four equal groups. In the first group MAC h. was assessed immediately after withdrawal from alcohol (at that time urine alcohol concentration was 21.5 $\pm$ 1 mg %). The other three, now drinking water, were tested for MAC h. after 4, 10 and 18 days. Thus, each mouse had only one exposure to halothane. While still on alcohol, but starved for 24 hours, the mice were tested for the speed at which they covered a maze containing the food on which they had been fed since birth. A further 7 mice received 0.33 micrograms of diazepam per gram body weight and another 6 mice 0.13 micrograms of scopolamine hydrobromide per gram, (both intraperitoneally) and tested in the maze.

Results. MAC h. in control mice was 1%. It fell to 0.6% immediately after withdrawal from alcohol and then rose, reaching control value within 4 days and 1.6% on the 18th day. After one day on alcohol, the mice failed to recall their way through the maze at the speed at which they could cover it while sober (73 $\pm$ 10 seconds and 178 $\pm$ 17 seconds, respectively, $P < 0.0005$). However, after 10 days they again learned to cover the maze statistically as fast as during their prealcoholic days (59 $\pm$ 8 seconds) figure 1. Mice who had never imbibed alcohol remembered the maze for over 10 days. Animals who had received diazepam or scopolamine hydrobromide were too sleepy to find their way through the maze on the next day. However, after a week they regained their learning capacity but not their memory.

Discussion. It is apparent that there is an inverse relationship between the MAC h. of alcoholic mice and their learning ability. This compound together with diazepam and scopolamine produces amnesia in these animals. The former appears to be mainly due to impaired brain cell function and the latter to the additive effect of both agents and cross enzyme induction (alcohol dehydrogenase which depends on the availability of NAD and NADPH oxidase in the mitochondria). Contrary to reported clinical experience[3] all agents produced retrograde amnesia, presumably because of the comparatively large doses used.

References.

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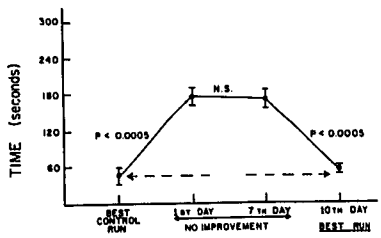

Figure. Comparison between ability to cover the maze in record time by control mice who have learned it, and alcoholic mice who have also learned it but cannot recall it after 1 and 7 days on alcohol, but which regain their learning power but not their memory on day 10, while still on alcohol.