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LETTER TO THE EDITOR

EFFECT OF EXPERIMENTER-ADMINISTERED ETHANOL ON AVOIDANCE LEARNING – A STUDY IN ETHANOL DEPRIVED RATS

Sir,

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In humans and laboratory animals, ethanol consumption is associated with morphological and functional alterations of brain structures involved in cognitive processes. Ethanol alters the neurophysiology of the hippocampal system and dependent behaviors (1). Voluntary ethanol administration improves performance in avoidance task (2). A negative correlation between avoidance performance and change in ethanol consumption from baseline exists in voluntary ethanol administered rats (3). Voluntary versus experimenter-administered routes of drug administration produce significant differences in central neurotransmitter responses (4). The present study was designed to study the sensitivity of cholinergic receptors in rats to experimenter administered ethanol on passive avoidance in male Wistar rats.

Male Albino rats of Wistar strain (10–12 weeks of age), weighing 100–120 g were housed in plastic cages of size 14"×9"×8" (3 rats in each cage) in a well-ventilated room at 22±2°C with a 12-hr light/dark cycle. All rats had free access to a standard diet and tap water. The Animal Ethics Committee, Manipal Academy of Higher Education, Manipal approved all the procedures used. Animals were divided into two groups of six rats each, control and ethanol treated. Ethanol treated rats received ethanol (Ethanol 99.9–100% “absolute”, Hayman Ltd., England) orally by gastric intubation at a dosage of 0.8 g ethanol/kg body weight/day for 1 week. Ethanol was diluted with double distilled water to get the desired concentration. The control animals received double distilled water alone for the same period. After the treatment period, all animals were subjected to passive avoidance training. The group II rats were ethanol deprived after that. After 24 and 48 hours later, the retention test for the passive avoidance task was conducted with all animals.

Passive avoidance test was done by the method of Bures et al., (5) with modifications. The apparatus was fabricated locally. It had two compartments, a rectangular larger compartment with a 50 × 50 cm grid floor and wooden walls of 35 cm height. It had a roof, which could be opened or closed. One of the walls had a 6 × 6 cm opening connecting the larger compartment to a dark smaller compartment. The smaller compartment had 15 × 15 cm electrifiable grid connected to a constant current stimulator, wooden walls of 15 cm height and a ceiling, which could be opened or closed. The connection between the two compartments could be closed with a sliding door made of Plexi glass. The larger compartment was illuminated with a 100 W

bulb placed 150 cm above the centre. The experiment included three parts. (i) Exploration test (ii) an aversive stimulation and learning and (iii) Retention test. During exploration test, each rat was kept in the centre of the larger compartment facing away from the entrance to the dark compartment. The door between the two compartments was kept open. The rat was allowed to explore the apparatus (both larger and smaller compartments) for three minutes. In each trial, the total time taken by the animal to enter the dark compartment was noted using a stop watch. At the end of the trial, the rat was replaced in the home cage, where it remained during intertrial interval of five minutes. After the last exploration trial, the rat was forced into the smaller compartment and the sliding door between the two compartments of the apparatus was closed. Three strong foot shocks (50 Hz, 1.5 mA, and 1 sec duration) were given at five second intervals. The ceiling was then opened and the rat was then returned to its home cage. Retention test was carried out after 24 and 48 hours. The rat was kept in the center of the larger compartment facing away from the entrance to the smaller compartment for a maximum period of three minutes. The sliding door was kept open during this period. The latency time required for the animal to enter the dark compartment was measured. Animals not entering the dark compartment within this period received a latency time of three minutes. Absence of entry into the dark compartment indicated a positive retention.

Statistical analysis were performed by Students 't' test and significance of difference was set at $P<0.05$.

The animals with the 24-hours ethanol-deprivation had increased percent (20%) avoidance. While 48-hours ethanol deprived rats showed decrease in the percent facilitation of avoidance behavior. The study supports that ethanol has an effect on avoidance behavior which is related to the time since last exposure. Avoidance behavior is motivated by fear or an expectancy of an aversive event. The findings supports that the 24-hours withdrawal from ethanol might have produced an adaptive neural change that increased the negative emotional state motivating avoidance behavior. Ethanol has the ability to increase freezing in rodents, which is a species-specific measure of fear (6). The decreased percent facilitation of avoidance behavior in 48-hours of ethanol-deprived animals indicates that the effect is related to the time since last exposure and it can also be explained that physiologic changes mediated the improved avoidance performance of the 24-hours ethanol deprived animals might have returned to normal in 48-hours ethanol deprived animals.

Ethanol effects the expression of motor behavior in escape/avoidance procedures (7).

TABLE I: Effect of alcohol on latency (in seconds) to enter the dark compartment during training and retrieval time. (Values are expressed as mean±SEM).

Groups	*Latency time during training time*	*Latency time during retrieval trial after 24-hours*	*Latency time during retrieval trial after 48-hours*
Group I (Control)	28±2.76	126±4.76	162±5.08
Group II (Ethanol treated)	31±2.89	151±5.09*	171±7.81

*P<0.05 compared with control group.

One of the physiological effects of exposure to ethanol is the development of tolerance to the sedative-hypnotic properties of ethanol caused by the down regulation of gamma-amino butyric acid type A receptors in several brain areas. As a result, one of the most common states accompanying ethanol withdrawal is an increase in anxiety (2). As indicated above, fear or anxiety is the major motivational variable underlying learning of avoidance behavior. Administration of anxiogenic beta-carboline compounds improves acquisition of a passive avoidance task (8). If basal anxiety is increased because of the 24 hours ethanol deprivation, the additional increase in fear created by exposure to foot shock may account for the improved avoidance behavior in the 24 hours ethanol deprived group. Both increased avoidance responding in the current study and increased immobility observed in response to uncontrollable stress, both represent facilitated learning in an aversive situation after ethanol deprivation (9).

In summary, results of the current study demonstrate that ethanol administration improves performance in an avoidance task and is related to the time since last exposure.

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