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DESIPRAMINE BLOCKS THE DEPRESSIVE EFFECTS OF ALCOHOL IN FEMALE WKY RATS

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INTRODUCTION

A number of epidemiological studies suggest an association between alcoholism and depression. However, a causal relationship for this comorbidity has not been established. Previously, it was observed that chronic alcohol administration to male Wistar Kyoto (WKY) rats results in increased immobility in the swim test, reflecting an exacerbation of the inherent depressive characteristics in these rats (*Tizabi et al., Alc Clin Exp Res 27(Suppl):132A, 2003*). In this study, we sought to determine whether similar results is obtained in female rats, and if so, would treatment with the antidepressant desipramine prevent the effect of alcohol.

METHODS

Animals

Age matched adult female WKY and Wistar rats (Harlan) were kept in a temperature-controlled room (24-26 ºC) on a 12:12 hour reversed light/dark cycle (lights on at 19:30). The animals had ad libitum access to food and water, except during experiments.

Drug Administration

A 16% (v/v) solution of ethyl alcohol (VWR International Inc, Bridgeport, NJ) was diluted in saline. The animals were administered 1 g/kg of alcohol i.p. once daily for 8 days. Desipramine (desipramine HCl, Sigma, St. Louis, MO) in a dose of 8mg/kg was dissolved in saline and was given i.p. once daily for 7 days ten minutes after alcohol administration.

Locomotor Activity Test

Thirty minutes post alcohol (1g/kg, i.p.) administration the locomotor activity test was conducted in an automated open field activity monitor measuring 27cm x 27cm x 20.3cm (Med Associates Inc, St. Albans, VT). Briefly, spontaneous locomotor activity, determined by the total horizontal distance traveled was automatically gathered. Animals were monitored continuously for 10 minutes. The activity-monitoring cage was wiped clean after each use. All behavioral tests were carried out during the early part of the dark phase, between 10:00 and 15:00hr

Forced Swim Test

The FST measures immobility of animals in an inescapable cylinder of water. The total amount of time the animal demonstrates this behavior reflects the animal's state of behavioral despair elicited by the inescapable nature of the tank. Rats were placed individually for 5 minutes in a round Pyrex cylinder pool (diameter of 17 cm and height of 60 cm) that was filled with 30cm of water (25±2 °C). A time sampling technique was used whereby the predominant behavior in each 5-s period of the 300-s test was recorded. Inactivity, swimming and climbing were scored as three behavioral states.

Statistical Analysis

Data is presented as means + SEM. Analysis of variance (ANOVA) were used to determine the differences between saline, alcohol, and desipramine-alcohol treated animals in behavioral parameters. Fishers LSD post hoc test was applied when the ANOVA showed significant differences at $p < 0.05$. All of the statistics were calculated using SPSS 13.0 standard version statistical software.

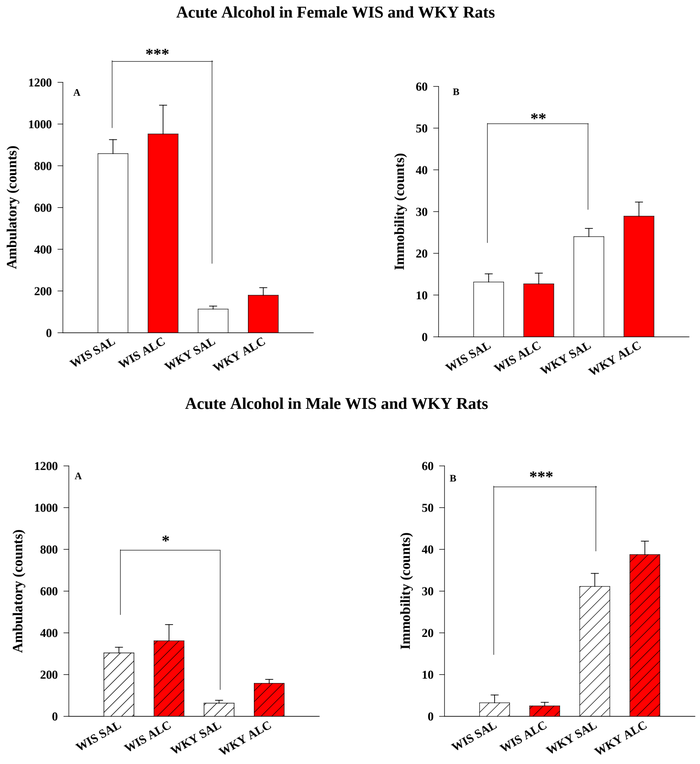

Fig-1 and Fig- 2 Effects of acute alcohol administration in the locomotor activity (A) and the forced swim test (B) immobility in WKY and WIS rats. Values are ± SEM. *** p < 0.001, ** p < 0.01, * p< 0.05 N= 6-9

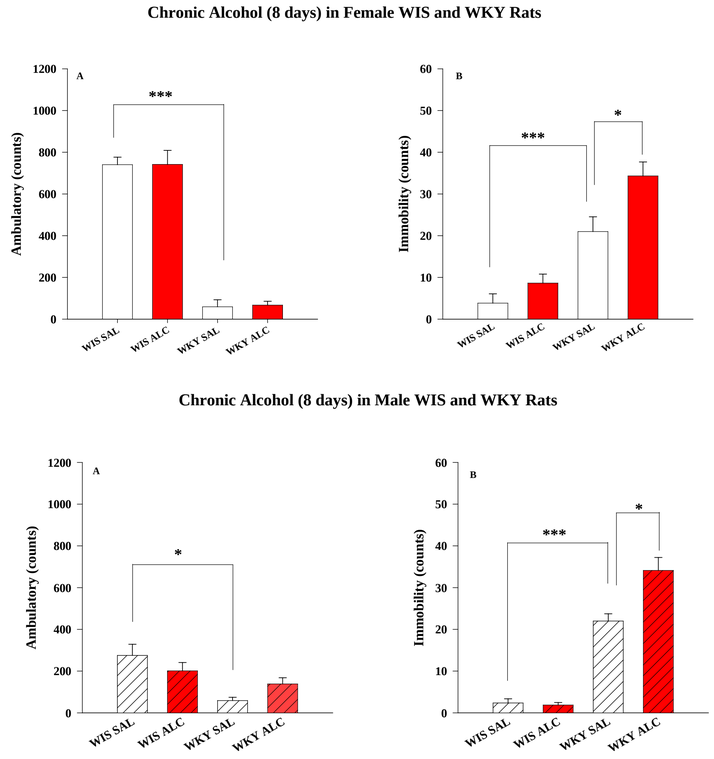

Fig-3 and Fig-4 Effects of chronic administration of alcohol in the locomotor activity (A) and the forced swim test (B) immobility in WIS and WKY rats. Values are ± SEM. *** p < 0.001 , *p < 0.05 N = 6-9

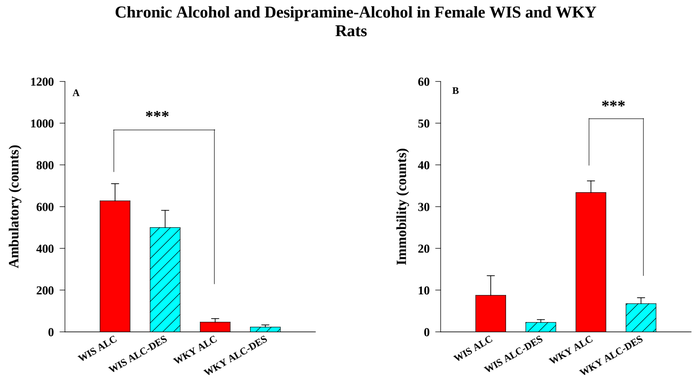

Fig-5 Effects of chronic administration of alcohol + desipramine in the locomotor activity (A) and the forced swim test (B) immobility in WIS and WKY rats. Values are ± SEM.
*** p < 0.001 N = 6-9

RESULTS

•Chronic, but not acute alcohol administration resulted in increased immobility in WKY rats only. These findings are similar to those previously observed in male Wistar and WKY rats.

•Daily administration of desipramine completely blocked alcohol-induced immobility in the FST in WKY rats.

•Locomotor activity in the open field was unaffected by ethanol or desipramine treatments in either strain.

CONCLUDING STATEMENT

These results provide further evidence that chronic alcohol may exacerbate the inherent depressive characteristics of certain rat strains, irrespective of the gender. Moreover, this "depressogenic" effects of alcohol may be effectively prevented by an antidepressant. These findings suggest therapeutic applicability of antidepressants in alcohol-induced depression.

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