REDUCTION OF ETHANOL DRINKING FOLLOWING CHRONIC ADMINISTRATION OF THE ANTIEPILEPTIC LEVETIRACETAM IN GENETICALLY SELECTED ALCOHOL PREFERRING RATS

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Ethanol is a drug with complex physiological effects on central system. The reinforcing and rewarding properties of ethanol and ethanol-seeking behaviour involves several neurochemical systems, including GABAergic and glutamatergic transmission. The possibility to use antiepileptic drugs for the treatment of alcohol dependence, thanks to the properties of these medications to inhibit neuronal excitation of glutamate receptors and enhance GABAergic neurotransmission, has been recently proposed. The objective of this study was to determine whether the antiepileptic agent levetiracetam (Keppra ®) is able to reduce ethanol drinking in genetically selected Marchigian Sardinian (msP) alcohol-preferring rats, a well established animal model of alcohol abuse. In the first experiment, using a two bottle choice paradigm (choice between water and 10% v/v ethanol), msP rats were trained to drink alcohol for 2 h a day. Water and food were available ad libitum. Once a stable baseline of ethanol drinking was established experiment begun. At the beginning of the dark cycle, levetiracetam (0, 100 and 150 mg/kg) was given per OS 60 min before access to ethanol. Ethanol, water and food consumption were monitored at 30, 60, 90 and 120 min. During the 2-h access rats drank up to 1.5 g/kg of ethanol. Alcohol intake was slightly but not significantly reduced by levetiracetam ($P>0.05$). Food and water intakes were not modified by drug treatment. In a following experiment other two groups of msP rats with similar baseline of daily ethanol drinking were given access to ethanol, water and food ad libitum. To study the effect of subchronic treatment with levetiracetam, for 7 consecutive days, 1 hour before light off (12:12 h light/dark cycle), rats were given the antiepileptic (150 mg/kg) or its vehicle. Ethanol, water and food intake was monitored at 2, 8 and 24 hours after the beginning of the dark phase of the light/dark cycle. Administration of 150 mg/kg of levetiracetam significantly decreased alcohol drinking ($P<0.05$) for the entire period of treatment. Water and food consumption was not affected by treatment. The result demonstrate that repeated administration of levetiracetam reduces ethanol intake in alcohol preferring-rats, suggesting that this drug might be of potential interest for the treatment of alcohol abuse in humans. *(Supported by Grant FAR 2006 University of Camerino)*