CHRONIC ETHANOL EXPOSURE AFFECTS ADENOSINERGIC MECHANISM IN BASAL FOREBRAIN

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Acute ethanol exposure promotes sleep. Chronic ethanol produces insomnia and disrupts sleep. Adenosine promotes sleep by inhibiting wakefulness-promoting neurons in the basal forebrain (BF) via the activation of A_1 receptors (A1R). Does chronic ethanol induce insomnia by affecting adenosinergic mechanisms in the BF? We performed two experiments to address this question.

Experiment 1: Since sleep deprivation (SD) increases BF adenosine levels, it can be used to evaluate the effects of chronic ethanol on BF adenosine release. Thus, our first experiment examined the effect of chronic ethanol treatment on SD induced adenosine release in adult male Sprague Dawley rats implanted with microdialysis probe in the BF. Chronic binge ethanol (35% v/v in milk based infant formula) treatment was performed for four days to induce alcohol dependency. Control animals were administered milk based infant formula. SD was performed on post-ethanol (withdrawal) day 1 for 6 hr by gentle handling and, microdialysis samples were collected at every hour and analyzed for adenosine levels.

Experiment 2: Chronic ethanol administration was performed as described above1. Rats were sacrificed on withdrawal day and BF was dissected out. Total RNA was isolated and A1R gene expression was examined by RT-PCR

Our initial results suggest that both, ethanol treated and control animals (statistics not performed due to small Ns) displayed increased adenosine during SD. However, A1R gene expression was significantly reduced following chronic ethanol treatment.

Our data suggest that chronic ethanol may induce insomnia by down-regulating A1 receptor gene expression without affecting adenosine release in the BF