POSTER 44

PROTRACTED ACTIVATION OF THE BASAL FOREBRAIN CHOLINERGIC NEURONS AFTER BINGE ETHANOL EXPOSURE

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Insomnia during alcohol withdrawal is a hallmark of alcohol dependency and a major cause of relapse in recovering alcoholics. The mechanism of insomnia in this patient population is poorly understood. Cholinergic neurons in the basal forebrain (BF) play an important role in promoting wakefulness. Recently, we have shown that acute ethanol/alcohol exposure inhibits these cholinergic neurons to promote sleep. Does chronic ethanol exposure lead to the persistent activation of the BF cholinergic neurons which may lead to insomnia?

Method: Male Sprague-Dawley rats were divided into experimental and control groups. Chronic binge ethanol administration protocol was used to induce alcohol dependency in rats. The protocol in brief: Experimental rats were intragastrically administered ethanol (35% v/v; ~9 g/kg/day) in three divided doses (depending on intoxication behaviors) for four days. Control group received sterile water (30ml/kg/day) instead of ethanol. Rats were euthanized on withdrawal day 1 and day 3 during the light (inactive/sleep) period and their brains were processed for c-Fos (a neuronal activation marker) and choline acetyltransferase (ChAT; cholinergic neuronal marker) immunohistochemistry to examine the activation of cholinergic neurons in the BF.

Results: Statistical analysis (Kruskal-Wallis Test and Mann-Whitney Test) revealed a significant increase in the number of ChAT positive neurons with c-Fos immunoreactivity in the BF of ethanol dependent rats as compared to controls.

Conclusion: These results suggest that chronic binge ethanol treatment causes persistent activation of the BF cholinergic neurons during normal sleep period. Persistent activation of these neurons is likely to cause protracted insomnia associated with ethanol withdrawal.