Thesis Title Influence of glucocorticoid on the alteratiion of choline acetyltransferase (ChAT) enzyme induced by ethanol in various brain areas of adult male rats.

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Abstract

During stress situation, there was an increase in the activity of hypothalamo - pituitary - adrenal axis (HPA- axis) resulting in the elevation of glucocorticoids. Ethanol was hypothesized to be an anxiolytic agent and widely used as agent to relief stressful condition. Both ethanol and glucocorticoids were reported to produce toxic effect on neuronal cells in various brain areas at high doses. However, glucocorticoid itself have been reported to exert both protective and toxic effect on the central nervous system (CNS) so the precise effect of glucocorticoids on brain function is still unclear. In this study, the effect of ethanol and glucocorticoids and the interaction of the two substances have been investigated, using the activity of ChAT as neuronal marker for the function of cholinergic system. The results showed that glucocorticoids administration 1mg/kg (s.c.) once daily for 5 days decreased ChAT activity in cerebral cortex, striatum and hippocampus significantly (p-value<.001).The mechanism may probably via the alteration in protein

content in the brain. Ethanol admistration produce a biphasic changes in ChAT enzyme activity. Low dose of ethanol treatment (0.1,0.5 g/kg) for 5 days increase ChAT activity while high doses of ethanol treatment (1g/kg) decreased ChAT activity in cerebral cortex,striatum and hippocampus. The effect of ethanol on ChAT activity is not a direct effect of ethanol but may probably occur via its metabolite or its by product. Ethanol plus dexamethasone, a synthetic glucocorticoid, reversed the action of ethanol both at low and high concentration significantly in cerebral cortex and striatum but not in hippocampus . The mechanism of action of ethanol and dexamethasone may occur via the alteration in affinity (Km) of ChAT enzyme for acetyl coenzyme A, a substrate for Ach synthesis. The interaction of ethanol, glucocorticoids and AF 64A, a cholinotoxin, on the function of cholinergic system which is an important system in learning and memory process were also studied. The result shown that AF 64A exacerbated the toxicity of ethanol treatment especially at low dose treatment (0.1g/kg).However, it does not exacerbate the toxicity induced by dexamethasone. The understanding about the effect and interaction effect of these substances may provide the information about the possible factors which contribute a significant role in pre - senile dementia.