ETHANOL INDUCED DYSREGULATION OF THE PSYCHO-NEURO-IMMUNE NETWORK

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ABSTRACT

ETHANOL INDUCED DYSREGULATION OF THE PSYCHO-NEURO-IMMUNE NETWORK

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Alcohol is one of the most harmful substance to the user and others that can be readily abused compared to other drugs (heroin, methamphetamine, etc.). In this study, we evaluated the roles of specific cytokines in the pathology of acute alcohol consumption in animal models. Two groups of NIH Swiss mice were treated IP with 1.8 g/kg (group A) and 3.0 g/kg of ethanol (group B) for 3 days. Controls (group C) were treated with saline. Tissue specific gene expression of key signal transducers, inflammatory cytokines, and their receptors (R) were evaluated with qPCR. Systemic cytokine levels were evaluated with flow-cytometry. Significantly higher gene expression of STAT-4, -5A -6 was observed in brain tissues of Group A animals compared to Group B. Compared to control animals, Group A animals exhibited increased gene expression of the T-bet and CXCL2(MIP2) in brain tissue. Splenic tissue of ethanol treated animals showed significant decreased gene expression of STATs, but increased gene expression of inflammatory cytokines TNFα and CXCL2. Plasma level of IL1 and CCL2(MCP1) were significantly higher in the Groups A and B compare to control animals. Subsequent study animals were treated similarly with ethanol agonist, Beta caryophyllene oxide (BCPO; Group O), to counteract alcohol-induced substance seeking behavior. BCPO treatment led to significant increase of plasma levels of TNFα, IFNγ, CCL2, IL23, and IL10

compared to Group A; and TNFα, IFNγ, IL10 and IL23 compared to Group C. This data suggests that alcohol consumption even with minimal doses leads to systemic inflammation and unequally affects systemic and tissue-specific cytokine equilibrium.