NIH Award from the National Institute on Alcohol Abuse and Alcoholism

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- Project: Mechanism of Alcohol and Nicotine Interaction
- Start Date: September 30, 2009
- Total Award Amount: $500,011

How the results of this project will benefit society:
This study of the interactive effects of ethanol and nicotine on microglia will have significant impact on preventing damages caused by the drinking-smoking combination and will lay the foundation of further mechanism of toxic effects of ethanol.

The problem the project is trying to solve:
The mechanisms of action of alcohol (ethanol) and nicotine on the nervous system have been studied extensively. However, it was not until a few years ago that microglia were recognized as an important site of action of alcohol and nicotine; alcohol for toxic effects and nicotine for neuroprotective effects. Heavy drinkers tend to be heavy smokers. We propose a hypothesis that microglia are a site where the drinking-smoking correlation resides. When activated by proinflammatory factors, microglia produce reactive oxygen species (ROS) such as NO and toxic cytokines such as TNFalpha. Electrons are moved across the membrane from intracellular NADPH to extracellular O₂ to generate O₂⁻·. This charge movement is compensated for by voltage-gated proton channels. Thus, both proton currents and electron currents are generated. The long-term goal of this project is to develop assessment of microglial function when alcohol and nicotine interact with each other. Specifically, we will elucidate the mechanism of alcohol-nicotine interaction through microglia. The results of this study will lay the foundation for understanding of alcohol and nicotine interaction.

How this project will work:
The proposed study comprises two parts: electrophysiological experiments and biochemical experiments. Proton currents are recorded from BV-2 microglial cell line as a measure of activation of microglia, and the effects of ethanol, nicotine and alcohol plus nicotine will be studied. Parallel biochemical experiments will be performed to measure ROS and toxic cytokines. We expect that ethanol augments the proinflammatory stimulation of microglia resulting in increases in proton currents, ROS and cytokines, and that nicotine suppresses the augmentation.

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