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2006 Program

Team Science Project
(2-year project)

Project Title: The Role of Nicotine in the Neural Control of Respiratory and Cardiovascular Systems

Project Summary: Cigarette smoking is a highly addictive behavior with both short-term and long-term deleterious effects on human health. Nicotine, which is considered the major addictive agent in cigarette smoke, is absorbed from cigarette smoke in the mouth and lungs and diffuses rapidly from the circulation into the central nervous system. Nicotine activates nicotinic receptors on neurons within the central nervous system to modify neural processing. The impact of nicotine on important respiratory and cardiovascular neural control centers is the focus of the research proposed by this team of investigators. This TSP will investigate the influence of nicotine on cardiorespiratory control from the level of specific receptor subtypes within the brain to the level of human cognition and circadian behavior. The four sub-projects are an integrated series of studies designed to develop a new understanding of the effects of nicotine on human respiratory cognitive sensory gating, respiratory reflex cough in humans and experimental animals, and the effect of prenatal nicotine exposure on respiratory neural control and the threshold for alerting responses during sleep. The central focus of this multi-dimensional project is the role of nicotine acting on the central nervous system, modulating and regulating the neural control of respiratory and cardiovascular behaviors. An integrated core will support the four interrelated sub-projects.

The TSP project will use animal models in combination with human studies to provide animal-human translational research on central neural effects of nicotine on the respiratory and cardiovascular systems. The primary research approaches for this project are: 1) the role of nicotine in the modulation of respiratory sensory neural processing and reflexes and 2) the role of prenatal nicotine on the neonatal brain pathways mediating respiratory and cardiovascular neural control. Sub-project 1 is an investigation of the role of nicotine administration and withdrawal in humans on central neural gating of respiratory afferents and the cough reflex sensitivity. Sub-project 2 is an investigation of the cough reflex in an animal model, directly related to the afferent and central neural mechanisms mediating the human respiratory sensations and cough. Sub-projects 3 and 4 will use pregnant rats exposed to nicotine to investigate the role of nicotine on newborn cardiorespiratory control. Sub-project 3 investigates the role of prenatal nicotine exposure on newborn impairment of upper airway defense mechanisms triggered by serotonin, directly related to cough reflexes and hypoxic responses. Sub-project 4 similarly investigates the role of prenatal nicotine exposure on newborn cardiovascular and respiratory responses to sleep, hypoxia, and hyperthermia, also related to cough reflexes and hypoxic responses.

The research investigators form an established integrated group that has a documented history of collaborative research. The current project is the natural convergence of their research interests onto the important topic of the role of nicotine in cardiorespiratory neural control. The outcome of this coordinated team effort will provide new and innovative insights into the role of nicotine on central nervous system function.