

## **Social Stress, Exercise, and the Brain: The Study of Mechanisms in an Animal Model**

**Introduction.** The present Great Journeys proposal will investigate specific mechanisms in the brain that underlie the consequences of social stress, and the potential protective effects of physical exercise. Using a unique animal model (prairie vole), these experiments will provide critical insight into the function of specific brain areas that are altered in the context of stress. The present experiments will extend the results generated from a previous Great Journeys award, which led to a funded R15 grant from the National Institutes of Health (NIH; *Mechanisms of social isolation and environmental enrichment in an animal model*; 1R15HL112350; 08/05/12 – 08/04/15; National Heart Lung and Blood Institute, NHLBI). The current Great Journeys project is necessary for the development of a successful NIH R01 grant proposal, to follow my R15 grant. This project includes integrative, translational methods conducted in an animal model, and will therefore provide excellent training for a Graduate Assistant in both technical and conceptual knowledge. The following sections will address the importance of studying social stress, health, and the brain, the timeline and plan for applying for external funding, and the involvement and mentoring of a Graduate Assistant.

**Goals and Significance of this Research.** Previous research from both humans and animal models indicates that social bonds are very important to psychological and biological health. Long-term social stress in humans has significant emotional and biological consequences including disrupted mood and emotion, cardiovascular problems, poor stress-coping ability, and altered hormonal and immune function. Regular exercise may have potential benefits for individuals experiencing stress, and can improve mood, stress-coping ability, and biological functions. However, the specific mechanisms in the brain that underlie the consequences of social stress and the potential benefits of exercise in this context are not well understood. Therefore, the present project will employ a unique animal model, the prairie vole, to investigate direct changes in the brain as a function of social stress and physical exercise. Prairie voles are rodents that provide an extremely powerful translational model for studying the interactions of social stress and the brain. Prairie voles – unlike nearly all other rodents – exhibit several social behaviors similar to those of humans, such as: (1) actively engaging in the surrounding social context, (2) forming long-term social bonds, (3) living in family groups, and (4) responding negatively to social stressors. The results from this project will have widespread implications for humans who suffer from social stress, emotional disturbances, and associated physical diseases. The specific goals of this project are the following:

**Goal 1: To investigate long-term changes in the brain that underlie behavior, responses to stress, and cardiovascular function following chronic social isolation in female prairie voles.**

**Prediction 1a:** 4 weeks of social isolation in female prairie voles (compared to social pairing) will lead to depressive and anxiety behaviors and exaggerated hormonal and cardiovascular reactivity to acute stress.

**Prediction 1b:** The altered behavioral and stress reactivity in socially isolated female prairie voles (compared to social pairing) will be mediated by increased activation of brain areas that regulate emotion and stress responses (hypothalamus and amygdala), and cardiovascular function (dorsal motor nucleus of the vagus, nucleus ambiguus, and ventrolateral medulla).

**Goal 2: To investigate the stress-buffering effects of exercise on behavior, responses to stress, and the brain following chronic social isolation in female prairie voles.**

**Prediction 2a:** Voluntary exercise in a running wheel (versus sedentary conditions) will protect against depressive and anxiety behaviors and normalize the hormonal and cardiovascular responses to acute stress in socially isolated female prairie voles.

**Prediction 2b:** Voluntary exercise in a running wheel (versus sedentary conditions) will prevent activation of brain areas involved in emotion and stress responses (hypothalamus and amygdala), and cardiovascular function (dorsal motor nucleus of the vagus, nucleus ambiguus, and ventrolateral medulla) in socially isolated female prairie voles.