The Hilda and Preston Davis Foundation Awards Program
for Eating Disorders Research: Senior Postdoctoral Fellows
2019 Award Recipients

- **Andrew Lutas, Ph.D.**
  Postdoctoral Fellow
  Beth Israel Deaconess Medical Center / Harvard Medical School
  Mentor: Mark Andermann, Ph.D.

  Neural circuits mediating hunger-dependent avoidance of aversive cues in anorexia nervosa

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Restrictive-type anorexia nervosa (AN) causes anguish in patients and families, and can often be fatal. Treatments remain inadequate, in part because we lack a good understanding of the underlying neural circuits and their pathology. The basal amygdala (BA) and insular cortex (InsCtx) are consistently implicated in AN by lesion and neuroimaging studies. For example, AN patients show enhanced InsCtx responses to aversive cues, and blunted responses to food cues. Our lab recently discovered an important pathway from AgRP neurons to InsCtx via paraventricular thalamus (PVT) and BA – two areas involved in assessing hunger-dependent salience of learned cues. PVT neurons projecting to BA (PVTBA) have been implicated in cued fear retrieval. I will directly test the hypotheses that hypothalamic hunger-promoting AgRP neurons suppress cued fear retrieval via inhibition of PVTBA projection neurons. Thus, the state of food restriction may shift from being net-negative to net-positive under conditions of heightened anxiety, as in many patients that subsequently develop AN. To investigate whether these circuits contribute to the etiology of AN, I will use two-photon calcium imaging to track PVTBA axons of behaving mice. I will test whether PVTBA responses to aversive cues increase following satiation or inhibition of AgRPPVT axons, and whether these responses are suppressed by activation of AgRPPVT axons in sated mice (Aim 1). I will then develop a novel mouse model of AN in which mice in a stressful context can voluntarily increase or decrease activity of AgRPPVT axons in a simple virtual reality environment. In this way, I will test the hypothesis that healthy mice avoid stimulation of AgRPPVT axons, while anxious/stressed mice learn to take specific actions that lead to increased activity in AgRPPVT axons. Together, these experiments provide novel approaches to understanding the neural circuits underlying learned behaviors that promote sustained food restriction in AN.

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- **Kimberly Smith, Ph.D.**
  Postdoctoral Fellow
  Johns Hopkins University
  Mentor: Timothy H. Moran, Ph.D.

  Real-Time Neurobehavioral Effects of Meal-Based Weight Restoration on Taste Preferences and Reward Circuitry in Anorexia Nervosa

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The goal of this pilot study is to investigate the neurobiological alterations and behavioral correlates that exist prior to and result following behavioral treatment and weight restoration in patients with Anorexia Nervosa (AN). AN is a complex disease of unknown etiology characterized by a chronic state of starvation and preoccupation with body weight and body image. Currently there is no cure for AN. At present, the primary treatment is weight restoration, which is essential for recovery and remission. Yet, the neural mechanisms responsible for the reduction in eating disorder psychopathology following weight gain are largely unknown. While the literature suggests profound differences in the neural activation patterns of reward regions in ill and recovered women with AN, few data exist demonstrating within subject changes that occur directly as a result of refeeding and weight gain. We hypothesize that nutritional rehabilitation and significant changes in weight, as seen in AN patients undergoing treatment with rapid refeeding through a meal-based approach, may affect brain reward circuitry that can be functionally assessed through taste responsivity to stimuli known to activate brain reward circuits. This research proposal discusses the strategies to be used to directly assess active reward processing and the concomitant changes in behavior in real-time as a function of treatment and nutritional rehabilitation in patients with active AN. In Aim 1, taste preferences of patients with AN to nutritionally relevant tastants will be assessed prior to and following treatment. In Aim 2, activation of a ventral reward circuit (including amygdala, insula, striatum, anterior cingulate, and orbitofrontal cortex) by these tastants will be measured before and after treatment using an fMRI approach. This study will identify potential reward-circuitry mechanisms involved in the progressive recovery from AN to be investigated in future research proposals.