COBRE Investigators

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Title of project: Epigenetic and Behavioral Outcomes Associated with Caregiver Experiences

Summary:

Caregiver experiences during early development profoundly affect development of the brain to impart either risk for (caregiver maltreatment) or resilience to (nurturing caregiving) later cognitive dysfunction, affect dysregulation, and psychiatric disorders. An emerging idea is that epigenetic marking of the genome may underlie the genesis of these outcomes. We have shown using a rodent model that we developed that caregiver maltreatment increases cortical methylation of *brain-derived neurotrophic factor* (*bdnf*) DNA. We have also shown using this model that female infants when adult display aberrant maternal behavior toward their own offspring. The present project will utilize our rodent model to explore whether epigenetic gene changes are a basis for behavioral outcomes associated with caregiver experiences (nurturing verses maltreatment). As aberrant *bdnf* gene activity is not only a leading candidate in the etiology of several psychiatric disorders but is also a leading candidate for the lasting changes in cognition incited by early-life stress, the studies outlined in this proposal utilize a candidate gene approach and focus on the *bdnf* gene. The goal of the first aim is to characterize epigenetic regulation of *bdnf* gene transcription across development in behaviorally-relevant brain regions (prefrontal cortex, amygdala, and hippocampus) of animals that have experienced either nurturing caregiving or caregiver maltreatment. The goal of the second aim is to determine whether there is a relationship between the observed epigenetic changes and adolescent behavioral performance on a variety of tasks that involve cortical, amygdala, and hippocampal function. Data generated from these studies will be the first to establish a systems-level understanding of epigenetic regulation of *bdnf* gene transcription across behaviorally-relevant brain regions during typical and atypical development, and whether these changes are related to behavioral outcome. Furthermore, data will validate an animal model of maltreatment that can provide a bridge from basic to clinical research and that may be of future use in pre-clinical drug screening and discovery.