

### **Impacts of Early Life Stress on the Neurobiology of Depression**

Currently there are 17 million Americans living with major depression, and for them, even basic tasks can seem overwhelming. In roughly half of people living with major depression medication and psychotherapy are of little use, and within this population there is a high incidence of early life stress (ELS). ELS causes lifelong changes to the brain, with environmental pressures leaving lasting marks on brain systems implicated in depression. However, very little is known of how ELS changes the young brain yielding a depressed state that persists into adulthood. The goal of this project is to understand the impacts of ELS on the adult brain and to gain an instrumental insight for treatments of adult depression. To accomplish this, we will test the hypothesis that ELS hijacks neural pathways that, under normal circumstances, carry out threat appraisal but after ELS are unable to “return to normal” –leading to a long-lasting depressed state in adulthood. We will test our hypothesis at two complementary levels. First, we will characterize the changes in morphology, connectivity, and function of brain cells from areas affected in depression, in a mouse model of ELS compared to unaltered control animals, as well as animals that undergo adult stress. Second, we will establish how ELS forges depressive behavioral symptoms (learned helplessness, anhedonia, social deficits –all observed in the DSM-V) in the mouse model of ELS compared to unaltered control animals. Completion of this work will help shed light on the poorly understood connection between the neurobiology of ELS and Adult depression. This could open up further research into novel targets for treatment that work differently than current methods, by giving us a clearer picture into the etiology of treatment resistant depression. This new approach, though in its infancy, has potential to give us a window into multiple areas of depression- causes, development, and possible treatments.