

Pediatric anxiety disorders affect approximately one in ten children resulting in marked social impairment. These individuals also carry a heightened risk for mood and anxiety disorders in adulthood, rendering this a public health issue relevant to the entire lifespan. Work to date characterizing the pathophysiology of anxiety disorders has focused on one sphere of anxious symptoms—hypersensitivity to cues of potential threat such as emotional faces or negative images (e.g., phasic responses), while biological markers for other key symptoms of anxiety, such as sustained hypervigilance and arousal (e.g., tonic responses), remain relatively unexplored. The objectives of this program of research are: 1) to delineate the typical development of brain systems involved in phasic and tonic processes that map onto threat processing and vigilance, 2) to provide preliminary evidence for their differential roles in representing tonic anxious phenotypes characteristic of generalized anxiety disorder; and 3) to test their predictive merit for risk in familial cases. The proposed work will first use functional neuroimaging and psychophysiology to characterize the functional properties of brain networks that mediate tonic and phasic symptoms of anxiety in a cross-sectional, typically developing sample (K phase). Then, deviant neural and behavioral signatures will be identified in a sample of individuals with pediatric Generalized Anxiety Disorder (GAD), a clinical syndrome marked by chronic apprehension and vigilance (K phase). Using these samples, we will assess whether biobehavioral markers of GAD are also evident in a sample of children at heightened risk for developing anxiety disorders based on family history (R phase). To accomplish these objectives, the candidate will receive extensive training in testing pediatric and clinical populations bolstered by education in developmental and clinical neuroscience, and advanced neuroimaging techniques including resting-state connectivity, diffusion tensor connectivity and network modeling methodologies. This work and training will prepare the candidate for initiating an independent laboratory capable of developmental, clinical and advanced neuroimaging research. Irrespective of the observed findings, this work will serve as a natural precursor to future R01 funding applications to track high-risk individuals longitudinally and/or utilize identified biomarkers in clinical research evaluating new therapies targeting the tonic system and its associated chronic anxious symptomatology. This work is progressing toward the ultimate goal of identifying predictive markers of risk for anxiety disorders that will facilitate early identification and prevention.