Research Statement

My research is motivated by the need to better understand the pathophysiology of brain dysfunction. Specifically, my interests include the neural basis of neuropsychiatric disorders and cognitive aging, including changes in social-emotional processing, memory and decision-making. Over the last 11 years I have built an arsenal of skills in cognitive and behavioral neuroscientific methods, including psychophysical testing, EEG, structural and functional MRI, diffusion tensor imaging and magnetic resonance spectroscopy, that are useful for evaluating brain-behavior associations. The primary purpose of my research is to strengthen empirical knowledge about brain and behavior associations to better understand cognitive disturbances, particularly in neuropsychiatric and aging populations. My long-term goal is to use advanced multimodal cognitive neuroscientific approaches to facilitate early identification of individuals at-risk for neuropsychiatric or neurodegenerative disease.

Currently, I am working on projects investigating the neurobehavioral and neuroimaging endophenotypes in the study of healthy community controls and multiplex multigenerational (MM) families with schizophrenia. We know that certain cognitive measures are heritable and differentiate individuals at-risk for schizophrenia from unaffected family members and healthy comparison subjects. These deficits in neurocognitive performance in patients with schizophrenia appear stable in the short term. However, the duration of most, but not all, longitudinal studies is modest and the majority of those have relied on traditional average performance measures to examine stability. In order to more precisely measure change over time I estimated performance variability within subjects as a complementary measure to traditional mean performance in neurocognitive performance. Intra-individual variability (IIV) reflects within-person fluctuations in neurocognitive performance, assessing the stability of cognitive processing. When within-person variability increases and is systematic, indexing performance based upon a single measurement (e.g. mean performance) may result in poor estimates of group differences. Thus, IIV has emerged as a useful construct for assessing cognitive performance in disorders such as ADHD and schizophrenia. Using an across-task measure of IIV confirmed previous results of more variability for neurocognitive measures in patients with schizophrenia compared to family members and healthy controls (Roalf et al., 2012; Schizophrenia Bulletin). Moreover, patients' IIV for speed increased over time relative to family members or comparison subjects. I have found that evaluating longitudinal neurocognitive performance using across-task IIV may provide a robust measure of neurocognitive performance and enable detection of change over time that better correlates with disease state. More recently, I have followed up on these findings by relating increased IIV to disruptions of white matter tracts in the brain of patients with schizophrenia (Roalf et al., in press; Schizophrenia Research).

In addition to behavioral comparisons, I have used functional neuroimaging to assess neurocognitive function. Most fMRI studies focus on single tasks, which limits applicability where assessment of multiple brain systems is needed. In order to assess comprehensive cognitive performance, I have used a computerized neurocognitive battery (CNB) at two independent sites to predict performance in over 200 healthy individuals. Using a cross-validated prediction model, brain activity was used to predict neurocognitive performance. Prediction of performance was robust for all tasks but prediction of performance during more complex tasks such as abstraction/mental flexibility, and visuo-spatial memory was best (Roalf et al., in submission). Thus, using a standardized computerized battery adapted for use in a 3.0T MRI we show stable, generalizable behavioral performance and brain activation patterns in healthy volunteers. These data may facilitate identification of neural dysfunction associated with poor neuropsychological performance, allow for identification of individuals at-risk for brain disorders, and be helpful for early intervention and rehabilitation of neurocognitive deficits. I look forward to using this approach in future studies as this method provides a robust comparison sample to which individuals with neurocognitive deficits can be compared. Ultimately it will enable us to link abnormal neurocognitive performance with aberrant brain activation patterns.

In addition to these projects I am engaged in several other lines of research, including using automated segmentation methods to identify regional volume differences in multiplex families with schizophrenia with Dr. Christos Davatzikos, examining chemosensory impairments in at-risk youth with Dr. Paul Moberg and Dr. Bruce Turetsky, including structural and diffusion MRI of the olfactory system. I am most excited by recent work with MRS spectroscopy with Dr. Mark Elliott and Dr. Hari Harihan. We are working to optimize a 7Tesla MRI acquisition protocol to acquire glutamate spectra from brain structures including primary olfactory cortex, amygdala (Roalf et al., under review) and hippocampus.

I have also continued my research from my graduate work including how alterations in decision-making are related to known age-related changes in the brain. In general, my work suggests that risk attitudes, particularly in older adults, influence economic decisions that involve social interaction. This is notheworthy as the elderly face many tough decisions that impact the remaining years of their lives such as health and end of life care, which are highly emotionally charged. They do this at the same time when they also have significant changes in the way emotion is processed (Roalf et al., 2011; Neurobiology of Aging), including changes in its neural underpinnings. Many situations, such as choosing a health plan, selling a house, or spending retirement money, have elements of uncertainty. How the brain integrates information and weighs the likelihood of risk, reward and trust is not fully understood. In recent work (Roalf et al., 2012; J Gerontol B Psychol Sci Soc Sci.), I found that older adults, in general, were less impulsive and were more risk averse than younger adults. This implies that older adults are less willing to disrupt social interactions with self-interested choices. I look forward to future studies that directly manipulate risk, measure decision-making in high or low risk-taking older adults, or determine how cognitive burden affects risk-taking during social economic decisions as these would add valuable insight into decision-making in older adults. Lastly, the nature and mechanisms underlying these difficulties are unclear; however, it is clear that age-related changes occur in brain regions known to underlie decision-making processes and more detailed cognitive assesment along with targeted neuroimaing methods will begin to elucidate these neural mechanisms. This research may prove critical for the development and testing of new interventions aimed to improve decision-making in impaired populations and may be used to measure the influence of social interaction in patients and other cohorts, in particular those with neuropsychiatric disorders.

My work in aging also extends into Alzheimer's disease (AD). Despite being a major research focus in recent years, establishing the diagnosis of the transitional stage of dementia, known as Mild Cognitive Impairment (MCI), with standard neuropsychological assessment instruments has remained challenging. Overall, our findings in a relatively large, community-dwelling cohort evaluated at a specialty memory clinic suggest that the individual screening measures (MMSE and MoCA) typically used in clinical practice to aid in the diagnosis of AD or MCI, offer reasonably high classification and diagnostic accuracy when compared to a more detailed neuropsychological evaluation (CERAD-NB). However, as a brief, stand-alone cognitive screening measure, the MoCA appears to be more sensitive than the older, but more widely used MMSE (Roalf et al., in press; Alzheimer's & Dementia). However, there is still a need for MCI-specific measures to increase the diagnostic specificity between AD and MCI.

My work is by nature interdisciplinary, and utilizes the most recent advances in cognitive neuroscience to understand the cognitive and neural basis of behavior in neuropsychiatric disease and aging. Data gathering and analysis would provide ample opportunities for undergraduate and graduate students to learn and contribute. The extension of my current work has real-world applications as a potential early identifier of neurologic impairment, which may lead to improved interventions. By pairing the knowledge and tools I have gained from this work with my desire to utilize novel scientific approaches and expand my research interests, I look forward to continuing my pursuits in the field of cognitive neuroscience.