**Overview**

The Anxiety and Traumatic Stress Disorders Laboratory conducts research on the neurobiological basis of posttraumatic stress disorder (PTSD) and anxiety disorders, which may help inform diagnosis and lead to new treatment development for these serious and often debilitating conditions.

The lab uses brain imaging technologies to study the function, structure, and chemistry of the brain in both healthy people and patients suffering from PTSD. anxiety, and depression. We also use behavioral paradigms, including tasks that assess learning and memory, so that we can study brain-behavior relationships in

Research questions of interest to our laboratory include:

* What are the cognitive and brain mechanisms underlying the development of persistent trauma-related mental disorders such as PTSD?
* What are the shared versus distinct brain changes across different anxiety and emotional disorders?
* What are the neural mechanisms underlying risk and resilience for emotional disorders? For example, why do some people develop PTSD after experiencing trauma while other people do not?
* Are there brain “markers” of risk and resilience to trauma?
* What are the brain changes that occur during successful treatment of emotional disorders?

### **Ongoing Research Projects at McLean Hospital**

### The primary focus of the Anxiety and Traumatic Stress Disorders Laboratory is understanding the neurobiological basis of posttraumatic stress disorder (PTSD), a and anxiety disorders.

*Cerebral GABA and fear conditioning in PTSD (PI: Rosso)*
This study uses a type of imaging called magnetic resonance spectroscopy (MRS) to examine whether PTSD patients compared with healthy subjects have abnormal levels of certain neurotransmitters in brain regions that mediate fear, and whether these neurochemical alterations are correlated with patients’ performance on a behavioral task of fear learning and extinction.

This will allow the lab to determine whether brain chemicals measured with MRS may hold promise as neurobiological markers of PTSD’s core behavioral features, whether they may inform biologically-based definitions of the disorder, or be used as targets for developing new treatments.

*Hippocampus neurochemistry in PTSD (PI: Rosso)*

This study is investigating levels of the neurotransmitter glutamate in the hippocampus of adults with PTSD, using MRS. There is evidence from animal research that chronic stress and trauma can lead to neuronal atrophy and death in the hippocampus, mediated by excess levels of the glutamate in this brain region.

The study examines whether in vivo glutamate, as detected with MRS, might be a biological marker of PTSD, and whether it is associated with certain types of clinical symptoms as well as measures of stress and anxiety.

*Internet-based cognitive behavioral therapy effects on depressive cognitions and brain function (PI: Rauch)*

This study strives to understand the effectiveness of Internet-based cognitive behavioral therapy (iCBT) treatment on improving depressive symptoms, coping and resilience skills, and cognitive processing. In this study, adults with major depressive disorder are assessed before and after a 10-week course of iCBT.

### Identifying and mapping the brain systems before and after treatment may help researchers guide future attempts to implement iCBT as a large-scale option for treating individuals with depression.

### **External Collaborative Projects**

*Neural Mechanisms of Fear Extinction Across Anxiety Disorders (PI: Milad)*

This study is in collaboration with Mohammed Milad, Ph.D. of Massachusetts General Hospital. The aim of the study is to investigate the neural substrates of fear extinction learning and extinction recall in healthy individuals and in patients with anxiety disorders. In this study, healthy human subjects and patients with anxiety disorders undergo a visual fear conditioning and extinction protocol using functional neuroimaging while measuring psychophysiological responses. We are interested in elucidating neural correlates of fear conditioning and extinction across different anxiety and stress-related disorders, including PTSD, generalized anxiety disorder, social anxiety disorder, specific phobia and obsessive compulsive disorder.

*Neurobiological Basis of Emotional Intelligence (PI: Killgore)*

This study is in collaboration with Scott Killgore, Ph.D. of the University of Arizona.

This study uses functional and structural brain imaging techniques to isolate the brain networks that are critical to adaptive coping, resilience, and emotional intelligence (EQ).  EQ is the ability to accurately perceive and identify emotions in oneself and others, and to understand, use, and manage these emotions to enhance cognitive processes, decision-making, mental health, and social functioning.  It has been suggested that in some cases, these emotional skills and attributes may contribute as much or more to an individual’s ultimate success at work, school, or social pursuits than the more commonly known aspects of cognitive intelligence or “IQ.”  Despite growing appreciation for the importance that emotional intelligence plays in mental health, resilience, and general life success, there is little known about the underlying brain processes associated with these abilities.

### *Bright Light Therapy to Improve Sleep following Mild Traumatic Brain Injury (PI: Killgore)*

This study is in collaboration with Scott Killgore, Ph.D. of the University of Arizona.

### The present study examines the efficacy of Bright Light Therapy in improving cognitive functioning, mood and sleep in individuals who have experienced a traumatic brain injury. We employ functional magnetic resonance imaging as well as diffusion tensor imaging to evaluate brain function and structure before and after a six-week course of light therapy. The goal of this line of research is both to evaluate the effectiveness of this therapy as well as to understand the effects of axonal damage on cognitive and emotional functioning in traumatic brain injury.

*Neuropredictors of cognitive resilience to sleep loss*

This study is in collaboration with Scott Killgore, Ph.D. of the University of Arizona.

Our lab is the first to combine multimodal neuroimaging techniques such as functional MRI, diffusion tensor imaging, resting state functional connectivity and MR spectroscopy to attempt to clarify why some individuals are coping well with sleep loss, while others are vulnerable to insufficient sleep. This study will therefore clarify the role of brain regions such as the medial prefrontal cortex in sleep deprivation and cognitive resilience to sleep loss.  Findings from this study could be used to identify brain regions that using behavioral or pharmacological interventions may specifically be targeted to increase performance in the context of insufficient sleep (e.g., military operations).

*Neurocorrelates of cognitive and emotional health following mild traumatic brain injury*

This study is in collaboration with Scott Killgore, Ph.D. of the University of Arizona.

This study will combine the MR imaging techniques diffusion tensor imaging and resting state functional connectivity to investigate neurocorrelates of cognitive and psychological health in 150 individuals with mild traumatic brain injury at different recovery stages (i.e., two weeks, one month, two months, six months, 12 months) compared to 30 healthy controls. Findings from this study will be used to inform a preliminary model regarding the relationship between white matter integrity and neuropsychological functioning following mild traumatic brain injury.

*Brain Function, and Structure, and Genes in Pediatric Obsessive Compulsive Disorder (PI: Stewart)*

This study is in collaboration with Evelyn Stewart, Ph.D. of the University of British Columbia.

The objectives of this line of work are to combine functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), and genotyping of risk genes in a cross-sectional study of youth with OCD. Specifically, the aims are: (1) To examine functional activation in the regions implicated in OCD (orbitofrontal cortex, striatum, insula), using three fMRI paradigms: a visuospatial priming task, a task-switching task, and an implicit facial affect recognition task, (2) To examine the relationship between brain structure and OCD-susceptibility genotypes in OCD subjects and healthy individuals. We are collecting anatomical and diffusion tensor imaging data, as well as specific allele and haplotype information in previously identified gene susceptibility regions. Individuals will be grouped based on risk genotypes and the risk groups will be compared in terms of regional brain structure. This work is done in collaboration with Evelyn S Stewart MD at the University of British Columbia.

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