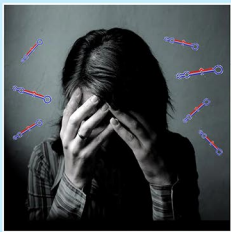




CATHLEEN RUECKEIS

Faculty Research Mentor: Dr. Sarah Linnstaedt
Department of Anesthesiology



Trauma-induced miRNA dysregulation
predicts pain and PTSD

MicroRNA -19b is a Sex-dependent Regulator of Posttraumatic Stress Symptoms and Widespread Pain

Chronic widespread pain (CWP) and posttraumatic stress symptoms (PTSS) are frequent forms of trauma that occur at different rates in women and men. Genetic approaches to study pathways using model organisms and mutants have identified hundreds of genes correlated with CWP/PTSS. Our lab sought to identify microRNAs (miRNAs) that contribute to sex-dependent differences in vulnerability to these outcomes. In the current study, we first identified miRNA that are predicted to regulate CWP/PTSS genes using Monte Carlo simulations. We found that the most significant miRNA predicted to target CWP/PTSS genes was miR-19b, a microRNA that has been shown previously to be regulated in response to estrogen and stress exposure. Next, we assessed whether miR-19b expression predicts CWP/PTSS in a cohort of individuals experiencing motor vehicle collision, one of the most common forms of trauma currently experienced by Americans. Logistic regression demonstrated a sex dependent relationship between initial miR-19b levels following motor vehicle collision and later development CWP/ PTSS. The sex-dependent expression of miR-19b was also observed in a rat model of single prolonged stress, which is thought to be analogous to PTSS. We found miR-19b to be regulated by 17- β -estradiol in rat dorsal root ganglion neurons and amygdala, neural tissues implicated in PTSS. The potential importance of miR-19b to CWP/PTSS pathogenesis is highlighted by results showing that miR-19b can directly bind a number of pain and PTSD associated transcripts including circadian rhythm pathway genes. Together, our results suggest that miR-19b plays a regulatory role in CWP and PTSS development following trauma/stress exposure. Thus, the level of miR-19b expression following motor vehicle collision may predict CWP/PTSD and enable preventative treatment.