

Female WMI rats with genetic stress hyper-reactivity show enhanced contextual fear memory without deficit in extinction of fear

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Abstract

The prevalence of post-traumatic stress disorder is higher in females than males, but pre-clinical models are established almost exclusively in males. This study is aimed to investigate the Stress Enhanced Fear Learning model of post-traumatic stress disorder in females. The model mirrors post-traumatic stress disorder symptomology, whereby prior stress leads to extinction resistant exaggerated contextual fear memory. As stress-reactivity is highly relevant to the study and risk for post-traumatic stress disorder, females of the stress hyper-reactive Wistar Kyoto More Immobile (WMI) and its nearly isogenic control the Wistar Kyoto Less Immobile (WLI) strains were employed. Adult females of both strains were either not stressed or exposed to a two-hour restraint stress, and 48 hours later underwent contextual fear conditioning. Fear memory was measured 24 hours later, followed by extinction trials for a week. Enhanced fear memory following contextual fear conditioning was found in WMIs compared to WLI females and was neither exaggerated by prior stress nor showed extinction deficit. The novel stressor of a glucose challenge test resulted in subtle strain- and prior stress-induced differences in plasma glucose and corticosterone responses. Hippocampal expression levels of learning and memory related genes, glucocorticoid receptor, estrogen receptors, and glucose transporter 1, only changed in WLIs by prior stress. Taken together, results indicate that stress hyper-reactive WMI females do not model post-traumatic stress disorder using the stress enhanced fear learning paradigm, and control WMI females are likely in a state of chronic stress, as additional stressors produced no effects in most measures.

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