Neuropathological Signatures Connecting Early-Life Trauma to Compulsive Eating behavior and Obesity

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Background: Childhood trauma heightens the risk of severe weight gain and adult obesity. However, how early-life traumatic experiences can lead to a lifelong struggle with obesity remain poorly understood. We reported that early-life trauma induces brain changes that may account for the added risk of eating disorders and obesity. Women exhibit an increased prevalence, severity, and burden of trauma and stress-related complications when compared to men. The present study identifies novel sex-dependent neuroadaptations mediating the elevated risk of overeating and obesity in a rat model of early-life traumatic stress.

Methods: Adolescent Lewis rats (n=96, 48 males, 48 females) were exposed to a two-hit model of predator-based psychosocial traumatic stress (PSS) followed by intermittent access to a high-saturated fat obesogenic diet (WD, 41% kcal from fat) or an ingredient-matched control diet (CD, 13% kcal from fat). The PSS paradigm combined unpredictable predator stressors and social instability. We evaluated longitudinally for physiological and behavioral markers of stress. The rats were subsequently exposed to intermittent WD feeding patterns to evaluate dieting-induced binge eating-like behaviors. The estrus cycle was monitored to assess the effects of PSS and WD in estrus cyclicity. Brains were scanned using MRI techniques to identify microstructural changes due to consumption of WD and challenges to their allostatic load.

Results: We found sex-dependent differences in rats that were exposed to traumatic stress and consumed the WD. Female rats displayed robust binge eating-like feeding behaviors when compared to males. This phenotype was associated with heightened traumatic stress-induced anxiety-like behaviors in the elevated plus maze. Interestingly, in female rats exposed to traumatic stress, estrus cyclicity evaluation revealed dysregulated length and variability of stage frequency. In addition, we identified several anatomical and molecular biomarkers that were affected in the rats that were exposed to traumatic stress and the obesogenic diet.

Conclusions: Our findings demonstrate that early-life traumatic stress and intermittent access to an obesogenic WD heightens behavioral vulnerabilities associated with risk for anxiety and stress-related eating disorders. Furthermore, we developed a new research model that recapitulates sex differences in how humans respond to childhood trauma. Given the cumulative effect of early-life adversities and nutrition on brain maturation and function, these findings significantly impact our understanding of neuroadaptations that may contribute to obesity.

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