Abstract

Background: Post traumatic stress disorder (PTSD) is a psychological disorder that often manifests as extreme anxiety and depression upon witnessing a non-threatening stimulus due to previous trauma. Most PTSD patients fail to respond to conventional therapies, necessitating improved treatments. Recent clinical studies have shown beneficial effects of acute 3,4-methylenedioxymethamphetamine (MDMA) administration in PTSD patients. Some of the proposed mechanisms for MDMA's unique effect in helping patients achieve symptom remission include modulating neuroimmune responses and acting through the hypothalamic-pituitary-adrenal (HPA) axis. HPA axis dysregulation has been observed in PTSD patients, marked by a decrease in cortisol and may promote maladaptive fear conditioning. MDMA activates the HPA axis, increasing cortisol levels, though its effects have not been isolated within the HPA axis. The dorsal hippocampus (DH) and amygdala have been associated with learning, memory, and fear-related emotions and behaviors associated with PTSD. However, the specific role that these brain regions play in the stress response pathway has been understudied. Therefore, to improve mechanistic understanding of MDMA as a potential PTSD treatment, its effect on HPA axis modulation in the DH and amygdala must be examined. As corticotropin releasing hormone (CRH) is an upstream regulator of cortisol release, this study hypothesized that MDMA exposure will increase CRH expression in the adult rat DH and amygdala.

Methods: Twenty adult male Sprague Dawley rats received either MDMA or saline, 24 hours and 1 hour prior to brain removal. DH and amygdala tissue was separately obtained via tissue punch. RNA was extracted and purified, and a cDNA library was created for RT-qPCR analysis. qPCR was used with a TaqMan assay to quantify CRH mRNA in the DH and amygdala among

MDMA- and saline-treated animals. The ΔΔCt method was used to compare mRNA expression in these brain regions among both groups.

Results: Compared to saline, MDMA exposure significantly increased CRH expression in the DH ($p=0.0111$) and amygdala ($p=0.0267$).

Discussion: This finding may explain a mechanism by which MDMA may attenuate anxiety-related PTSD symptoms through HPA axis activation. Supplemented with behavioral testing and immunohistochemistry, further investigations could test the effects of MDMA on anxiety-like PTSD symptoms through this pathway.