Individuals with opiate use disorder (OUD) have an increased prevalence of post-traumatic stress disorder (PTSD). Prior research suggests that heroin withdrawal leads to a similar inflammatory phenotype seen in PTSD, involving increased expression of the cytokines tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) from immune cells like microglia and astrocytes. This expression is upregulated in the dorsal hippocampus (DH) and contributes to enhanced fear learning, a rodent model of hyperarousal seen in PTSD. Prognosis and treatment for comorbid OUD and PTSD is poor, but clinical trials involving the psychedelic compound 3,4-methylene-dioxymethamphetamine (MDMA) have shown promising efficacy for treatment-resistant PTSD. MDMA has an immunomodulatory effect in the DH for PTSD, decreasing pro-inflammatory cytokine expression and hyperarousal behaviors. We examined whether MDMA works similarly in heroin withdrawal, focusing on glial fibrillary acidic protein (GFAP), an astrocyte marker, and TNF-α immunoreactivity in the DH. We found no significant differences in GFAP or TNF-α immunoreactivity across treatment groups, potentially indicating that rats did not undergo heroin withdrawal. Future studies may repeat the procedure and collect weight measurements to determine if withdrawal is present, as well as study the influence of MDMA on IL-1β expression and microglial activation.