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Sex Differences in Inflammation and Brain Function in Methamphetamine Use Disorder.

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Abstract

Introduction

Effective treatments for methamphetamine (MA)-use disorder (MUD) are critically needed. Treatment outcomes, however, are variable, especially for women, as sex differences in treatment efficacy have not been adequately studied. With rates of MUD recently tripling in women, it's critical to identify sex-specific mechanisms and targets for tailored medications.

Women exhibit higher levels of inflammation and greater activation in emotional centers of the brain. These differences may explain why women resort to MA more frequently to alleviate negative emotions. Despite evidence of sex differences in biological mechanisms, there is a lack of studies extending these results in MUD. This proposal therefore aims to address the knowledge gap in sex differences in MUD, focusing on inflammation and brain function.

Results

Preliminary results in 22 MUD and 35 controls, the MUD group exhibit higher levels of inflammation (IL-1β: $p = 0.03$, IL-6: $p = 0.07$). A significant sex by group interaction on IL-6 ($p = 0.013$) show women with MUD exhibit the highest levels of inflammatory markers compared to all other groups ($p = 0.013$). Neuroimaging analysis show that women with MUD compared to men exhibit greater connectivity between the reward and emotion centers of the brain. With respect to the relationship between inflammation and brain connectivity, results show that the connectivity between striatum, amygdala, hippocampus and insula ($p < 0.05$, whole-brain corrected) and Il-6 is positive in the MA group and negative in controls. Post-hoc tests reveal that women with MUD drive the positive relationship between IL-6 and striato-limbic RSFC ($p = 0.005$).

Conclusion

Taken together, our data support our hypotheses that women with MUD exhibit higher levels of inflammation and limbic connectivity. This preliminary work has the potential to advance our understanding of sex-specific markers and provide a framework of biological risk factors that influence disease severity and may provide targets for precision medicine.