Exploring the Effects of MDMA on APP and CRH Gene Expression in the Dorsal Hippocampus

UNC PSYCHOLOGY & NEUROSCIENCE

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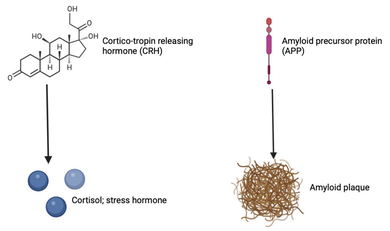
Introduction

- 3,4-methylenedioxymethamphetamine(MDMA), used recreationally as a sensation enhancing party drug, is growing popularity as a pharmacotherapeutic treatment for post-traumatic stress disorder (PTSD), has been linked to increases in cortisol and amyloid pathology, and causes similar dorsal hippocampal (DH) based memory deficits as those seen in Alzheimer's Disease (AD).[1,2,3,4]



- Corticotropin-releasing hormone (CRH) is released as a physiological response to stress and signals Cortisol release.[5]
- Amyloid precursor protein (APP) precedes amyloid pathology, a distinct characteristic of AD.[6]
- AD research has linked CRH and amyloid pathology.[7]
- No direct studies analyzing the effect of MDMA on CRH and APP gene expression.

Methods

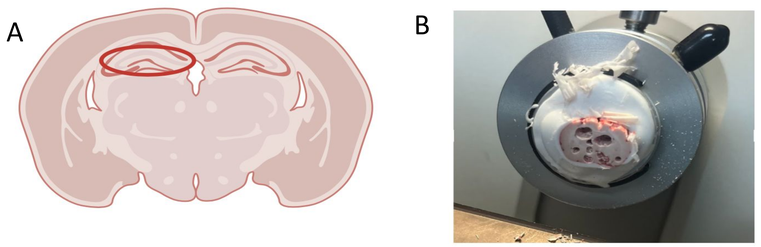


Figure 1. Brain region studied in mice subjects. **A.** Dorsal hippocampus represented on a coronal slice **B.** 1.25mm dorsal hippocampal punches performed using cryostat and tissue punching tools.

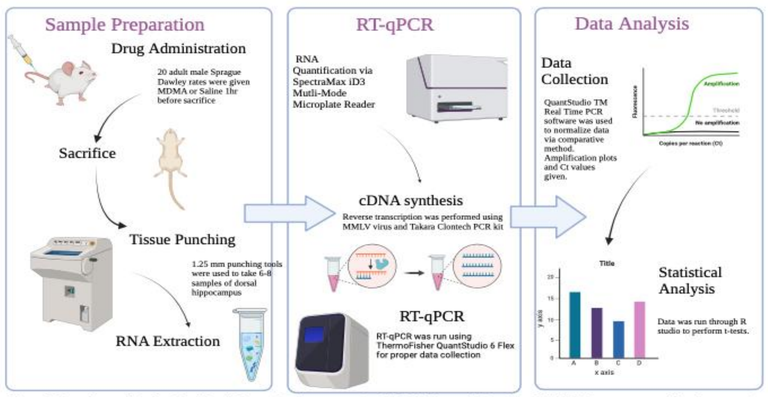


Figure 2. Experimental Design. 20 adult male Sprague Dawley rats were given MDMA before sacrificing. Leica CM1860 UV cryostat was used for subsequence tissue punches of brain tissue. Following tissue punches, RNA was extracted from sample and quantified to ensure proper extraction procedure. cDNA was synthesized via reverse transcription and run through PCR for data collection. Final data analysis was done by performing t-tests on Ct values derived from amplification plots.

Hypothesis

Acute MDMA exposure will *upregulate* both CRH and APP gene expression in the dorsal hippocampus of male rats.

Results

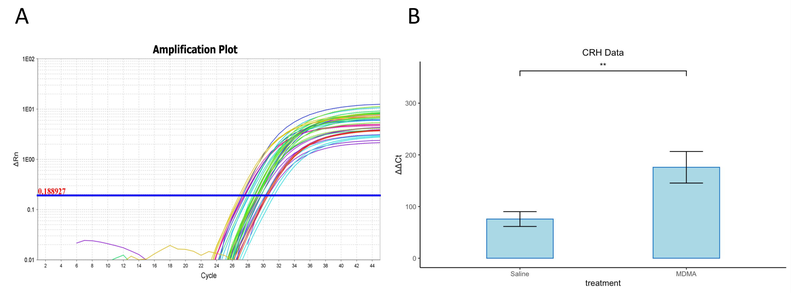


Figure 1. CRH Gene Expression qPCR Data
A. qPCR amplification plot for CRH gene. Results from 60 samples, crossing threshold at a Ct value between 26 and 31. NTP control data shown at bottom. **B.** CRH gene expression levels as a measure of ΔΔCt values. Significant increase in ΔΔCt value of MDMA treated mice as compared to saline (**p < 0.05).

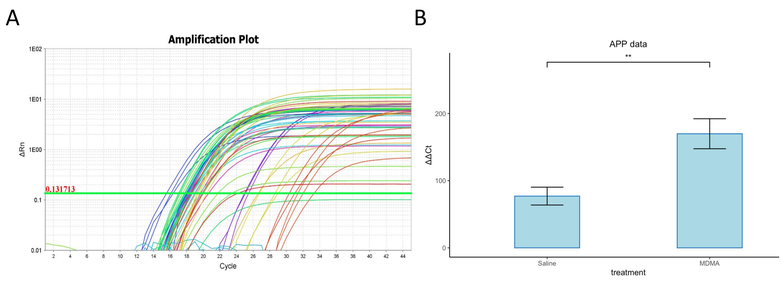


Figure 2. APP Gene Expression qPCR Data
A. qPCR amplification plot for APP gene. Results from 60 samples, crossing threshold at a Ct value between 15 and 34. NTP control data shown at bottom. **B.** APP gene expression levels as a measure of ΔΔCt values. Significant increase in ΔΔCt value of MDMA treated mice as compared to saline (**p < 0.05).

Discussion/Future Directions

- MDMA exposure associated with significant increase in APP & CRH gene expression levels in DH
- Only male rats⟶ both sexes considered in future, or a separate study with females
- Did not use AD animal model
- Explore how higher levels of CRH could be advantageous in everyday life⟶ elevated cortisol can lead to a more relaxed state, better alertness, and activeness
- Further research into relationship between CRH and APP⟶ look to see if elevated stress is associated with more aggregation of amyloid plaques and vice versa
- Continue to conduct research into MDMA being used as therapeutic intervention for PTSD and other disorders ⟶ ensure administration is not causing or associated with long term damage (i.e the onset of neurodegenerative disorders like AD).[1]

References

Acknowledgements

We would like to thank Dr. Donald Lysle for donating the rodent brain tissue and the College of Arts and Sciences as well as the Department of Psychology & Neuroscience for funding and support of the undergraduate NSCI laboratories. We would also like to thank the Office for Undergraduate Research for supporting our course's GRC: Jenny Fiedler who was instrumental in our course R analysis. Finally, we would like to thank Dr. Elena Vidrascu and ULAs Brandon, Ashton, and Neha for all of their help and support this semester!