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

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Background

- **Alzheimer's disease (AD)** is a progressive neurodegenerative disorder that affects memory, cognitive function, and the ability to perform everyday tasks. It is characterized by the accumulation **amyloid plaques**, formed by deposits of the amyloid precursor protein (APP).[1]
- The **dorsal hippocampus (DH)** is significantly involved with spatial and recognition memory, and is shown to be damaged in AD.[2]
- The DH has projections into the **amygdala**, an area responsible for fear and emotional memory.[1]
- Studies showed MDMA exposure **decreases** the production of APP in the cortex.[3]
- Examining the **effect** of MDMA treatment on APP gene expression in the DH and amygdala could help determine if the drug has **therapeutic use** for AD.

Experimental Design

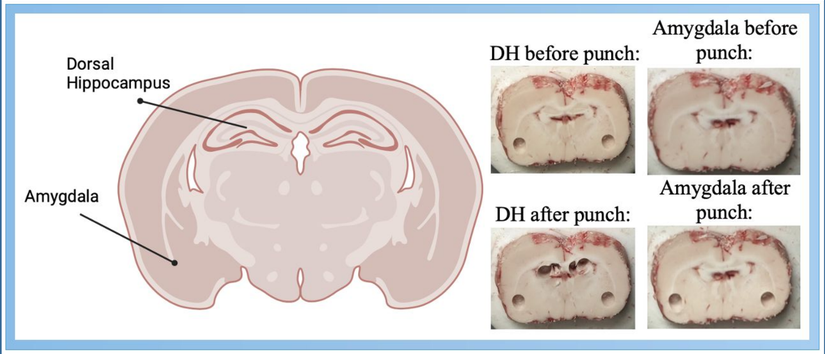

Figure 1. Brain Regions of Interest. The dorsal hippocampus and amygdala were chosen for this study.

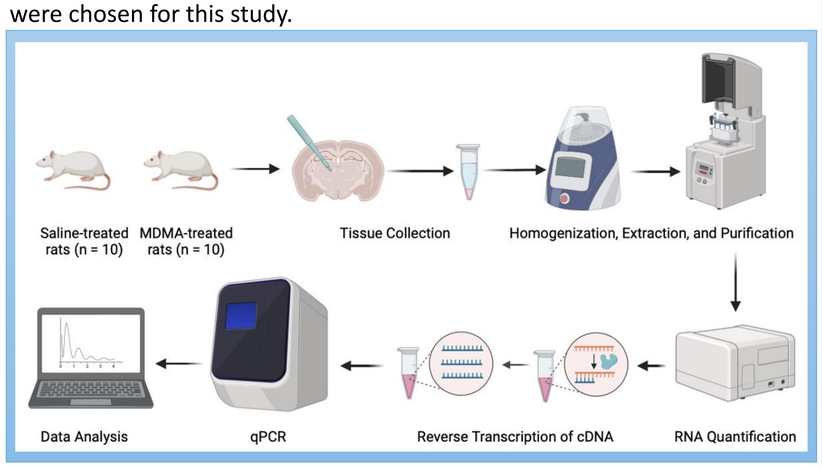

Figure 2. Experimental Schematic. Methods of RNA collection, purification, and quantification shown, with the addition of qPCR and data analysis.

Hypothesis

MDMA-treated rats will exhibit decreased APP gene expression in the dorsal hippocampus and amygdala.

Results

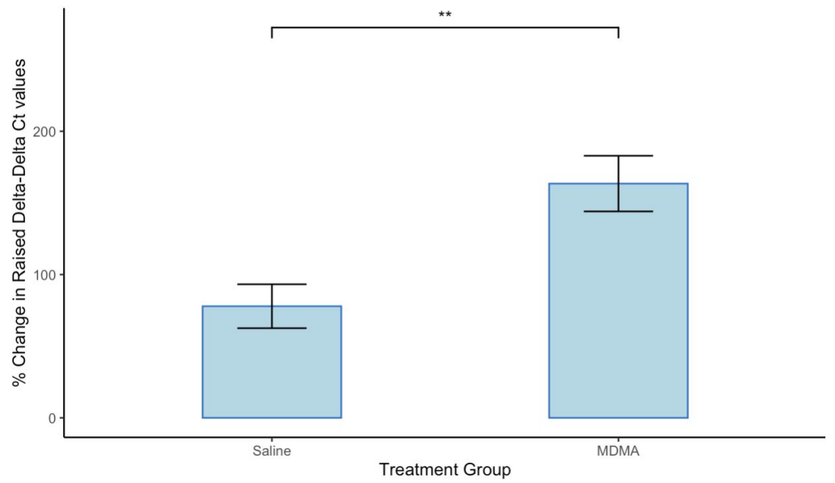

Figure 3. Effect of MDMA Treatment on APP Gene Expression in the DH. The graph shows the % change in $2^{-\Delta\Delta CT}$ values for the gene of interest (APP), across both saline and MDMA treatment groups. A statistically significant increase in APP gene expression was seen in the DH as a result of MDMA treatment. **p < 0.05; error bars represent standard error.

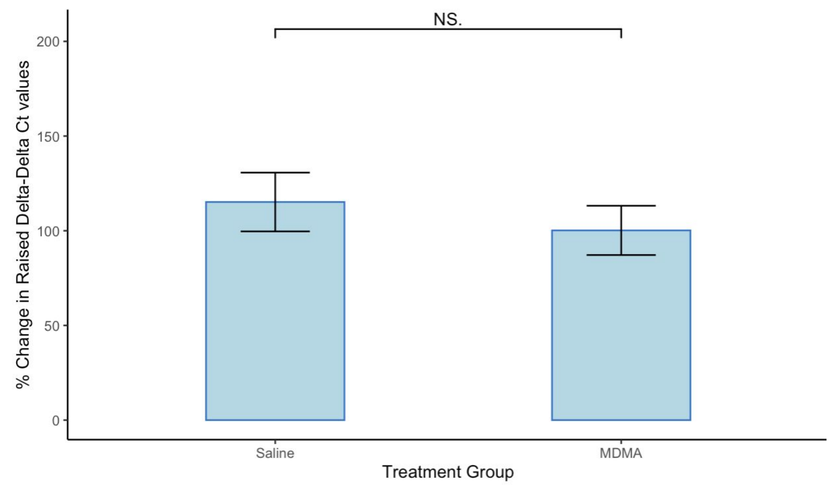

Figure 4. Effect of MDMA Treatment on APP Gene Expression in the Amygdala. The graph shows the % change in $2^{-\Delta\Delta CT}$ values for the gene of interest (APP), across both saline and MDMA treatment groups. No statistically significant difference in APP gene expression was seen in the amygdala as a result of MDMA treatment. N.S. p >> 0.05; error bars represent standard error.

Results, cont.

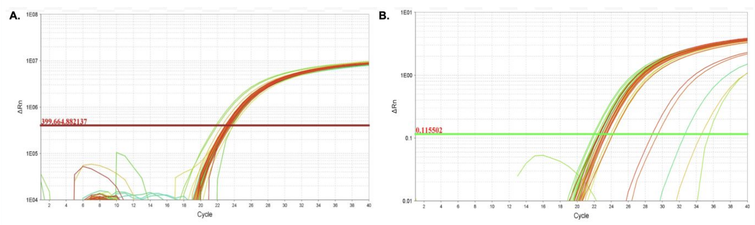

Figure 5. Overall qPCR Amplification Plots. For both the DH and amygdala, 20 qPCR samples were run in triplicate, resulting in 60 lines on the overall amplification plots. The y-axis represents the accumulated fluorescence signal, while the x-axis represents the number of qPCR cycles. Panel A (left) represents the data from DH qPCR; Panel B (right) represents amygdala qPCR data.

Conclusions

- **In MDMA-treated rats, APP gene expression significantly increased in the DH, and was unchanged in the amygdala.**
- Suggests that MDMA could play a role in the abnormal **development of beta amyloid plaques**.
- Results conflict with other studies that have shown MDMA decreases APP in the cortex[3], warranting **further exploration** into the relationship between MDMA and APP gene expression in **memory regions** of the brain like the hippocampus, amygdala, and neocortex.
- Using MDMA therapeutically for AD patients is **not likely**, at least until the effects of MDMA on amyloid plaque deposition are further solidified.
- MDMA has been investigated as a treatment for other conditions including **PTSD**, but further research needs to be done to prevent any possible damage that may arise from **chronic** therapeutic use.[4]

References & Acknowledgements

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References: