COLLEGE OF ARTS AND SCIENCES
Psychology and Neuroscience

Acute MDMA Exposure Increases BDNF Gene Expression in Rat Amygdala and Dorsal Hippocampus

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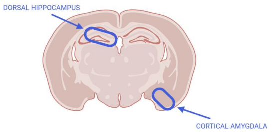
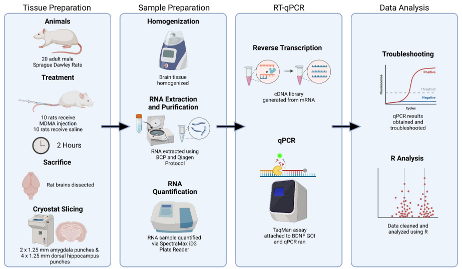
Introduction

- Post Traumatic Stress Disorder (PTSD) occurs after traumatic events and causes anxiety and depression.
- MDMA (3,4-methylenedioxymethamphetamine), commonly known as ecstasy, is a synthetic drug renowned for altering mood and perception, with potential therapeutic applications for PTSD[1], such as decreased fear recalling the traumatic event,
- MDMA's effects on the brain, especially the serotonergic system, can be detrimental[2] from short term mood-swings and fatigue to long-term cognitive impairment.
- Brain-derived neurotrophic factor (BDNF), a crucial protein for neural health, is intricately linked to the serotonergic system and cognitive function[3].
- The amygdala and dorsal hippocampus are key brain regions in fear and memory processing[4].
- Understanding how MDMA influences BDNF expression in the amygdala and dorsal hippocampus is key to understanding its effects on fear learning and PTSD development.

Acute MDMA administration alone will increase BDNF gene expression in the amygdala and dorsal hippocampus of rats.

Experimental Design & Regions of Interest (ROIs)




Tissue Preparation
Animals
20 adult male Sprague Dawley Rats
Treatment
10 rats receive MDMA injection
10 rats receive saline
2 Hours
Sacrifice
Rat brains dissected
Cryostat Slicing
2 x 1.25 mm amygdala punches & 4 x 1.25 mm dorsal hippocampus punches
Sample Preparation
Homogenization
Brain tissue homogenized
RNA Extraction and Purification
RNA extracted using BCP and Qiagen Protocol
RNA Quantification
RNA sample quantified via SpectraMax iD3 Plate Reader
RT-qPCR
Reverse Transcription
cDNA library generated from mRNA
qPCR
TaqMan assay attached to BDNF GOI and qPCR ran
Data Analysis
Troubleshooting
qPCR results obtained and troubleshooted
R Analysis
Data cleaned and analyzed using R

Figures

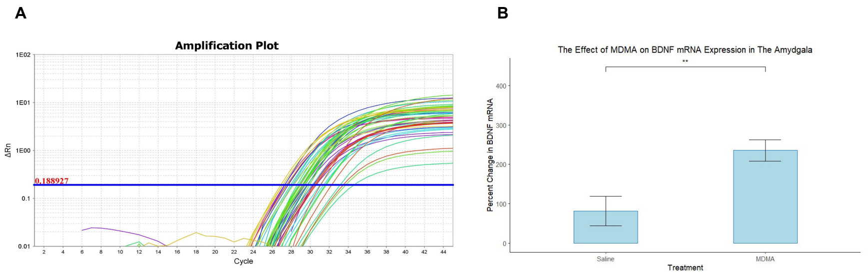


Figure 1. The Difference in Expression of BDNF in The Amygdala Due to MDMA. An RT-qPCR was run to identify differences in BDNF mRNA expression across n = 10 rats for each saline and MDMA administered group (**A**). The percentage change in BDNF mRNA expression is shown for amygdala of MDMA administered rats and saline administered rats ($t = 3.33$, $df = 16.19$, $p = 0.00$). The percent change is based on the mRNA expression of GAPDH in the amygdala (**B**). Legend: MDMA, 3,4-methylenedioxymethamphetamine. BDNF, brain derived neurotrophic factor. ** $p<0.05$.

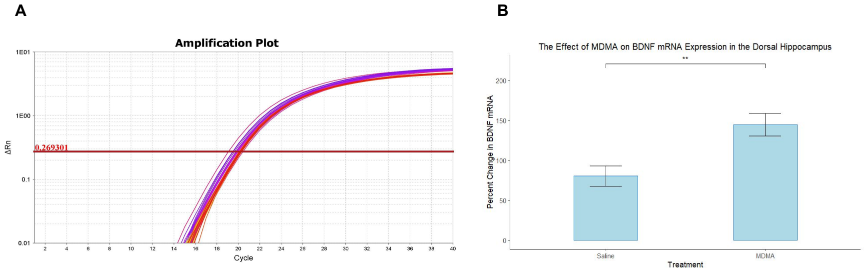


Figure 2. The Difference in Expression of BDNF in The Dorsal Hippocampus Due to MDMA. An RT-qPCR was run to identify differences in BDNF mRNA expression across n = 10 rats for each saline and MDMA administered group (**A**). The percentage change in BDNF mRNA expression is shown for dorsal hippocampus of MDMA administered rats and saline administered rats ($t = 3.36$, $df = 17.84$, $p = 0.00$). The percent change is based on the mRNA expression of GAPDH in the amygdala (**B**). Legend: MDMA, 3,4-methylenedioxymethamphetamine. BDNF, brain derived neurotrophic factor. ** $p<0.05$.

Results and Conclusions

- MDMA, administered to the amygdala and dorsal hippocampus lead to a statistically significant increase in BDNF mRNA expression in those regions compared to just saline.
  - *In the **amygdala**, the MDMA administered group had **significantly greater** BDNF expression (**Figure 1B**)*
  - *In the **dorsal hippocampus**, the MDMA administered group had **significantly greater** BDNF expression (**Figure 2B**)*
- The increase in BDNF in both the amygdala and dorsal hippocampus suggests that BDNF is intrinsically correlated with MDMA's mechanism of action and, in particular, memory encoding and extinction.

Future Implications and Limitations

- Deeper understanding of MDMA's impact on molecular pathways in the brain, particularly in regions associated with emotional processing and memory formation.
- Increased BDNF expression in the amygdala and dorsal hippocampus suggests a potential mechanism through which MDMA may facilitate therapeutic outcomes in PTSD treatment.
- Development of therapies for PTSD that lack the side effects of MDMA.
- Development of targeted therapies that modulate BDNF expression for disease and conditions with low BDNF, such as Alzheimer's Disease[5] and memory deterioration from aging[6].

Limitations:

- **Only male rats** - Excludes potential gender-specific responses, limiting the generalizability of the findings.
- **Rats were not models for PTSD** - Limits the reliability of the findings in accurately contextualizing stress-related disorders
- **One dosage** - Fails to explore dose-dependent effects.
- **Single tissue collection time** - Overlooks dynamic biological changes over time.

Future Directions:

- Determine how BDNF expression in PTSD rat models responds due to 1 mg/kg of MDMA to confirm if MDMA alone is enough to increase BDNF expression.
- Analysis of BDNF expression in rats over various time points.

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References

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