Effects of Acute MDMA Exposure on Sert1, Psd-95, 5-Ht2ar, and Grin2b in the Dorsal Hippocampus

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Background

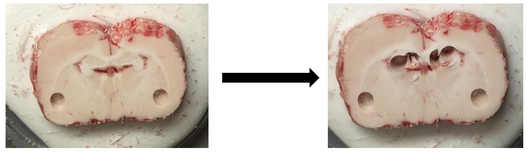
- MDMA has been studied as a possible treatment for PTSD[8]
  - Clinical trials have shown that it has better therapeutic effects on severe PTSD than SSRIs[5]
- The mechanism behind fear extinction learning associated with PTSD treatment with MDMA is unknown[2]
- Dorsal Hippocampus is known to be involved in memory[2]

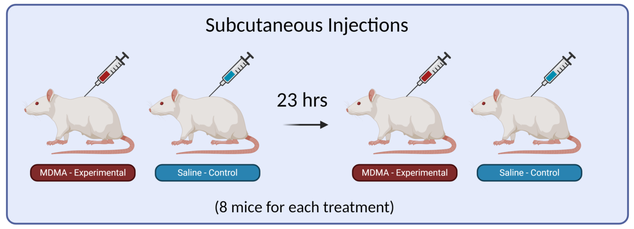
Genes of Interest based on previous studies on fear learning:

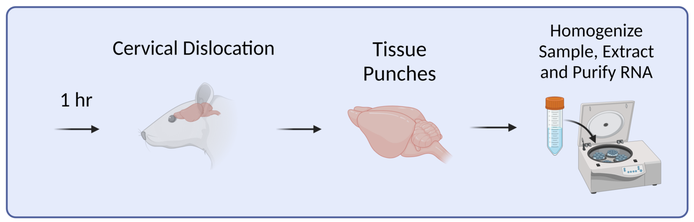
- SERT1 (serotonin transporter) knockout rats displayed enhanced acquisition of fear and delayed extinction of fear[4]
- PSD95 (scaffolding protein) is required for fear memories to be maintained, hallucinogens may act through PSD95 mediated signaling[3]
- 5-HT2AR (serotonin receptor) antagonists led to blocking of enhanced fear memory while agonists led to enhanced fear memory[9]
- GRIN2B (NMDA receptor subunit) found to interact with serotonin receptors to influence synaptic plasticity[1]

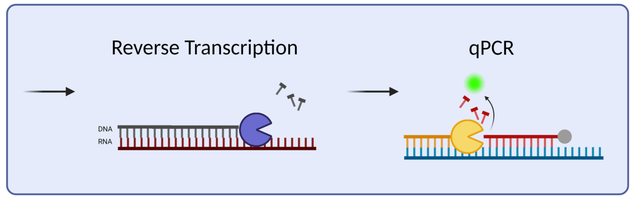
Methods

ROI: Dorsal Hippocampus









Results

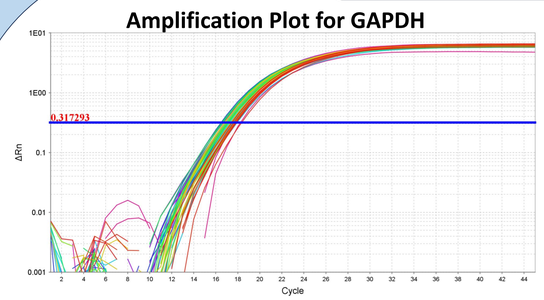


Figure 1. Amplification Plot for GAPDH using Taqman primer Rn01775763_g1 in the dorsal hippocampus with an average CT value of 22.814.

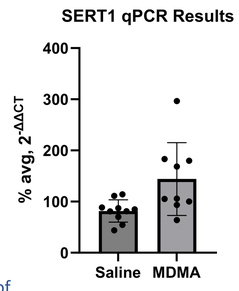


Figure 2. SERT1 qPCR results. The average percent change in expression of SERT1 for the MDMA and Saline groups were 144.017 and 81.634, respectively. The p value for an unpaired t-test was 0.0109, showing statistically significant results. SERT1 had a higher level of expression in the MDMA group compared to the Saline group.

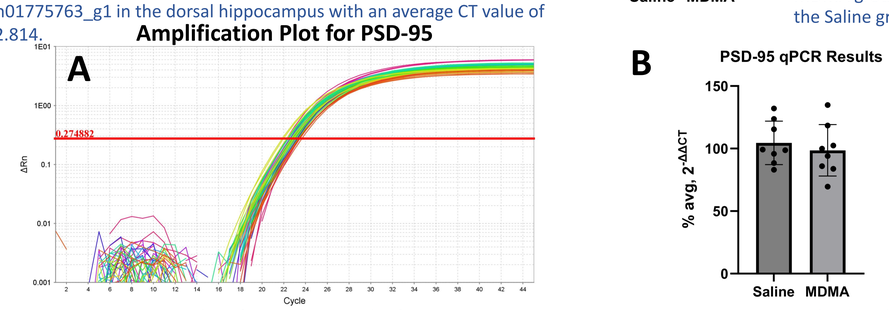


Figure 3. PSD-95 qPCR results. A) Amplification Plot for PSD-95 using Taqman primer Rn00571479_m1 in the dorsal hippocampus. **B)** The average percent change in expression of PSD95 in the dorsal hippocampus for the MDMA and Saline groups were 98.608 and 104.552, respectively. The p value for an unpaired t-test was 0.4931, showing non-significant results, PSD95 had no significant differences in level of expression in the MDMA group compared to the Saline group.

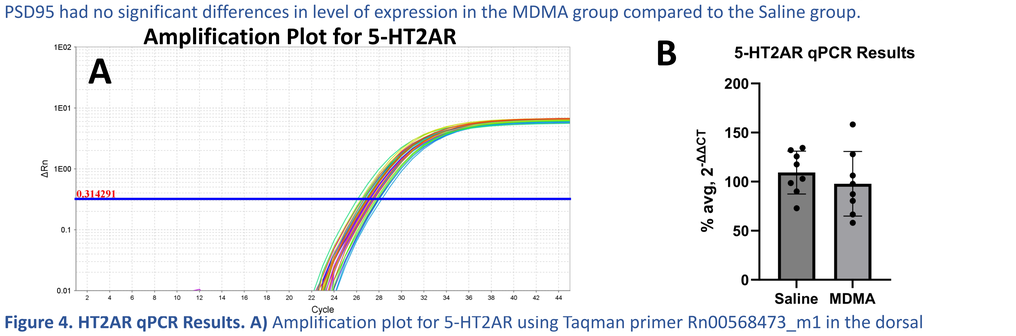


Figure 4. HT2AR qPCR Results. A) Amplification plot for 5-HT2AR using Taqman primer Rn00568473_m1 in the dorsal hippocampus. **B)** The average percent change in expression of PSD95 for the MDMA and Saline groups were 97.817 and 109.308, respectively. The p value for an unpaired t-test was 0.3298, showing non-significant results, PSD95 had no significant differences in level of expression in the MDMA group compared to the Saline group.

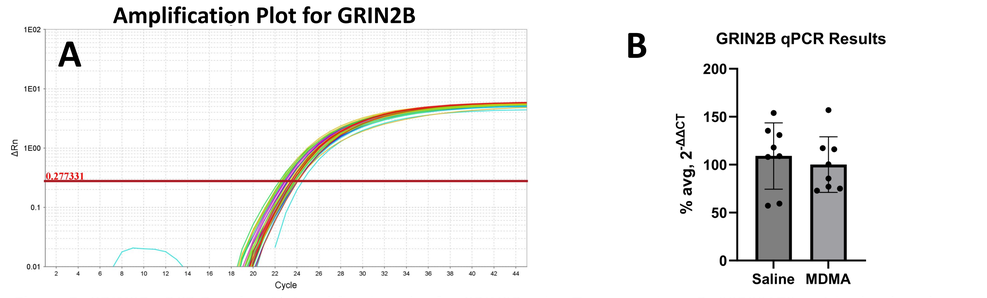


Figure 5. GRIN2B qPCR Results. A) Amplification plot for GRIN2B using Taqman primer Rn00589173_m1 in the dorsal hippocampus. **B)** The average percent change in expression of PSD95 for the MDMA and Saline groups were 100.145 and 109.018, respectively. The p value for an unpaired t-test was 0.5873, showing non-significant results, PSD95 had no significant differences in level of expression in the MDMA group compared to the Saline group.

Discussion

- SERT1 expression increased in rats treated with MDMA compared to control rats treated with saline (control)
- There were no significant changes in expression of GRIN2B, PSD-95, or 5-HT2AR in rats between the MDMA and saline (control) groups
- Upregulation of SERT1 in the dorsal hippocampus with administration of MDMA would have the opposite effect of SSRIs on serotonin levels, which may contribute to the differences seen in patient outcomes for those prescribed MDMA vs SSRIs
- GRIN2B, a subunit of the NMDA receptor, and PSD-95 are involved in LTP and synaptic plasticity, both long term changes and changes in gene expression may not be seen with acute MDMA exposure[7]
- 5-HT2AR has been shown to be associated with long-term learning associated with stressful situations and changes in gene expression may not be seen with acute MDMA exposure[6]

Future Directions:

- Look at more genes related to acute MDMA exposure
- Conduct qPCR analysis of GRIN2B, PSD95, 5-HT2AR in rodents that have had chronic exposure to MDMA

References

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