3,4-methylenedioxymethamphetamine (MDMA) impairs the extinction and reconsolidation of fear memory in rats

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Experimental Goal

To characterize the effects of MDMA on extinction, relapse, and reconsolidation of conditioned fear memory in rats.

Background

Traumatic memories are a central component of post-traumatic stress disorder (PTSD). Current therapeutic strategies for PTSD thus focus on either inhibition of fear memories, or establishment of stronger competing memories.

Currently, these strategies have demonstrated poor long-term efficacy.

In human studies, psychotherapy paired with moderate-dose MDMA has shown promise in reducing symptoms of PTSD, but the means by which MDMA reduces fear is unknown.

MDMA administered during psychotherapy could enhance fear extinction (learning that trauma cues no longer predict threat), prevent relapse (return of fear after the passage of time or in environments different from where extinction took place), or interfere with fear memory reconsolidation (the process of strengthening fear memories after recall).

Exercise Behavioral Neuroscience Laboratory

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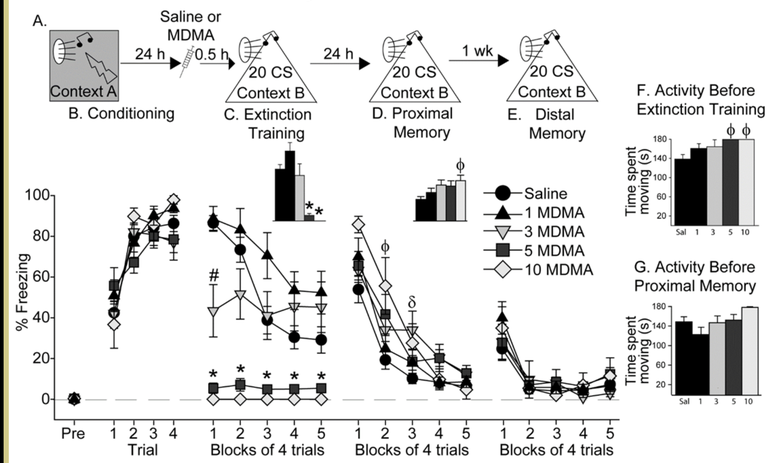
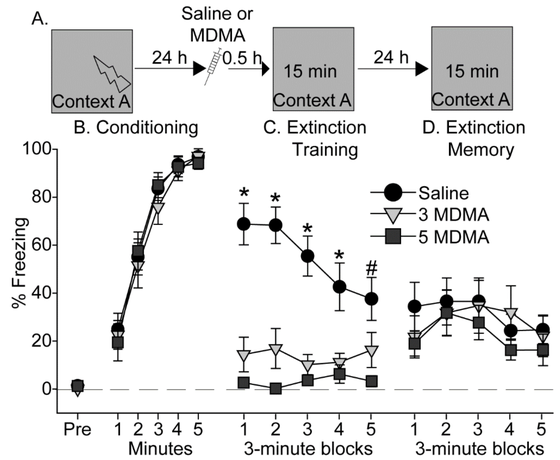
MDMA increases locomotor activity during fear extinction and impairs extinction retention at high doses

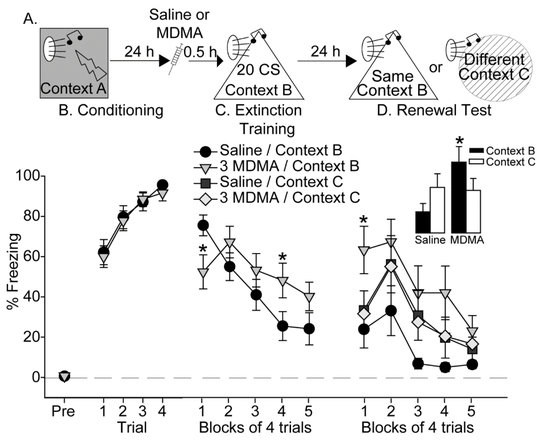
Auditory Fear Extinction



Contextual Fear Extinction

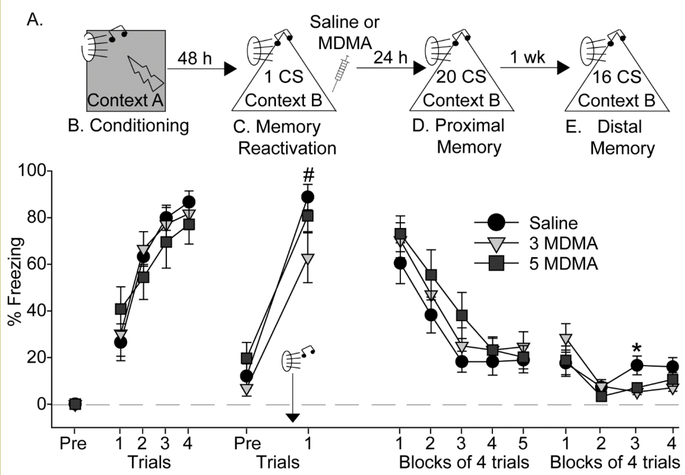


MDMA has no effect on renewal of auditory fear conditioning

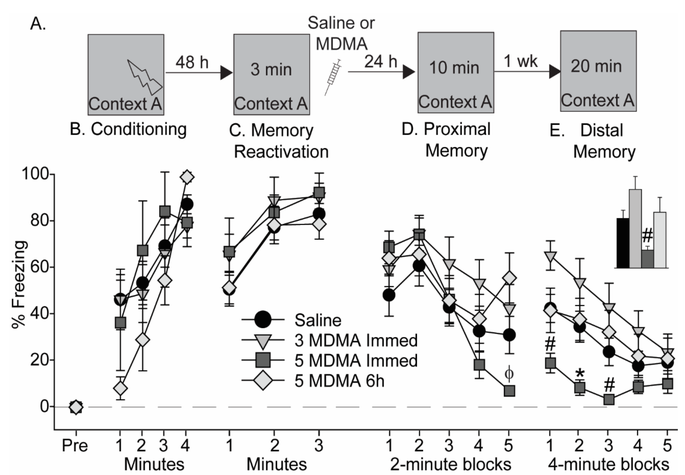


MDMA administered immediately after conditioned fear memory recall impairs fear memory reconsolidation

Auditory Fear Reconsolidation



Contextual Fear Reconsolidation



Conclusions

- MDMA fails to facilitate fear extinction, and at higher doses, interferes with fear extinction recall.
- Despite impaired extinction recall at the proximal time point, MDMA has no impact on the relapse (spontaneous recovery or renewal) of conditioned fear after extinction.
- MDMA interferes with fear memory reconsolidation, and these effects are delayed and persistent.
- Results suggest that MDMA could augment psychotherapy by interfering with reconsolidation of traumatic memories that resurface during MDMA-assisted psychotherapy.
- Further research is needed to elucidate the neuro-chemical mechanisms by which MDMA impairs conditioned fear memory reconsolidation.