Effects of S-methamphetamine, 3,4-methylenedioxymethamphetamine (MDMA) and its enantiomers on place conditioning in C57BL/6 and BTBR T+Itpr3tf/J mice

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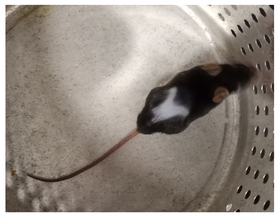
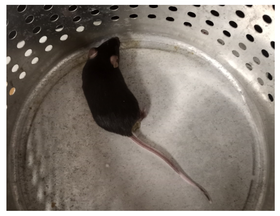
INTRODUCTION

- 3,4-methylenedioxymethamphetamine (MDMA) elicits psychostimulant-like and psychedelic-like effects, and it and its analogues are being explored as potential treatments for social withdrawal secondary to Autism spectrum disorder (ASD).
- We used place conditioning to investigate abuse-related effects of methamphetamine (S-METH), MDMA, and its enantiomers in C57 and BTBR mice.
- The BTBR T+Itpr3tf/J (BTBR) mouse is an inbred strain generated from C57BL/6 (C57) stock, and is the "gold standard" model for ASD research.

BTBR mouse



C57 mouse



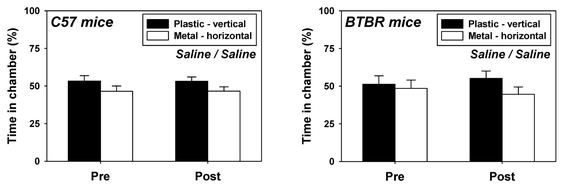
APPARATUS

- We built 2-chamber CPP boxes differentiated by floor texture (rough black plastic vs steel punch plate) and wall pattern (vertical vs horizontal stripes).
- Chambers were connected by a hallway equipped with photobeams to detect entries.
- An associated computer calculated time spent in each chamber and chamber entries.

METHODS

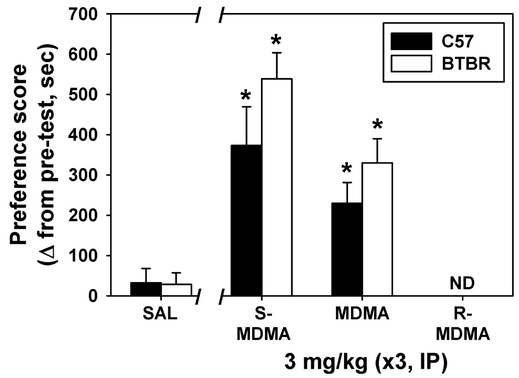
- An initial preference test was conducted prior to drug exposure. Mice were then assigned to receive drug on their non-preferred side (if there was one).
- Across the next 3 days, a total of 3 saline and 3 drug pairings occurred. Thirty min after injection, mice were placed into the appropriate compartment, and remained there for 30 min.
- Saline pairings occurred in the mornings, and drug pairings were conducted in the afternoons.
- A final preference test was then conducted, identical to the initial preference test.
- All tests were conducted under low light conditions.

RESULTS - SALINE

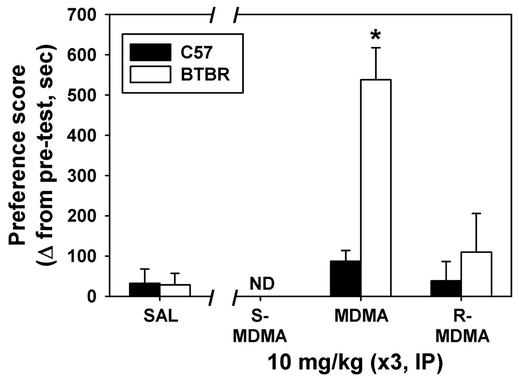


- A group of C57 and BTBR mice received saline on both sides of the apparatus to determine any potential strain differences.
- No apparent initial preference was observed for either compartment, and no preference emerged with repeated exposure.
- No strain difference in apparent initial compartment preference was observed, and no strain difference emerged with repeated exposure.

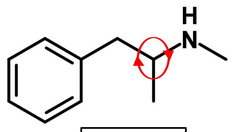
RESULTS - MDMA



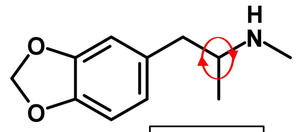
- Pairings with 3 mg/kg S-MDMA and racemic MDMA elicited significant place preferences in C57 and BTBR mice.
- The effects of R-MDMA were not determined at this unit dose in either strain.



- Pairings with 10 mg/kg racemic MDMA induced a significant place preference only in BTBR mice.
- R-MDMA did not induce place preference in either strain.
- The effects of S-MDMA were not determined at this unit dose in either strain.

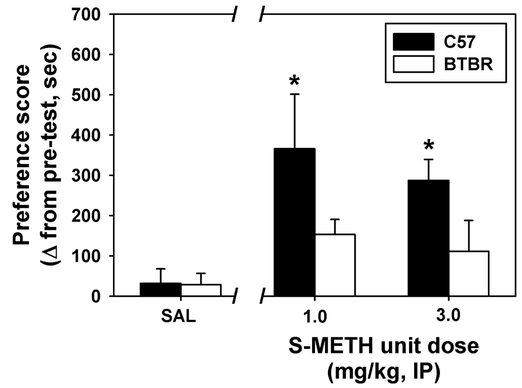


METH



MDMA

RESULTS – S-METH



- Pairings with S-METH elicited significant place preference only in C57 mice at both the 1.0 and 3.0 mg/kg unit doses.

CONCLUSIONS

- These studies show that MDMA elicits abuse-related CPP in mice that is dependent on the presence of the S-enantiomer.
- BTBR mice exhibit more robust CPP with MDMA than C57s, but may be resistant to METH-elicited CPP.
- Importantly, these studies suggest that novel formulations of MDMA biased toward the R- enantiomer may elicit reduced abuse-related effects.

FUTURE DIRECTIONS

- Effects of other MDMA-like entactogens and their component enantiomers should be determined in BTBR and C57 mice.
- Apparent sensitivity of BTBR mice to MDMA should be investigated further.

ACKNOWLEDGEMENTS

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