Investigating the Effects of PMAT Deficiency on Cocaine- and Amphetamine-Induced Locomotor Sensitization

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Reduced function of the transporter **PMAT** contributes to **D-amphetamine-**induced **stereotypy,** but not **locomotion**

Background

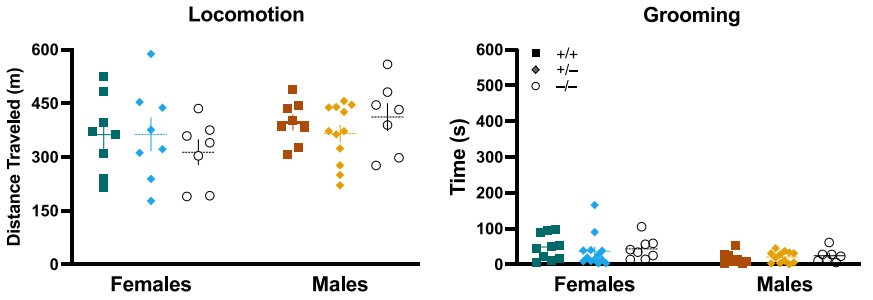
- PMAT = Plasma membrane monoamine transporter
- PMAT takes up dopamine and serotonin faster than other monoamine transporters
- Functional contribution of PMAT emerges when higher affinity transporters are impaired
- No studies have evaluated the contribution of PMAT to psychostimulant-induced locomotor sensitization with cumulative doses
- Mice constitutively deficient in PMAT were used, because no selective inhibitor of PMAT currently exists
- We **hypothesized** that relative to wildtype (+/+) controls, **mice with reduced (+/-) or ablated (-/-) PMAT function would exhibit *increased* cocaine- and D-amphetamine-induced locomotor sensitization**

Methods

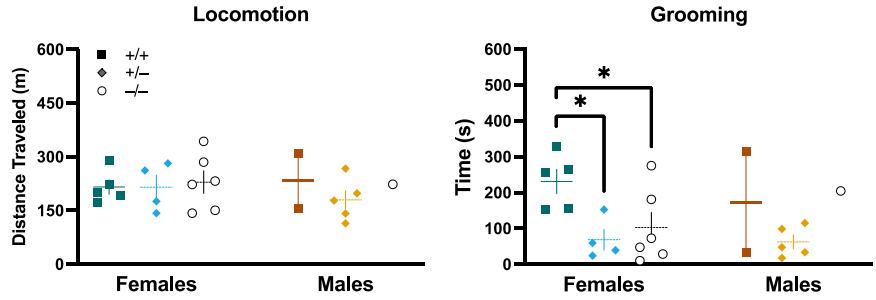
- Adult male & female PMAT-deficient mice
- Cocaine- and D-amphetamine-induced locomotor sensitization
- Cumulative doses of 5-40 or 0.27—9.98 mg/kg, respectively
- Mice injected every day for cocaine, and every 3 days for amphetamine; total of 5 injection days
- Graphed data are from the final injection day: day 5 for cocaine and day 13 for D-amphetamine
- Stereotypy data are from the highest dose on the final injection day
- Data analyzed with two-way ANOVAs and Dunnett's post-hocs; ***p<0.05**
- Note: lower amphetamine doses were explored, but those data are not presented here.

Results

PMAT Deficiency does not Influence **Cocaine**-Induced Locomotor Sensitization or Grooming Behavior



PMAT Deficiency does not Affect **D-Amphetamine**-Induced Locomotor Sensitization, but does Attenuate Grooming Stereotypy in Females



Summary & Conclusions

- PMAT deficiency sex-selectively attenuates D-amphetamine-induced grooming stereotypy in **females**
- PMAT is not necessary for the effects of cocaine or D-amphetamine
- PMAT might sex-specifically contribute to select behavioral effects elicited by D-amphetamine
- Natural genetic variation in human PMAT function might influence sex-specific responses to D-amphetamine

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