Sex Differences in Anxiety-Like Behaviors During Withdrawal from Morphine

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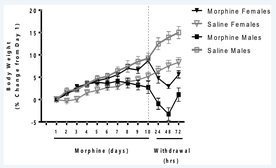
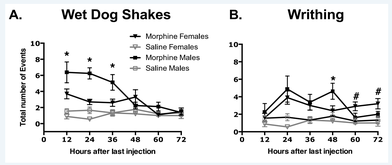
Introduction

- Most knowledge of opioid withdrawal comes from studies on males.
- Studies on sex differences or opioid withdrawal in females are lacking.



- Body weight decrease after morphine withdrawal (W/D) in both sexes (Bobzean et al., 2019).



- Morphine withdrawal induces somatic symptoms of withdrawal in both sexes (Bobzean et al., 2019).

Materials and Methods

Animals

- 29 adult Long Evans rats (Males: *N* = 17, Saline – *n* = 9, Morphine – *n* = 8; Females: *N* = 12, Saline – *n* = 6, Morphine – *n* = 6)

Drugs and Dose

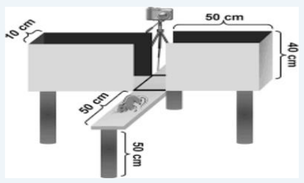
- Morphine sulfate in 0.9% saline – Injected subcutaneously (s.c.) twice daily for 10 days (escalating dose from 2.5 mg/kg to 40 mg/kg)
- Saline controls were injected with 0.1 mL/kg with 0.9% saline s.c.

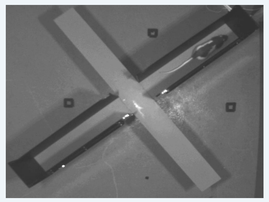
Elevated Plus Maze (EPM)

- Time spent and entries into open and closed arm - measures of anxiety-like behavior

Body weight

- Somatic marker for morphine withdrawal

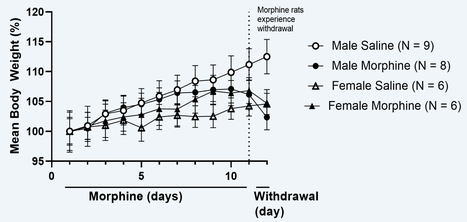


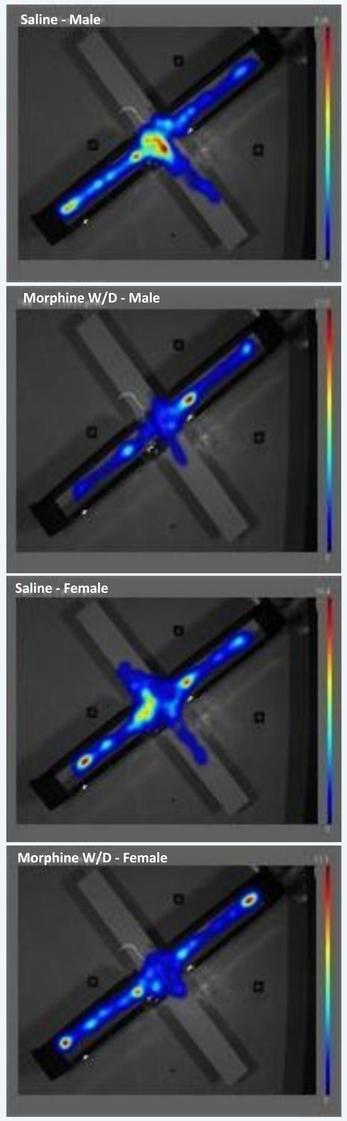


Elevated Plus Maze setup

Results

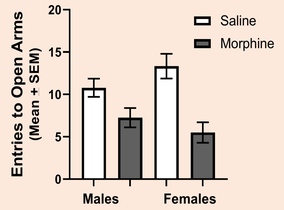
Morphine W/D decreased body weight in males and females



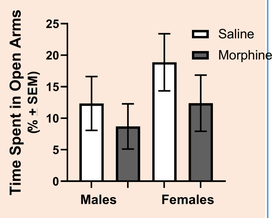


Results

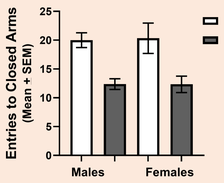
Entries into open arm decreased during Morphine W/D



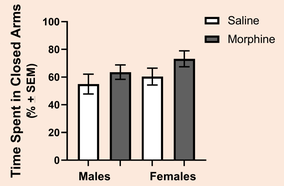
Time spent in open arm decreased during Morphine W/D

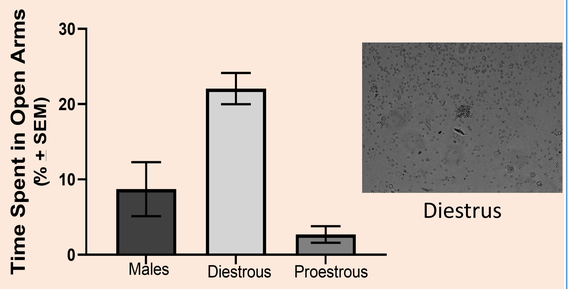


Entries into closed arm decreased during Morphine W/D



Time spent in closed arm did not change during Morphine W/D





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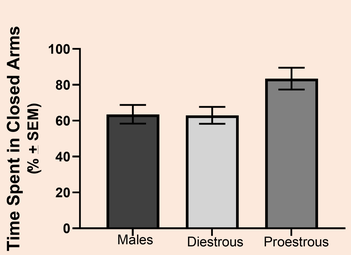

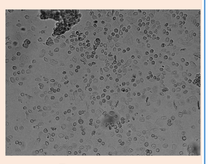

Proestrous

Discussion

- Morphine treated rats anxiety-like behavior in EPM shows animal model of addiction beneficial for studies
- Next step, investigating drugs to alleviate anxiety in a rodent model

Conclusions

- EPM good measure of anxiety-like behavior; anxiety important self-reported feature with human addicts
- Females' anxiety differs by stage of estrous cycle; important to consider sex and hormone levels with morphine withdrawal

Future Directions

- Western blot
- Additional Estrous Cycle Data
- Ketamine

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