The Dopamine D3 Agonist Pramipexole Decreases Symptoms of Morphine Withdrawal in Opioid-Tolerant Animals

Alissa Davis[1], Dylan Marshall[2], Martina De Cristofaro[2], Stefan Clemens, PhD[2], Kori Brewer PhD[1,2].

Brody School of Medicine, East Carolina University, Department of Emergency Medicine[1] and Physiology [2], Greenville, NC 27834

INTRODUCTION

- Despite dangerous side effects, opioids remain the standard of care for moderate to severe pain because they are highly effective analgesics with few alternatives.[1]
- We have shown that using a dopamine 3 receptor agonist as an adjuvant to morphine can decrease the opioid dose needed to achieve analgesia and can prevent the development of tolerance to morphine in rats.
- It is not known if this same adjuvant can be used to safely reduce the dose of opioid after tolerance has developed which may decrease tolerance, dependence, and withdrawal.

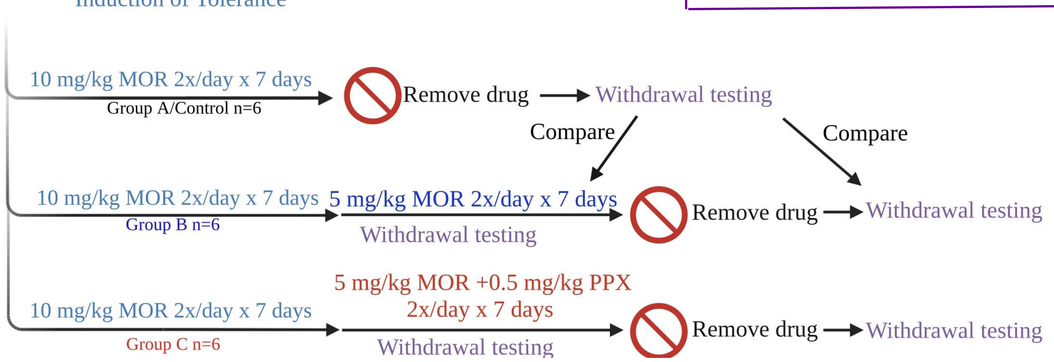
OBJECTIVE

- Determine if using the dopamine receptor agonist pramipexole (PPX) as an adjuvant can attenuate opioid withdrawal in animals that are opioid tolerant.

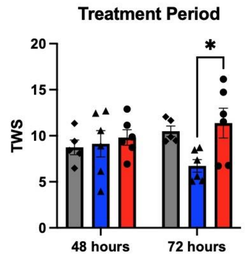
BACKGROUND LITERATURE

MATERIALS & METHODS

- Morphine tolerance was induced in 18 male Long-Evans rats
- Withdrawal symptoms were measured and compared across groups at each change in drug regimen.

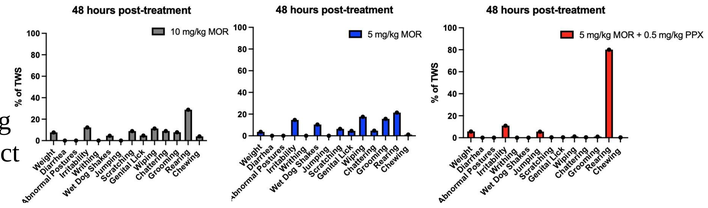


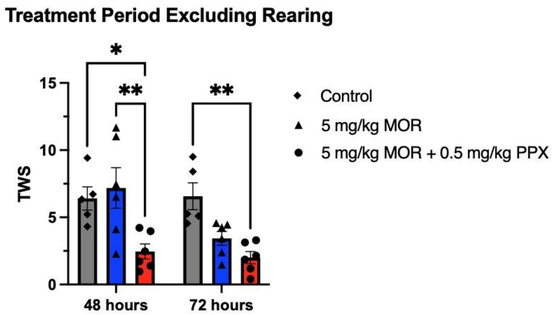
RESULTS



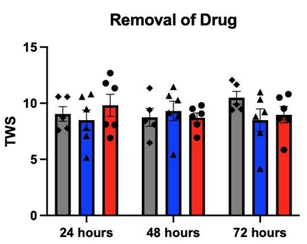
1. Total withdrawal scores (TWS) were similar between control vs. either treatment group 48 and 72 hours after the onset of treatment in morphine tolerant animals.

2. In contrast to the other groups, the TWS for PPX treatment group was driven almost exclusively by rearing behavior - a known side effect of PPX.

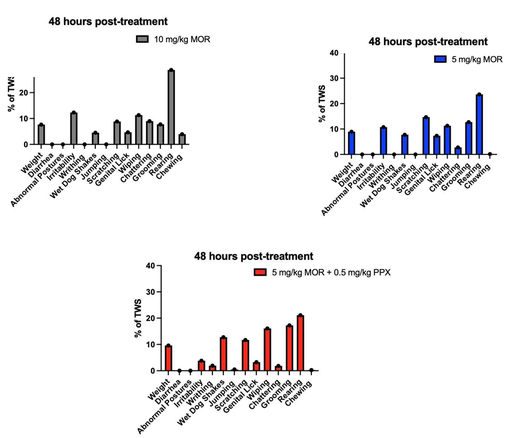




3. When controlling for rearing behaviors there was a significant reduction in withdrawal symptoms in the PPX-treatment group.



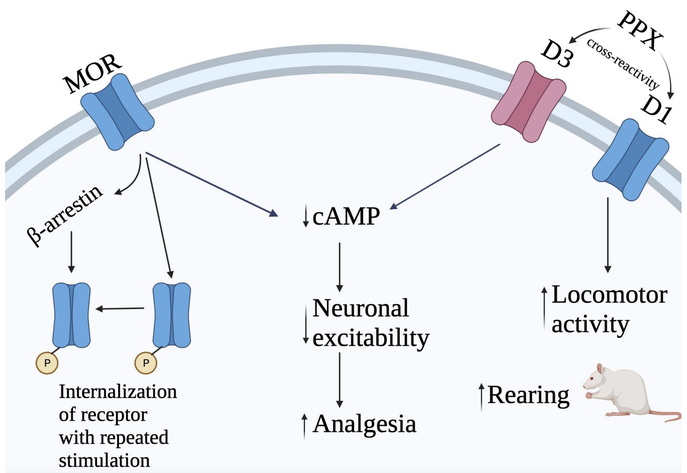
4. No significant differences existed between groups in TWS or behavioral profile after removal of all drug.



SUMMARY & CONCLUSIONS

- By adding pramipexole, we were able to reduce the dose of morphine given to a tolerant animal without inducing withdrawal symptoms.
- The addition of pramipexole did induce increased locomotor activity, suggesting the need to lower the dose of that drug in future studies.
- This preclinical data supports investigating a role for pramipexole in opioid replacement therapy.
- Signs of withdrawal were still evident when drug treatments were stopped in all groups.
- Future research should investigate if a stepwise decrease in doses of the morphine/pramipexole combination over time can also reduce withdrawal after complete removal of drug in morphine tolerant animals.

5. Model of morphine and PPX interactions at cellular level



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- [1]NIDA. 2021, June 1. Prescription Opioids DrugFacts. Retrieved from https://nida.nih.gov/publications/drugfacts/prescription-opioids on 2023, July 18

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