

# Behavioral effects of Pre-Natal Opioid Exposure in Mice



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## Background

- If a mother is taking opioids while she is pregnant, it can cause cognitive and developmental effects to the exposed child (Fodor et al. 2014) and neonatal abstinence syndrome (NAS).
- Buprenorphine is an opioid that is commonly given to addicted mothers to substitute the harmful opioid drug they are abusing and to lessen the withdrawal symptoms and the chance of death.
- The effects of maternal buprenorphine in mice are unknown, although studies in humans show, “reduced performance on tests of cognitive function compared to unexposed children” (Konijnenberg and Melinder 2011)

## Hypothesis

- Morphine and buprenorphine treatment during pregnancy will cause long term cognitive effects in the offspring

## Methods

- The mice used were bred in house and are a hybrid of a male DBA mouse and a female C57BL6 mouse strain.
- The dams were injected daily with a dose of saline, morphine, or buprenorphine until the pups were weaned. The pups were split into 3 groups based on what drug they were exposed with 12 mice per group
- Open Field Test: Each mouse was placed in an open chamber and was able to roam around the chamber for five minutes. This test was run for two days. The first day the mice were exposed to red light and 24 hours later they were exposed to white light.
- Social Interaction Test: The mice were placed in a cage with a DBA mouse with no other distractions other than the new mouse for 10 min.
- Novel Object Recognition Test: The mice were shown two of the same objects and were placed into the same chamber as the open field test. 24 hours later the mice were placed in the same chamber again, however one of the objects was different from the one previously seen.
- The mice were placed in an operant testing chamber to complete various cognitive tests, starting with fixed ratio 1 (FR1).
- qPCR was conducted on a select array of genes

## Results

Fig 1. (a) MO group significantly expressed more itgam gene in the amygdala (b) MO group significantly expressed more tlr2 gene in the amygdala, (c) no significant difference between groups for tlr4 gene expression

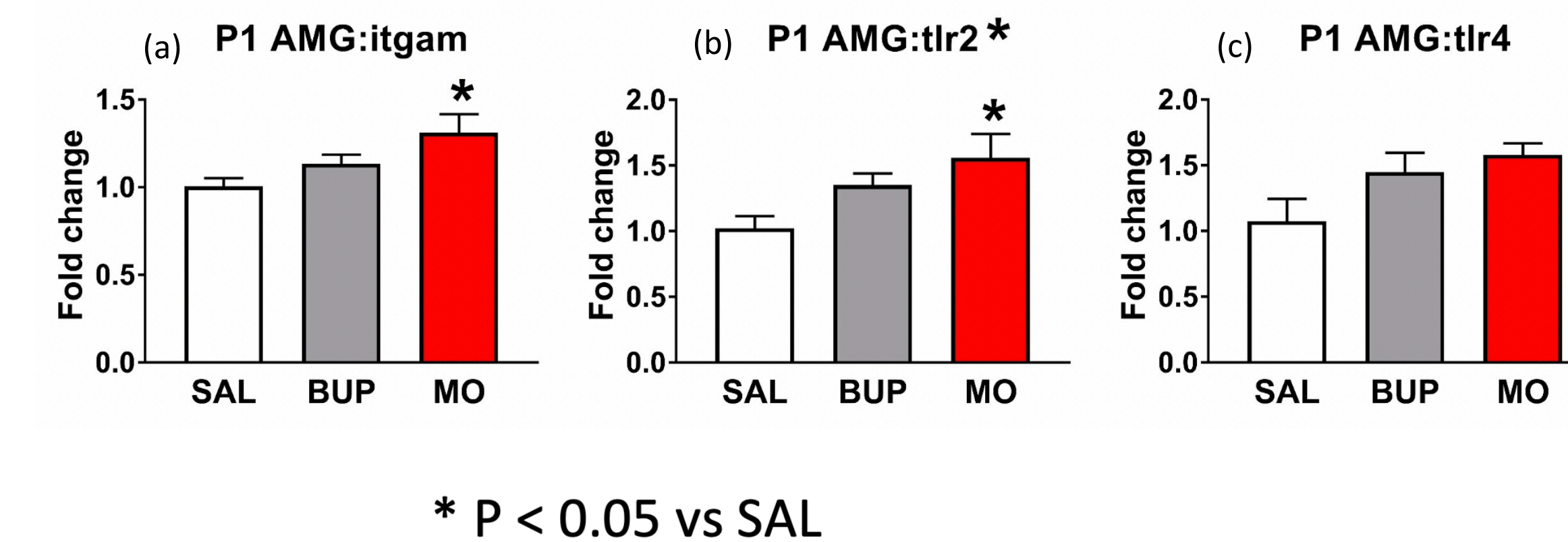


Fig 2. results of FR1 operant tests for each drug group and gender (a) significant increase in trials for female BUP, (b) no significant difference, (c) no significant difference, (d) no significant difference, (e) significant difference in blank touches between drug groups, (f) significant difference in accuracy between drug groups

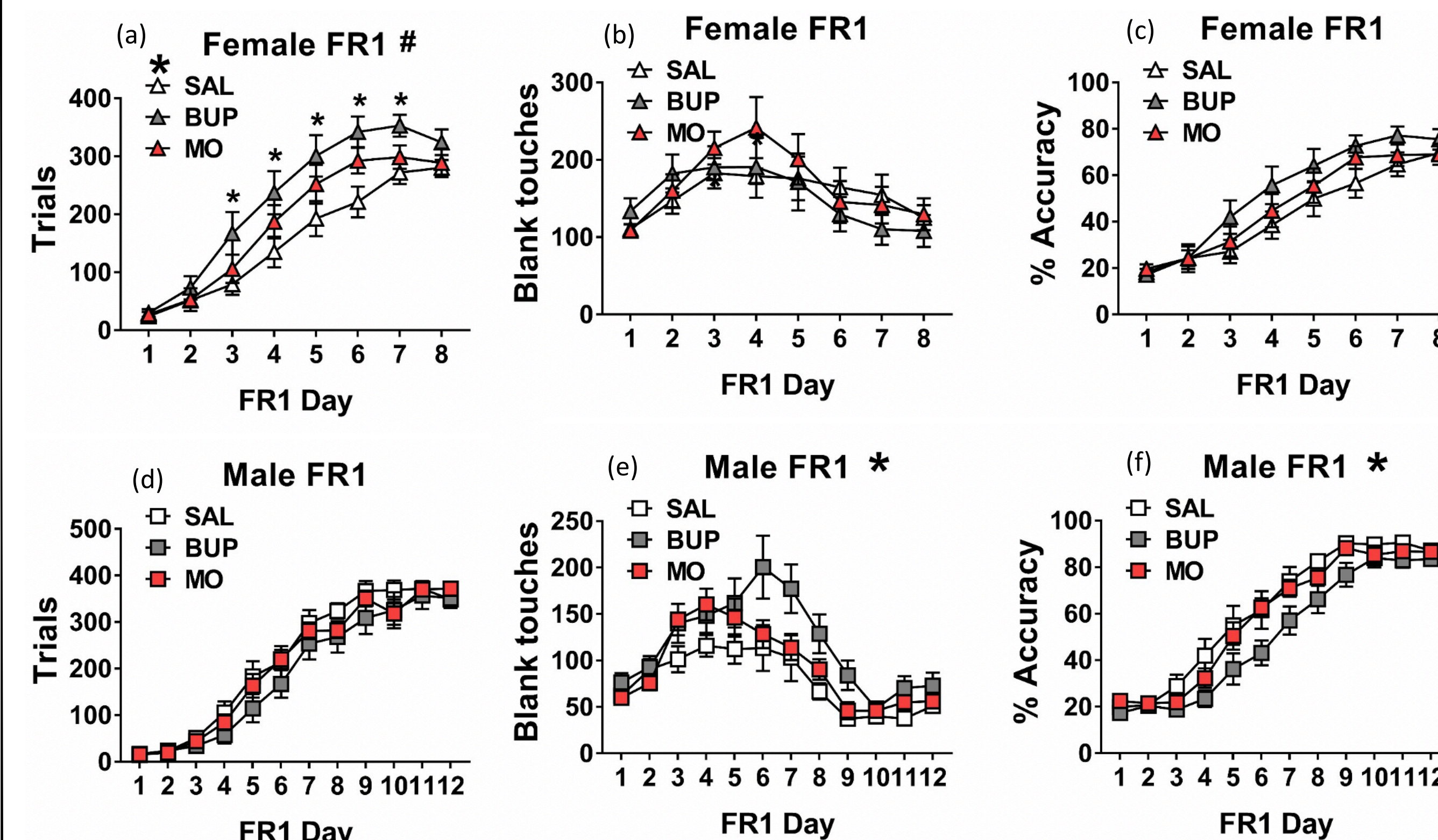


Fig 3. (a) Male MO and BUP groups had a recognition index significantly different from 50% (b) Female MO group had a recognition index significantly different from 50%

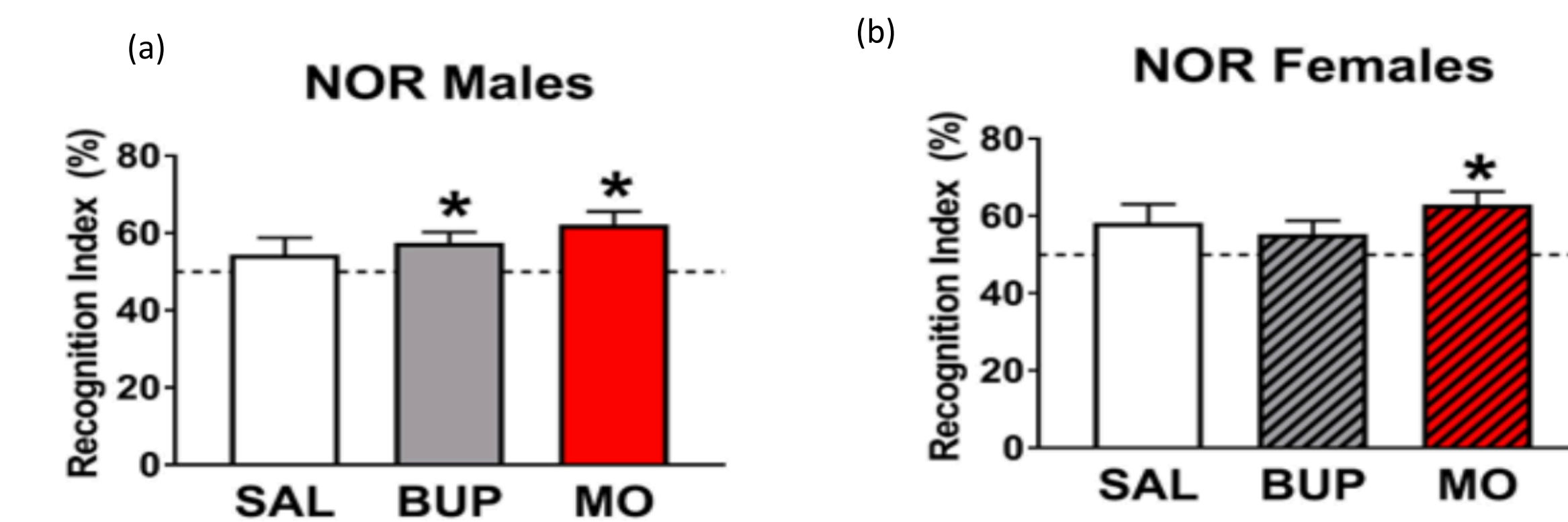


Fig 4. (a) Male MO group spent significantly more time in the center and (b) had a greater frequency in comparison to the SAL group, (c) no significant difference in distance traveled

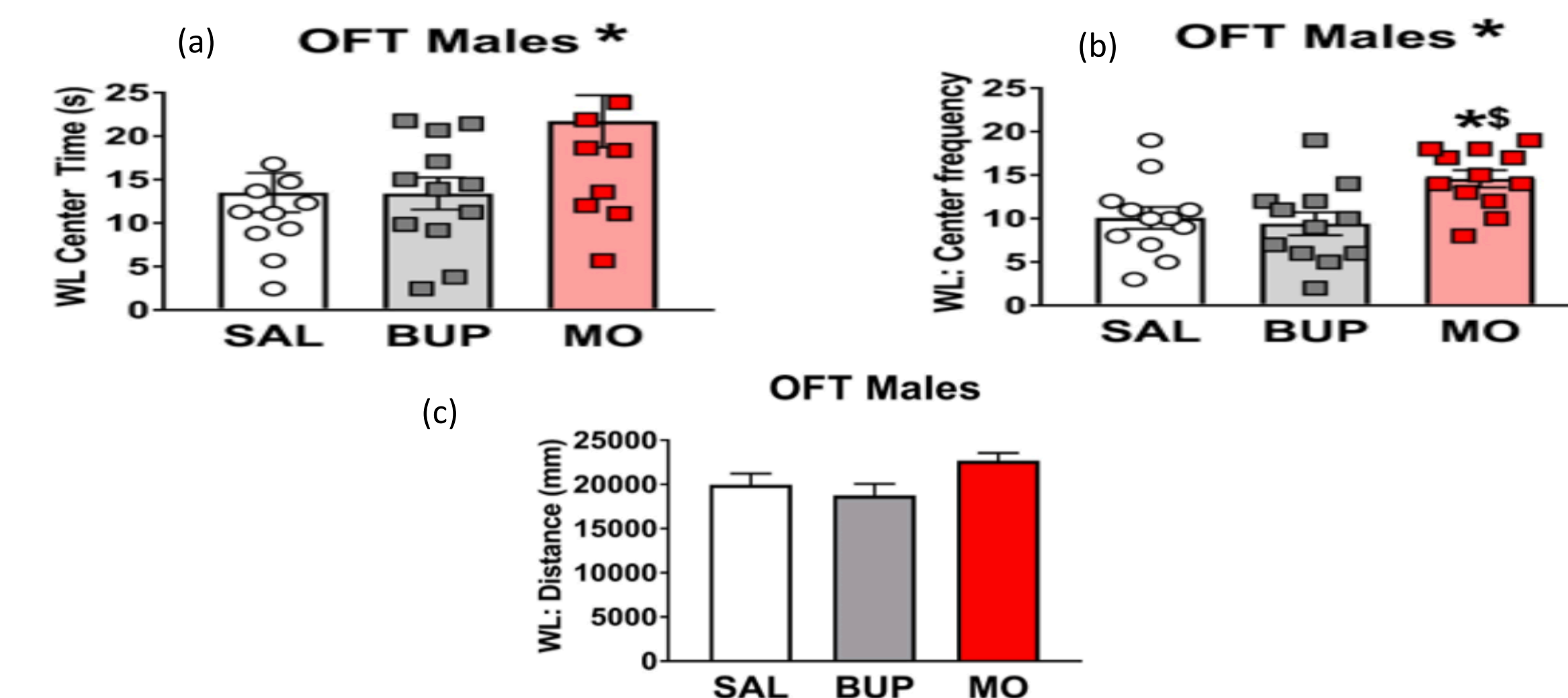
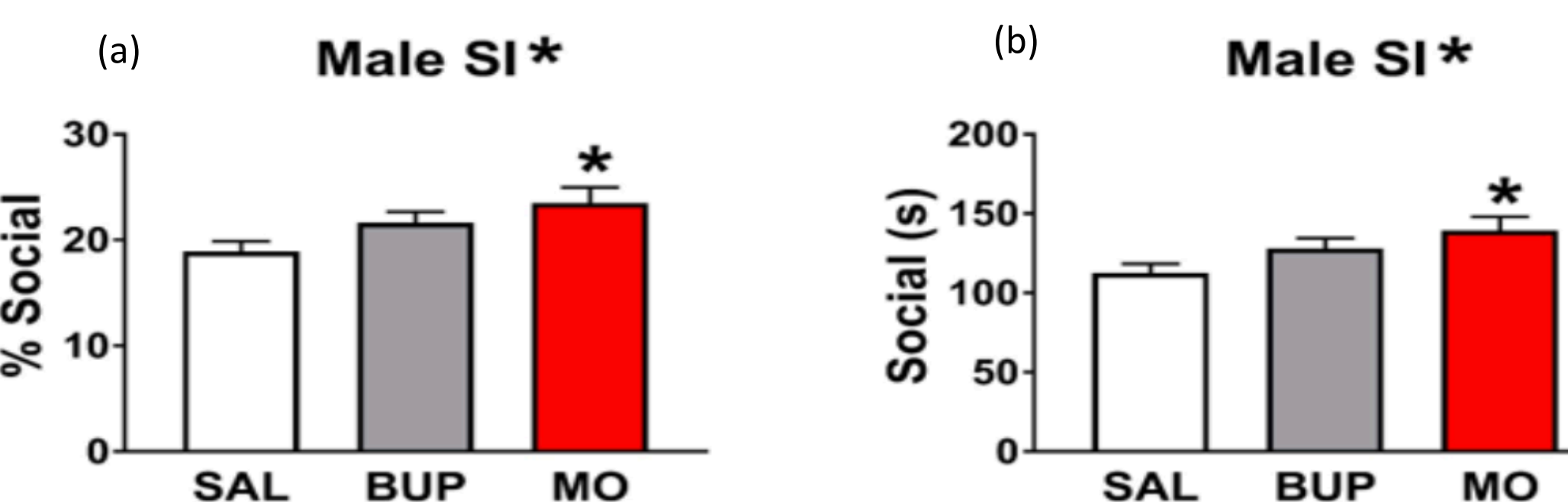


Fig 5: (a) Male MO group was significantly more social than the SAL group by percentage and by (b) time spent in seconds



## Summary

- The main findings of this study show that:
  - (i) in the open field test, the male MO exposed offspring would spend significantly more time in the center of the arena,
  - (ii) in the novel object recognition test the males exposed to either of the opioids and the females exposed to morphine spent significantly more time with the novel object,
  - (iii) the male MO group was significantly more social than the other groups and,
  - (iv) fixed ratio 1 shows the female group exposed to buprenorphine completed a significant amount of more trials and that the male buprenorphine group was slightly less accurate .

## Conclusion

- These results suggest that the mice exposed to an opioid in utero may be more novelty seeking and impulsive in comparison to the control saline group.
- The subtle effects of the opioids could be due to needing slightly higher or longer lasting dose for BUP
- It is also possible opioids alone are not problematic unless combined with other factors such as nicotine use, maternal stress, maternal mental illness etc.
- MO has been shown to activate immune cells in the brain. Our findings show an increase in expression of itgam and tlr2 in the amygdala which are both involved in the cells of the immune system

## Citations

- Fodor, A., Tímár, J., & Zelena, D. (2014). Behavioral effects of perinatal opioid exposure. *Life Sciences*, 104(1-2), 1-8. doi:10.1016/j.lfs.2014.04.006
- Konijnenberg, C., & Melinder, A. (2011). Prenatal exposure to methadone and buprenorphine: A review of the potential effects on cognitive development. Retrieved from <https://www.ncbi.nlm.nih.gov/pubmed/21480011>