Mu-Opioid Receptor Deletion Contributions to Neuroeconomic Decision Making

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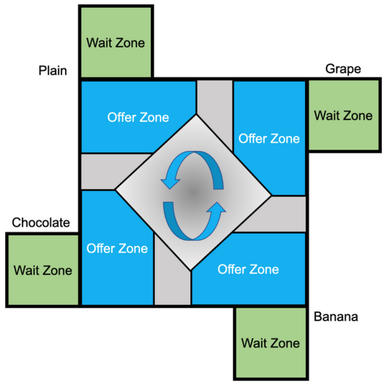
Abstract

There exist three types of endogenous opioid receptors: mu (MOR), delta (DOR), and kappa (KOR) receptors, which are found throughout the brain and influence different aspects of the opioid system[1]. MORs are involved in the motivational salience of rewards in rodents[2]. We are specifically interested in the mu-opioid receptor because MOR antagonism decreases the selection of the most valuable option when multiple rewards are available[3].

There is little understood about how endogenous mu-signaling is involved in neuroeconomic decision-making, especially in the context of competing reward values. Therefore, we will eliminate the genetic instructions for producing MOR proteins by deletion of the *Oprm1* gene[4] to determine if the knockout of these receptors will impact neuroeconomic decision-making.

We predicted that mice with *Oprm1* deletions would not make the most optimal economic decisions compared to controls – they would not budget their time as efficiently during the maze, they will wait longer delay times, receive fewer rewards, and quit offers more often than the control mice.

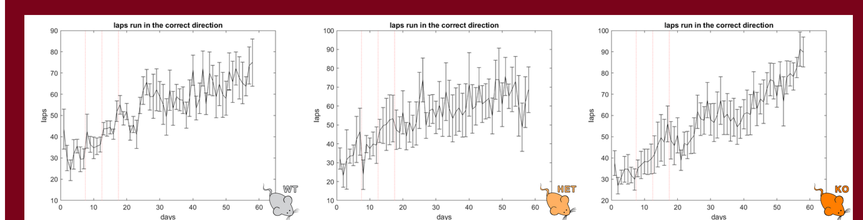
Methodology



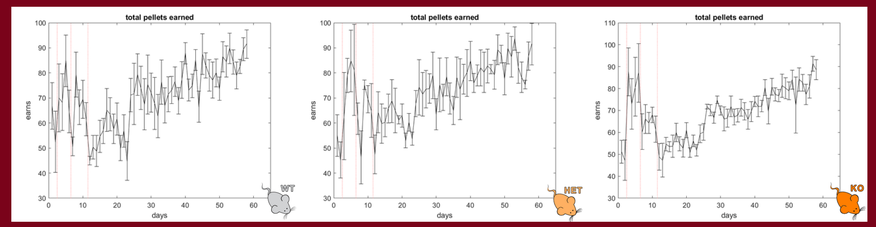
- Mice that were wild type (WT), heterozygous (HET), and knockout (KO) for the *Oprm1* gene were trained on the maze for 70 days.
- Each corner of the maze contained a different flavored food pellet.
- When a mouse entered the Offer Zone, a tone played whose frequency indicated how long they had to wait for the reward.
- A mouse could accept or reject the offers. On accepted offers, the animal could quit during a countdown. It only earned when it waited for the entire countdown.
- The mice were food-restricted and had 1 hour to budget their time and maximize their earnings for the day.

Results

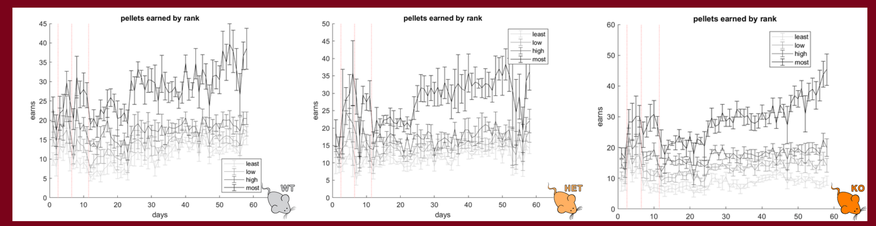
Laps Run in the Correct Direction Over Training Period



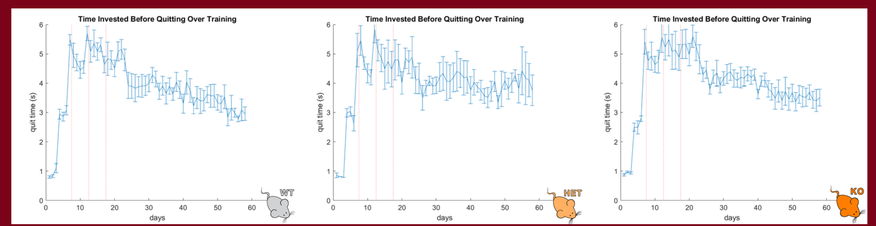
Total Pellets Earned Over Training Period



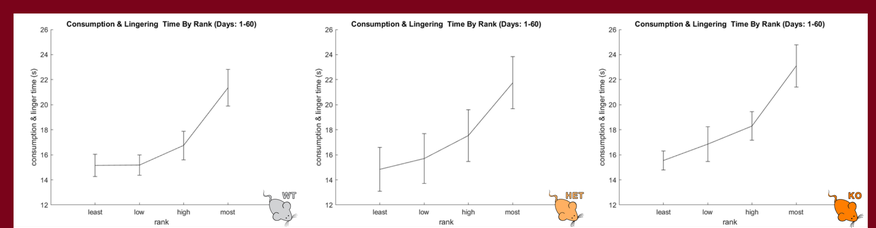
Pellets Earned by Preference Rank Over Training Period



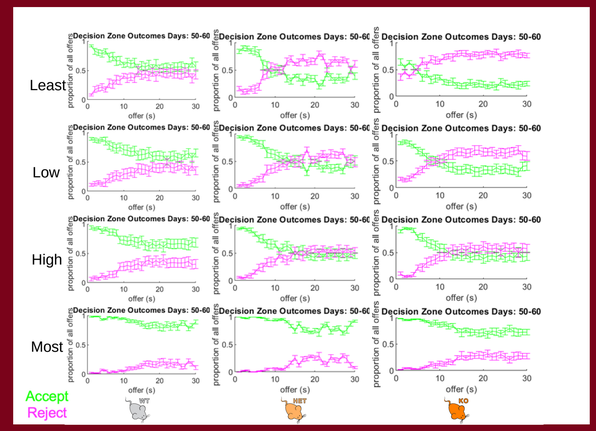
Time Invested Before Quitting Over Training Period



Mu-opioid receptor deletion does not impact consumption time



Offer Accept Threshold Changes With Degree of Mu-Opioid Deletion



Discussion & Conclusion

- There were no differences in genotypes on the following metrics:
  - Laps, pellets earned, pellets earned by preference rank, time invested before quitting, consumption time, and lingering time.
- Mice remained longer in the Wait Zone when their most preferred food pellet was earned. This could be explained by a place preference, in which the mice linger around their most-preferred flavor to learn and solidify that preference.
- **Offer accept threshold changes with the degree of mu-opioid deletion.** WT mice have the highest accept threshold while KO mice have a low and strict threshold, with HET mice falling in the middle. This indicates that there is a gene dose-dependent effect on the offers mice are willing to take for certain rewards. KO mice exhibited stricter thresholds for lower offers in their neuroeconomic decision-making process.
- These findings contradict our initial predictions. The difference in thresholds across genotypes may indicate the importance of endogenous opioid signaling on tolerance – that is, when mu-opioid signaling is present, the mice are more likely to tolerate longer wait times. Another explanation is deleting the MOR alters their valuation process so that they only accept extremely low offers and become extremely selective.
- **Future Directions**: Replicate these findings to verify that the trend is consistent. The same experiment could be conducted with different rewards besides food pellets, such as opioid drugs. Finally, the deletion of the DOR and KOR could be explored in the same way as the MOR was explored here.

Citations

1. Kieffer, Brigitte L., and Claire Gavériaux-Ruff. "Exploring the opioid system by gene knockout." *Progress in neurobiology* 66.5 (2002): 285-306.
2. Chelnokova, Olga, et al. "Rewards of beauty: the opioid system mediates social motivation in humans." *Molecular Psychiatry* 19.7 (2014): 746-747.
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4. Peciña, Susana, and Kent C Berridge. "Hedonic hot spot in nucleus accumbens shell: where do mu-opioids cause increased hedonic impact of sweetness?." *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* vol. 25,50 (2005): 11777-86. doi:10.1523/JNEUROSCI.2329-05.2005.