



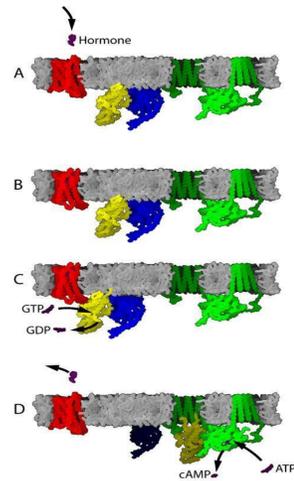
GPR171 Expression in Female Mice

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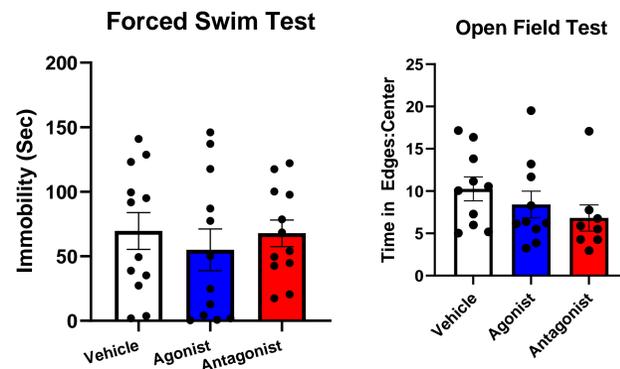
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Background

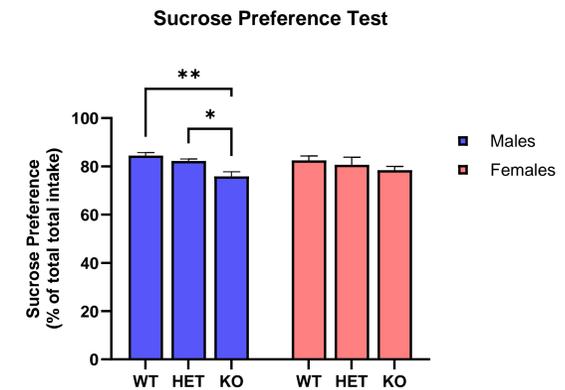
- GPR171 is a hypothalamic G protein-coupled receptor for BigLEN (a GPR171 agonist and ProSAAS-derived neuropeptide which regulate food intake in mice).
- It is highly expressed in areas involved in both anxiety and depression- primarily the nucleus accumbens, basolateral amygdala, prefrontal cortex, and ventral hippocampus.
- This protein is theorized to play a role in mood and eating disorders.



Experiment 1



Effects of Genotype and 171 Expression



There are 3 different genotypes of mice that were tested:

- Homozygous Wildtype
- Heterozygous
- Homozygous Knockout

Male KO are more depressed than their WT counterpart. Females don't show the same results, meaning that sex and genotype likely play a part in GPR 171 expression.

Hypotheses

- Experiment 1:**
 - Does acute GPR171 agonism or antagonism modulate anxious and depressive behaviors in female mice?
- Experiment 3:**
 - Does estrogen interact with GPR171 actions and neural expression in female mice?

Experiment 1 Results

After subjecting the mice to a series of stimuli/experiments (Forced Swim Test and Elevated Plus Maze), we were able to conclude a few pieces of interesting data:

- Unlike males, where we were able to see some significant differences between those who received the vehicle, agonist, or antagonist, the drugs didn't show significant differences in the female mice subjected to the same experiments.
- Because the results differed significantly from the male mice, this led us to believe that Estrogen, a predominantly female hormone, could be playing a critical role in the expression of GPR171 in female mice.
- Experiment 3 was born out of our conclusions from this experiment.

Experiment 3 Results

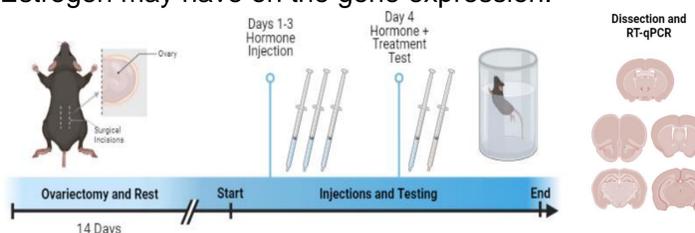
Based off of our results from Experiment 1, we were led to believe that Estrogen played a role in the expression of GPR171 in female mice. In order to control for estrogen, all the female mice received ovariectomies and were allowed 2 weeks rest afterward to allow their hormones to normalize again. Afterward, the mice were randomly injected with either a placebo drug or estrogen and then subjected to a Forced Swim Test.

The results showed that in a forced swim, the agonist is pro-depressant under estrogen, but anti-depressant under placebo. These results are further confirmed while looking at the number of GPR171 expressions using qPCR.

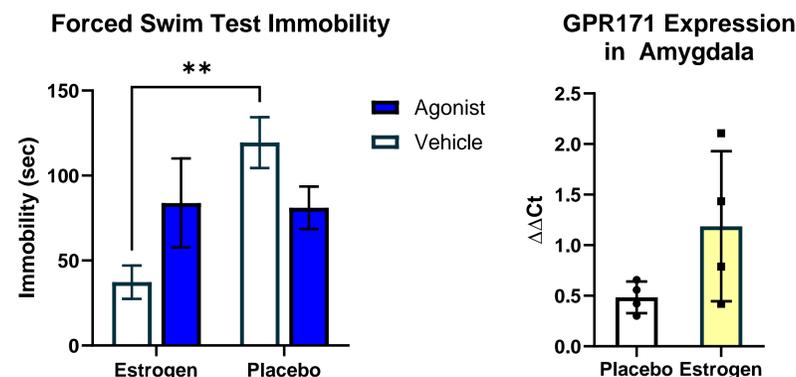
Methods

- Experiment 1:**
 - Female mice were subjected to a variety of tests and stimuli. These tests were performed at any point during the menstrual cycle of the mice.
 - 15 minutes following the injection of a vehicle, agonist, or antagonist or GPR171, the female mice were subjected to an elevated plus maze and forced swim test. This is designed to simulate moments of anxiety and/or depression.
- Experiment 3:**
 - Female mice received ovariectomies, and then injections of either placebo or Estrogen, as shown below.
 - They were subject to the forced swim test again, had their brains dissected and tested with qPCR, to determine the effect Estrogen may have on the gene expression.

Measuring Interaction between GPR171 agonist and estrogen



Experiment 3



Conclusions

- Experiment 1:**
 - Unlike the male mice, the evidence from our experiment suggest that when GPR171 agonists or antagonists are administered to female mice, the anxious or depressive behaviors that result are insignificant.
- Experiment 3:**
 - While the effect that Estrogen has on GPR171 expression isn't completely understood, we are led to believe that its impact in neural expression is significant and requires further study.

References

- [https://www.mdscsystems.com/products/biglen-mouse_6304#:~:text=BigLEN%20\(mouse\)%20is%20a%20GPR171,activation%20of%20postsynaptic%20G%20proteins.](https://www.mdscsystems.com/products/biglen-mouse_6304#:~:text=BigLEN%20(mouse)%20is%20a%20GPR171,activation%20of%20postsynaptic%20G%20proteins.)
- <https://www.ncbi.nlm.nih.gov/gene/229323>