

The Effect of Estradiol on GnRH mRNA Expression in Old Mouse Hypothalamic Tissue

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Introduction

- Gonadotropin releasing hormone (GnRH) is known to be the primary regulatory molecule in control of the hypothalamic-pituitary-gonadal axis, through which the brain regulates reproductive function.
- Estradiol (E_2) provides feedback to regulate the production and secretion of GnRH. However, little is known about the mechanisms by which estradiol regulates GnRH release. Estradiol typically has a negative effect on GnRH secretion, but positive feedback occurs in a time-of-day specific manner.
- Our lab has recently shown that E_2 treatment in the young animal significantly reduces GnRH mRNA expression on both the hypothalamic tissue and single cell level.
- It is now widely accepted that the aging brain contributes to reproductive senescence. However, it is unknown if E_2 can regulate GnRH mRNA expression in old animals.

Figure 1. Proposed Feedback Mechanism of Estradiol on GnRH Neurons

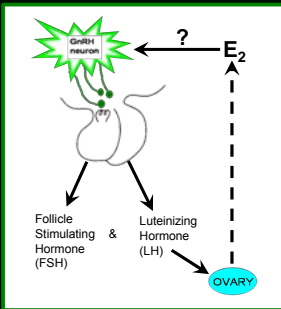
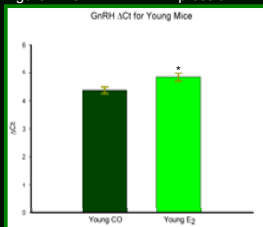


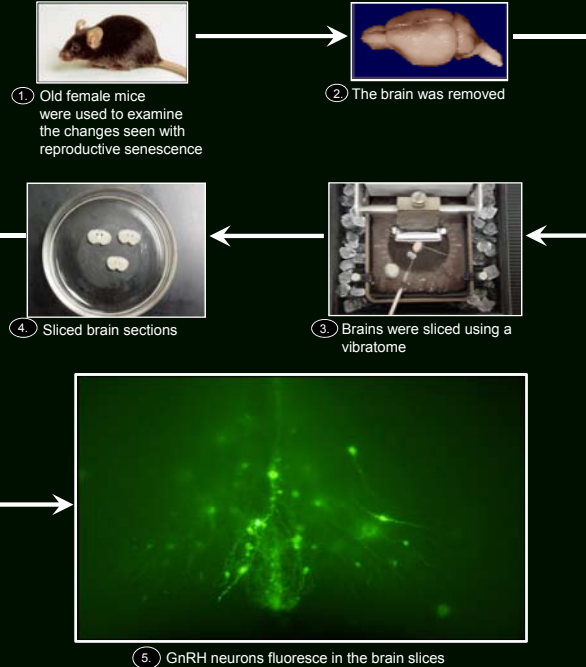
Figure 2. GnRH mRNA Expression in Young Mice



This graph demonstrates that GnRH mRNA expression is reduced in the hypothalamus of young E_2 -treated animals when compared to young controls.

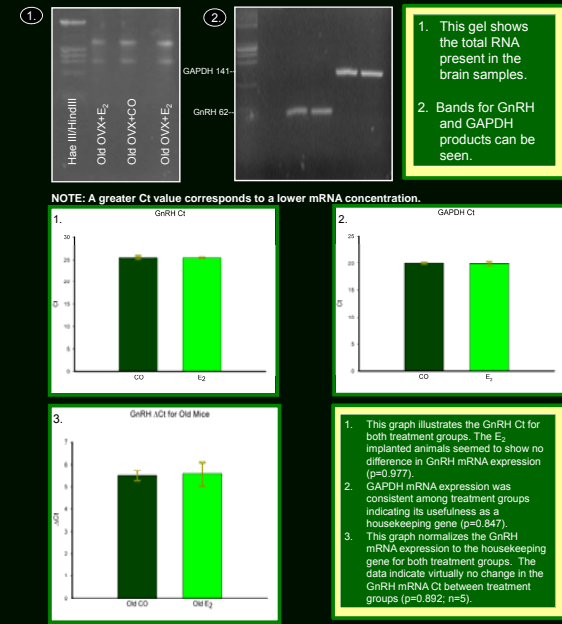
Methods

Figure 3. Procedure to isolate neurons from brain slices



- Old (≥ 15 mo.) mice were ovariectomized and implanted with E_2 (0.625 μ g) or control capsules.
- Mice were sacrificed 5-7 days post-OVX.
- Total RNA was isolated from the hypothalamic tissue.
- Quantitative RT-PCR with primers specific for GnRH and a housekeeping gene (GAPDH) was performed.
- ANOVAs were performed to compare GnRH expression for the treatment groups.

Results



Conclusions

- OVX+ E_2 animals showed a statistically insignificant downregulation of GnRH mRNA in comparison to OVX+CO animals ($p=0.892$; $n=5$).
- This result suggests a decreased responsiveness of the aging brain to E_2 .
- Future studies will add more samples to increase the power of the study. Time of day will also be analyzed to determine its significance on GnRH mRNA expression in old mice.
- Western blots may be performed to determine if changes in mRNA expression affect protein concentrations.

Acknowledgements

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