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The Effects of Estrogen and Arousal on Latent Inhibition

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Introduction

The behaviors of humans and animals are dependent on neurotransmitters and hormones that affect attention, alertness, and associative learning. These include the hormone estrogen (which plays an interesting role in cognition and attentional processes) and the neurotransmitter orexin (involved in wakefulness, arousal and goal-directed behaviors). Here we evaluated the roles of orexin receptors and estrogen in Latent Inhibition (LI), a measure of attention and associative learning. Latent inhibition is a behavioral phenomenon in which an organism's ability to associate new meaning to a familiar previously inconsequential (pre-exposed) stimulus is reduced when compared to associating meaning to a novel stimulus (non pre-exposed) in a classical conditioning paradigm. We hypothesize that orexin and estrogen have synergistic effects on latent inhibition (LI).

Methods

Subjects

- Female mice, aged 3-4 months, $n = 33$
- All mice underwent ovariectomy surgery

Experimental Design

- Alterations to the experimental subjects included condition (non-pre-exposed and pre-exposed), genotype (wild-type vs. orexin receptor knock-out), and treatment (estrogen vs. placebo).

Latent Inhibition Paradigm

- In a 5-phase experiment, about half the mice were pre-exposed to a stimulus and then conditioned with a foot shock, while the others did not receive pre-exposure.
- Freezing time was then manually recorded upon subsequent exposure to the stimulus as a measure of LI.

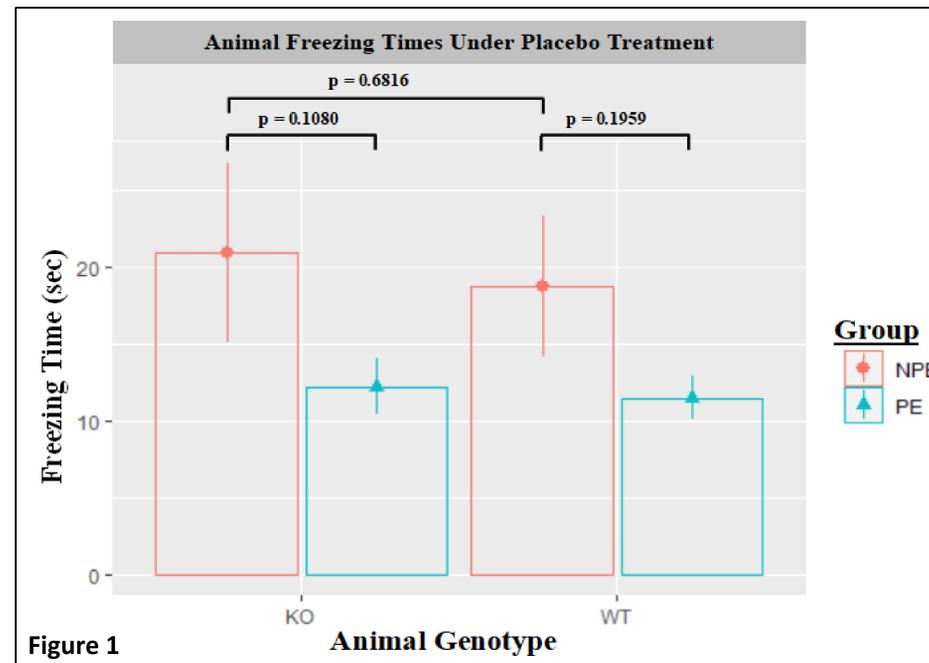


Figure 1

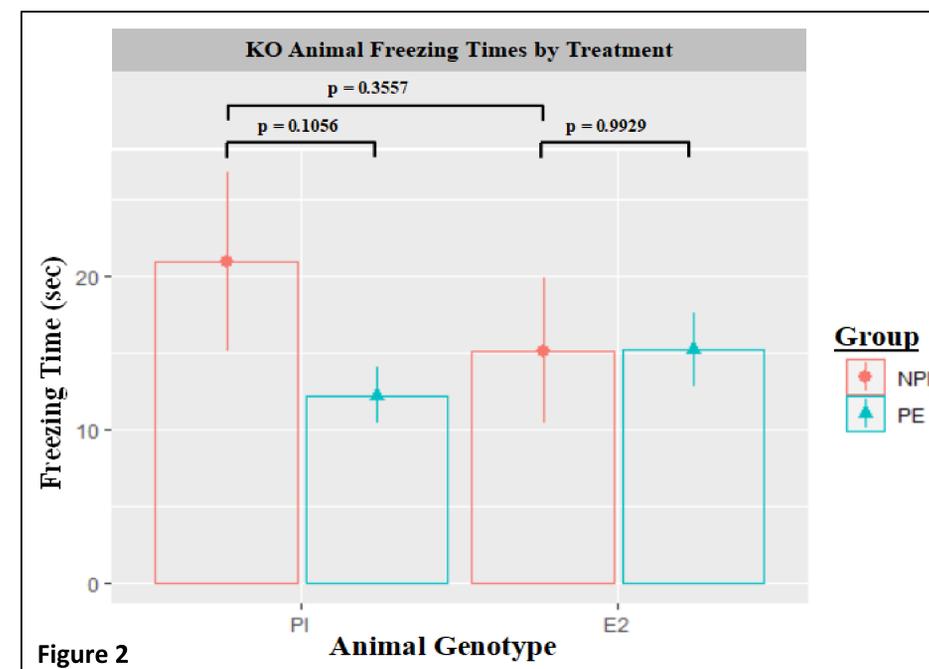
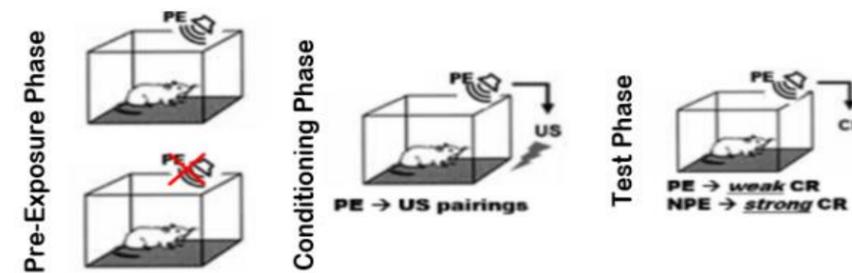


Figure 2

Results and Conclusion

The average time spent freezing during the NPE and PE stimuli during the test session in animals receiving placebo treatment is shown in Figure 1. A two-way ANOVA indicates a main effect of group ($F(1, 17) = 4.584, p < 0.05, \eta^2 = 0.215$). Under placebo, both KO and WT animals in the NPE condition showed elevated freezing times as compared to PE condition. Overall, the results trend towards a display of LI in both the KO and WT animals under placebo treatment.

The average time spent freezing during the NPE and PE stimuli during the test session in KO animals receiving placebo or estrogen is shown in Figure 2. A separate two-way ANOVA did not indicate any main effect of treatment ($F(1, 14) = 0.064, p > 0.05$) or group ($F(1, 14) = 1.822, p > 0.05$). However, as seen in Figure 1, the KO under placebo that were not preexposed froze slightly more than those who were pre-exposed to the stimuli. While this is not statistically significant, the result trend toward a display of LI in KO receiving placebo but not in KO animals receiving estrogen. While the results that were obtained are of great interest, there exists a necessity to further clarify the roles that orexin and estrogen play in a latent inhibition paradigm.

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