SJSU SAN JOSÉ STATE UNIVERSITY

SJSU Undergraduate Research Grants

Molecular Mechanisms of Ethanol-induced Feeding Dysfunction

Manae Matsubara, Rachel Vasquez, and Rachael French

Department of Biological Sciences, San José State University

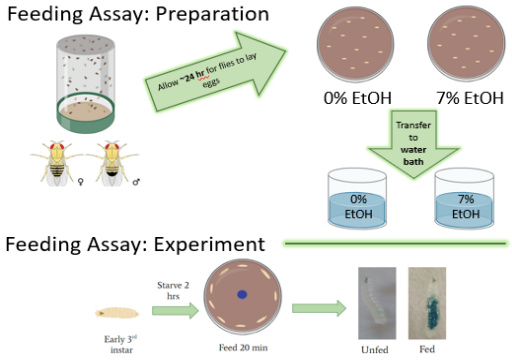
Abstract

Animal feeding behaviors are governed by conserved physiological mechanisms that promote sufficient feeding for developmental progression and survival. Developmental alcohol exposure (DAE) alters feeding behavior through multiple mechanisms, including suppressed feeding motivation and feeding abnormalities. These changes likely contribute to the detriment associated with fetal alcohol spectrum disorder (FASD).

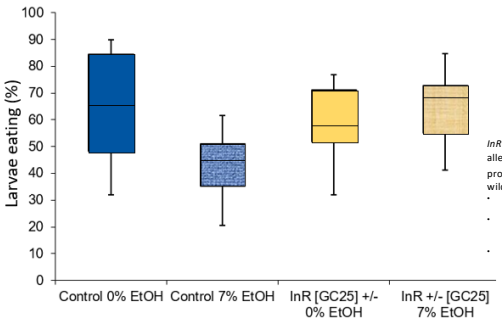
We have established *Drosophila* as a genetic and developmental model for FASD, and have demonstrated that DAE results in reduced feeding at every developmental stage in flies. The neuropeptide F (NPF/NPY) pathway regulates rewarding behaviors and is positively associated with increased feeding across all taxa. We have shown that in the presence of DAE, NPF signaling is increased in *Drosophila* larval brains indicating that NPF is necessary for larval survival. These data suggests that NPF is increased to compensate for reduced feeding caused by an as-yet-unidentified ethanol-dependent mechanism. Insulin negatively regulates NPF/NPY release, resulting in reduced feeding. We have previously demonstrated that insulin signaling is reduced by DAE, and we hypothesized that this reduction is a survival mechanism by which DAE-exposed larvae increase NPF release. We will present data in support of this hypothesis - mutations disrupting insulin signaling suppress ethanol-induced anorexia.

Finally, both dopamine and octopamine signaling are regulated by insulin and enhance feeding. Both neurotransmitter receptors are reduced in DAE-exposed animals, and we hypothesize that one or both of these signals is the target for DAE-induced anorexia. We will perform genetic and molecular epistasis experiments to test the signaling relationships between insulin, NPF/NPY, octopamine, and dopamine.

Methods



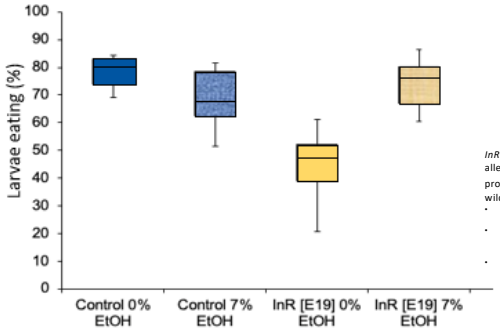
InR^{GC25} heterozygotes are resistant to DAE-induced anorexia



InR^{GC25} is a loss of function allele that reduce InR protein levels to 57% of wildtype.

- p = 0.3067 for the effect of genotype.
- p = 0.1561 for the interaction between. genotype and ethanol
- Two-way ANOVA with Tukey HSD post-hoc analysis

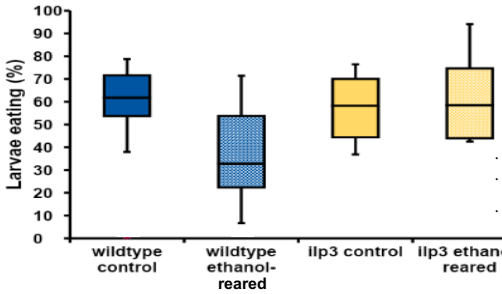
InR^{E19} heterozygotes are resistant to DAE-induced anorexia



InR^{E19} is a loss of function allele that reduce InR protein levels to 50% of wildtype.

- p = 0.5197 for the effect of genotype.
- p = 0.5197 for the interaction between. genotype and ethanol
- Two-way ANOVA with Tukey HSD post-hoc analysis

Flies homozygous for a null mutation in *insulin-like peptide 3* (*ilp3*) are resistant to DAE-induced anorexia



- p = 0.14 for the effect of genotype.
- p = 0.17 for the interaction between. genotype and ethanol
- Two-way ANOVA with Tukey HSD post-hoc analysis

Conclusions

1. Larvae with *InR* mutations suggest that insulin receptor are resistance to the deleterious effects of DAE on feeding motivation.
2. *Dilp3* and *Dilp5* may be responsible for anorexia in ethanol-reared third instar larvae.