Bidirectional brain-gonad interactions generate context-dependent behaviors. Lee, E.L.Q., Horvitz, H.R.

The drive to reproduce distinguishes living from non-living things. The brain and gonad interact to generate physiology and behaviors that optimize reproductive success. If and how these organs coordinately interact to produce context-dependent responses beyond those of reproductive behaviors is largely unexplored. In studies of the nematode roundworm *Caenorhabditis elegans* we discovered a brain-gonad signaling system that controls how worms sense time patterns of experiences. Specifically, we found that C. elegans can be traceconditioned, showing that it has the ability to process timing durations. Furthermore, these sensitivities to temporal durations can be modulated intergenerationally in the progeny if parents are primed with stimuli in a specified temporal pattern. We found that the adrenergic system is key to both the processing of time durations in the parents as well as the transmission of the modulated signals to the progeny. The only adrenergic tissues in C. elegans are the two RIM and two RIC neurons and the somatic gonad. We showed that intergenerational temporal modulation is implemented by a brain-gonad-embryo feedforward adrenergic relay to produce birth cohort-specific behavioral responses. Within an animal, brain-gonad interactions might be predicted to be bidirectional. In subsequent studies of germline-brain interactions, we found that mutant worms lacking a germline preferentially seek proteinaceous food sources over carbohydrate and lipid sources compared to wild-type worms. Our results thus begin to define an understanding of bidirectional brain-gonad communication — a unique organ-organ interaction that spans timescales beyond an individual's lifespan and that is key to reproduction and thus survival.