C. elegans intergenerationally modulates learned timing behavior through a gonadal signal

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Organisms utilize parentally-derived information to help them adapt to and survive in a given environment. How such information is transmitted intergenerationally in a flexible manner, tailored to specific environments, is a fundamental problem. We show that *C. elegans* is able to transmit learned signals to alter its progeny's sensitivity to the relative temporal patterning of stimuli. We have developed an associative learning paradigm in which *C. elegans* learns to associate a neutral odor stimulus with a noxious light stimulus when these stimuli are paired in an ordered temporal pattern in which the odor is predictive of subsequent light exposure. Trained worms produce progeny with altered responses to such temporally-patterned stimuli. Interestingly, the intergenerational transmission of behavior is dependent on the ordering of the temporal pattern and is not merely a response to exposure to a stressful stimulus – worms exposed to equal levels but randomly ordered patterns of learning stimuli do not exhibit any intergenerational inheritance. Thus, this example of intergenerational information transmission contrasts with previously described intergenerational phenotypes that involve pure stressors e,g., heat shock, *Pseudomonas* PA14 infection, etc. Organisms live in ever-changing environments, and we have observed that this intergenerational information transfer is not only temporally context-specific but also is flexibly tuned to the progeny's potential environment. Specifically, in this learning paradigm, parental worms undergo only brief learning sessions lasting 12.5 minutes; it might not be advantageous for all progeny generated post-learning to rigidly inherit an adaptation derived from a parental experience that was relatively transient. Consistent with this notion, we have observed that the time window for the intergenerational transfer of information is short: only oocytes fertilized directly after the learning session for a period spanning ~150 minutes carry the learning-induced information. Progeny derived from eggs fertilized after the initial permissive 150 minutes do not display the intergenerational behavior. This finding further suggests that the critical period for the transmission of this learned information ends around the time of fertilization. We screened mutants defective in specific biogenic amines and showed that tyramine, a neuromodulator, is involved in mediating this information transfer. Tyramine from the gonad and not from neurons is the likely source of the intergenerational modulation of timing sensitivity, suggesting that information transfer might involve direct communication from the gonad to the oocyte. We hope that an understanding of how the learned intergenerational signal is established and how this signal is then passed to the oocyte will reveal new aspects of how cells can transfer learned context-specific information across multiple tissues, and in particular across the soma-germline Weismann barrier – which was proposed to prevent characteristics acquired through parental experience from being transmitted to the next generation, i.e. Lamarckian inheritance. Determining the mechanism by which this intergenerational learning occurs should provide insight into how inherited information can be transiently transmitted to a limited number of progeny and yet be sufficiently persistent to be expressed in the relevant cells long beyond the initial stages of development and manifest its effects in adulthood.