Searching for the Genetic Components of Long-term Memory of Operant Self-learning in *Drosophila*

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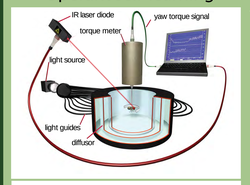
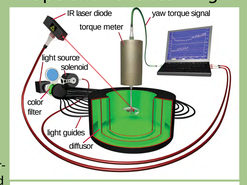
Two genetically distinct forms of operant learning

Operant self-learning



Operant world-learning



In self-learning, only the fly's own behavior is predictive of the heat punishment

World-learning occurs when a predictive external cue is added to a self-learning experiment

Self-learning was found to be independent of cAMP singalling, but dependent on Protein Kinase C (PKC) and the transcription factor FoxP. No further genetic components have been identified so far. In this work, we test polymorphisms in the Protein Kinase G (PKG) gene foraging (for), the *radish* mutants, defective in anesthesia-resistant memory (ARM) and the adenylyl cyclase mutant *rutabaga*.
In addition, we probe for long-term memory (24h) of operant self-learning.

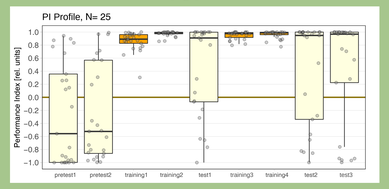
When a predictive stimulus is added to a self-learning experiment, flies preferentially learn about this stimulus' predictive relationship to the heat punishment, rather than about their own behavior controling the heat. Consequently, the genetic components involved in these experiments are the same as in, e.g., Pavlovian situations, i.e., the cAMP cascade. Neither PKC nor FoxP are involved in this form of learning, despite the similarities to self-learning.

Motivations

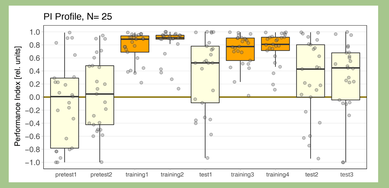
The operant self-learning mechanism appears to be evolutionary conserved among bilaterians. The dependence on PKC has been reported for the marine snail *Aplysia*, songbirds and mice. FoxP-dependent self-learning was found in humans, birds and mice. PKC manipulations in mice suggest that the mechanism may be implemented as PKG-dependent cerebellar long-term depression (LTD) in these animals. Therefore, we tested two variants of the *Drosophila* PKG gene *foraging*, rover (*for*^{R}) and sitter (*for*^{s}). In *Drosophila* olfactory conditioning, two parallel processes encode two different forms of memory, the *rutabaga*-dependent cAMP cascade and RAP-like GTPase activating protein (*radish*)-dependent anesthesia-resistant memory (ARM). To test for interactions of these genes with operant self-learning, we tested both *rut* and *rsh* mutants in a short version of the self-learning experiment, in which wild-type flies fail to show a learned preference.

Is Protein Kinase G involved in operant self-learning?

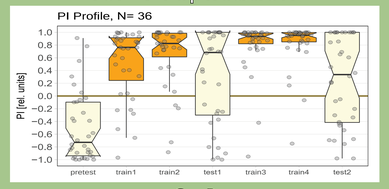
for^{R}



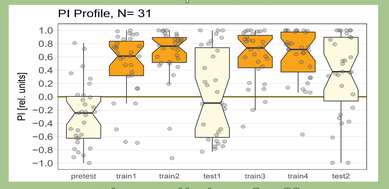
for^{S}



for^{R}: replication

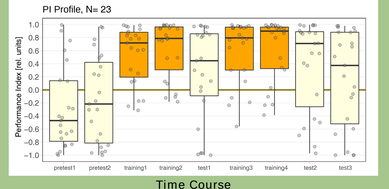


for^{S}: replication



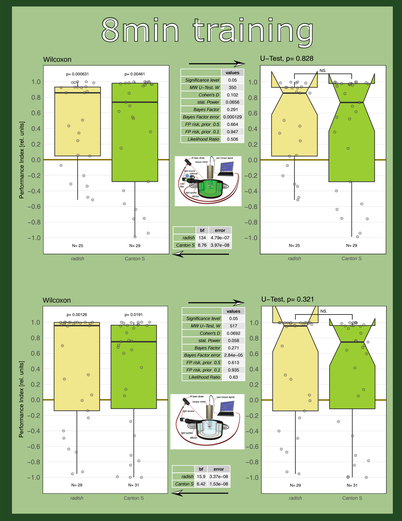
for^{R}

other allele: for^{S2}

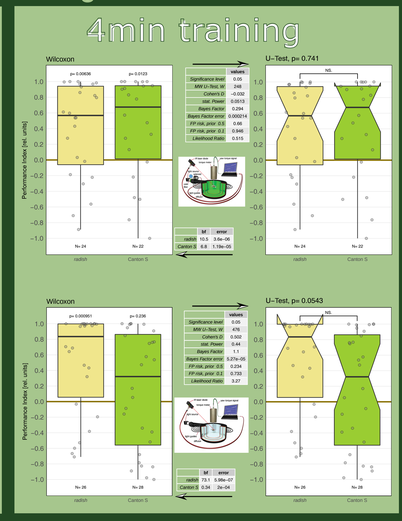


ARM interacts with self-learning

8min training

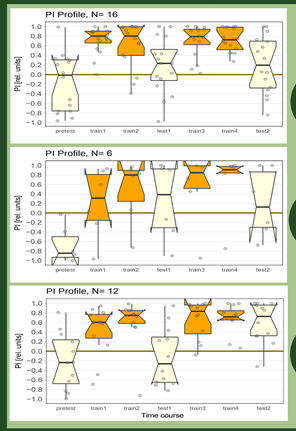


4min training

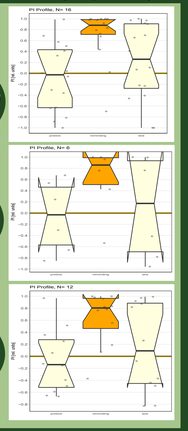


Is there LTM after self-learning?

Learning



Memory (24h)



Wild-type Berlin

for^{R}

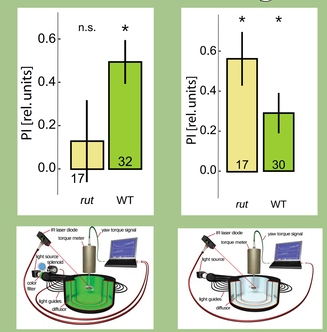
for^{S}

Summary

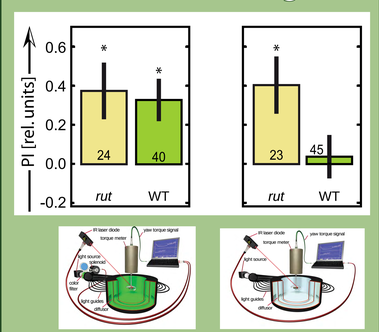
We tested various candidate genes for their involvement in operant self-learning as well as for the existence of long-term (24h) memory after self-learning. We found tentative evidence for a weak long-term memory 24h after self-learning. We did not find conclusive evidence for variants of the PKG gene to show any difference in their long-term self-learning memory. We also could not find clear differences between the two PKG variants in immediate recall of self-learning. However, there seemed to be a difference in avoidance of the punishing heat-beam, which may be explained by different heat-sensitivity between *rover* and *sitter*. The *radish* mutant, defective in a RAP-like GTPase activating protein, appears to show self-learning in a short version of the self-learning task where wild-type flies fail to show a significant learning score. This result is reminiscent of analogous experiments with *rutabaga* mutants, where the mutants also showed superior self-learning in the shortened task.

Improved self-learning in *rutabaga* mutants

8min training



4min training



SfN meeting 2017, Washington D.C.