LEARNING AND MEMORY

Austerity measures for memory

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Efficient management of energy homeostasis is essential for survival. Although it is known that under conditions of food shortage, the brain takes priority with regard to energy allocation, it is not known whether the brain itself adopts energy-conserving measures. Formation of some types of long-term memory (LTM) requires energy-intensive protein synthesis and two new studies show how LTM formation in the brain of *Drosophila melanogaster* adapts under conditions of food shortage.

Both studies used an associative conditioning paradigm for the formation of olfactory memories in which flies are trained to associate a stimulus with an odour. 'Aversive' LTM (which is the formation of an association between an odour with an aversive stimulus) formation requires multiple spaced training sessions (spLTM), whereas 'appetitive' LTM (which is the formation of an association between an odour and sugar) formation can be established in starved flies following a single training session. Aversive consolidated memory can be of two distinct types: anaesthetic-resistant memory (ARM) results if the training sessions run consecutively (that is, without rest intervals) and is protein synthesis-independent, whereas spLTM is protein synthesis-dependent.

The crammer (*cer*) and tequila (*Teq*) mutations disrupt spLTM but not ARM. Plaçais and Preat found that *cer* and *Teq* mutant flies that were starved before and after spaced training were able to form consolidated memories. However, although pre-treatment with the protein-synthesis inhibitor cycloheximide reduced memory formation in fed wild-type flies that were exposed to spaced training sessions, it had no effect on starved flies. Together, these findings suggest that by directing memory consolidation mechanisms towards the less energy costly ARM under conditions of reduced food supply, the flies could enhance their chance of survival.

The authors then stimulated specific dopaminergic neurons whose synchronized oscillatory activity is known to drive spLTM consolidation. Forcing starved flies to form LTM rather than ARM shortened survival duration by about one-third, further supporting the pro-survival role of an LTM-to-ARM switch when food availability is severely restricted.

Insight into the molecular mechanisms underlying appetitive and aversive LTM was provided by the study by Hirano *et al.* In their experiments, flies were submitted to mild fasting before training and put back on food after training. They found that although fasting before multiple spaced training sessions had no effect on the aversive spLTM formation, mild fasting prior to an aversive single training session enhanced LTM formation (fLTM). Importantly, food supply after training is an essential for formation of the both types of LTMs.

Activation of cyclic AMP (cAMP) response element-binding protein (CREB) is involved in aversive LTM, and the authors found that fasting activated the CREB coactivator CREB-regulated transcriptional coactivator (CRTC) in mushroom body neurons. Conversely, interfering with the activity of another CREB co-activator, CREB-binding protein, reduced spLTM but not fLTM.

Blocking the activity of CRTC suppressed aversive fLTM but had no effect on spLTM. Furthermore, expression of active CRTC in flies exposed to a single training session caused formation of aversive fLTM (but not spLTM), suggesting that CRTC is sufficient to generate fLTM, even in the absence of fasting.

CRTC phosphorylation is regulated by insulin signalling. Flies defective in insulin signalling displayed enhanced CRTC-dependent LTM after a single training session, suggesting a possible mechanism for fLTM formation in which fasting reduces insulin signalling, resulting in activation of CRTC and CREB and activation of protein-synthesis-mediated LTM.

Taken together, these two studies indicate that under different conditions of reduced food availability, the brain of *D. melanogaster* responds by altering the mechanisms by which LTM is formed; mild starvation only before the training launches CRTC to facilitate LTM, and severe starvation before and after the training switches LTM to ARM.

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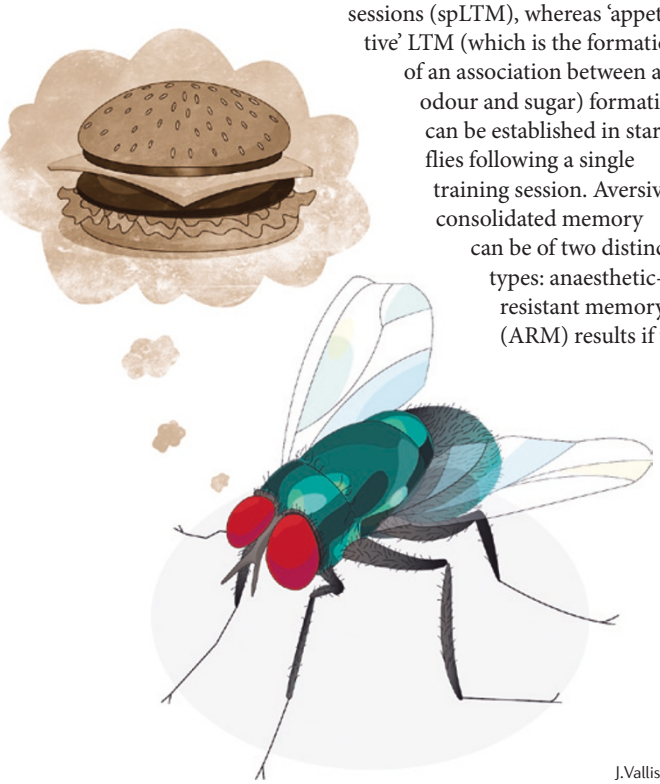

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ORIGINAL RESEARCH PAPERS Plaçais, P. -Y. & Preat, T. To favor survival under food shortage, the brain disables costly memory. *Science* **339**, 440–442 (2013) | Hirano, Y. *et al.* Fasting launches CRTC to facilitate long-term memory formation in *Drosophila*. *Science* **339**, 443–446 (2013)