Dopamine signaling

https://doi.org/10.1038/s41594-024-01458-5

Balancing reproductive pursuit and visual danger

Humans and other animals wittingly or unwittingly run risk–benefit analyses daily. For animals of reproductive age, a prime example of such analysis is assessing the benefit of reproductive success versus the cost of being preyed upon. The scale needs to be sensitive: over-prioritize survival at the risk of a lack of progeny, or undermine danger at the risk of perishing. While previous studies and empirical knowledge have suggested that males become less preoccupied about potential danger upon permissive cues indicating increased probability of successful copulation, the molecular mechanisms orchestrating this behavior have remained ill-understood.

Writing in *Nature*, Cazalé-Debat et al. remedy this gap in understanding and provide notable mechanistic and functional insight into the neurons, receptors and signaling cascades that regulate the trade-off between survival and propagation in *Drosophila*. Using sex–danger conflict assays, the authors demonstrate that though male flies abort courtship upon danger cues at early stages, they increasingly disregard visual threats as courtship progresses and copulation becomes more likely. The initial abortive response seems to be regulated by visual activation of LC16 neurons, which then turn on 5-HT^{PMPD} neurons (serotonin neurons in the posterior medial dorsal cluster) and activate the release of serotonin; the latter inhibits P1 and plP10 neurons, thus turning off key hubs that are known to be activated during courtship. This allows flies to prioritize survival over reproduction.

However, things dramatically change later during courtship, with dopamine levels increasing and dopamine-activated cascades, also via proprioceptive loops, gradually taking over. The authors hypothesize and then show that PPM1/2 dopamine neurons crosstalk with LC16 neurons, inducing their progressive shutdown through the suppression of LC16 activity. This phenotypically translates into male flies not translating visual cues of danger. Importantly, Cazalé-Debat et al. provide multiple lines of evidence that the characterized cascades are specific to the interplay between courtship and visual danger cues, as PPM1/2 inhibition of LC16 output does not occur in solitary male flies. Finally, it is shown that dopamine D2-like receptors are instrumental in the initiation of this dopamine-induced inhibiting cascade; this is notable because such receptors have key human homologues that are implicated in sensory perception.

In summary, the authors here provide important insight into some of the mechanisms underlying the societal trope of being 'love blind' and implicate dopaminergic cascades as a potential gradual sensory filter system.

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Original reference: *Nature* **634**, 635–643 (2024)