

Optogenetic study shows that male flies find ejaculation pleasurable

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A male fly being exposed to red light to trigger optogenetic activation of CRZ neurons, which causes ejaculation. Credit: Avi Jacob, BIU Microscopy unit

Researchers reporting in Current Biology on April 19 show that male



fruit flies find sex—and more specifically ejaculation—to be an inherently rewarding experience. The study is the first to show that the rewarding nature of ejaculation is conserved among animals, from flies and mammals. It also adds to evidence that manipulating sexual experience in flies affects their interest in consuming alcohol, the researchers say.

"Successful mating is naturally rewarding to <u>male flies</u> and increases the levels of a small peptide in the brain called Neuropeptide F," says Galit Shohat-Ophir of Bar-Ilan University in Israel. "Male flies that are sexually deprived have increased motivation to consume alcohol as an alternative <u>reward</u>."

Shohat-Ophir, along with the study's lead author Shir Zer-Krispil and their colleagues, in collaboration with HHMI Janelia Research USA, came to these conclusions by taking advantage of optogenetic tools. These tools enable researchers to genetically engineer <u>fruit flies</u> such that it's possible to activate particular neurons with light. In their studies, they used flies in which neurons expressing the neuropeptide corazonin (CRZ) could be switched "on" by exposure to <u>red light</u>. Earlier evidence shows that CRZ neurons in the fly abdomen trigger the release of sperm and seminal fluid. By examining flies in this way, the researchers were able to explore the rewards associated with ejaculation apart from other aspects of a sexual encounter.

"We wanted to know which part of the mating process entails the rewarding value for flies," Shohat-Ophir says. "The actions that males perform during courtship? A female's pheromones? The last step of mating which is sperm and <u>seminal fluid</u> release?"

To find out whether ejaculation produced an immediate pleasurable response, the researchers used an arena in which one side emitted a red light to trigger optogenetic activation of CRZ neurons and tracked where



male flies chose to spend their time. Those experiments showed that flies showed a strong preference for the red light, implying that ejaculation in itself is a rewarding experience.

Next, they trained the flies to associate the red light and ejaculation with a particular odor. They then tested whether the flies preferred the scent that reminded them of that past experience of ejaculation. And they did.

After a few days of repeated activation of CRZ neurons, the fruit fly males had high levels of neuropeptide F in their brains, similar to males that actually mated with female partners. When those males were given the choice between liquid food and liquid food spiked with alcohol, they preferred the non-alcoholic food. In contrast, control <u>flies</u> and engineered males not exposed to red light preferred the alcohol.

"The principles by which the brain processes reward are extremely conserved in all animals; this is a really basic every day machinery that helps animals survive," Shohat-Ophir says. "Drugs of abuse use the same systems in the brain that are used to process natural rewards. This allows us to use simple model organisms to study aspects of drug addiction, including the interplay between natural and drug rewards and the connection between experience and the mechanisms that underlie the risk to develop drug addiction."

The researchers say they will continue to explore how information about ejaculation or successful mating reaches the brain. They also want to use their findings to further understand an individual's risk for developing an addiction, noting that addiction risk is influenced by a combination of molecular and neuronal mechanisms that influence the likelihood of progressing from initial drug exposure to repeated use.

"Our studies suggest that the state of the animal (i.e., undergoing successful mating or being rejected) affects the motivation to consume



drug rewards," says Shohat-Ophir. "An analogy for reward states can be proposed in which a high-reward state is illustrated by a full 'reservoir' and low state by an empty 'reservoir.' One can speculate that vulnerability to addiction is related to the size of the 'reservoir' that needs to be filled, or to different sensitivity to changes in the reward levels."

More information: *Current Biology*, Zer-Krispil et al.: "Ejaculation Induced by the Activation of Crz Neurons Is Rewarding to Drosophila Males" <u>www.cell.com/current-biology/f ... 0960-9822(18)30368-3</u>, <u>DOI: 10.1016/j.cub.2018.03.039</u>

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