Fruit fly post-mating behavior controlled by male-derived peptide via command neurons, finds study

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Scientists have succeeded in pinpointing the neurons within a female fruit fly's brain that respond to signals from the male during mating.

Male fruit flies transfer a substance called a sex-peptide during mating in the seminal fluid together with sperm. This sex pheromone influences the female fly's behavior, so she will start to lay eggs and be less inclined to mate further.

This is a common phenomenon in insects but until now, it was not known where in the nervous system the neurons are located that direct these so-called "post-mating behaviors."

Researchers at the University of Birmingham have now found a way to identify which specific groups of neurons in the fly's brain were responding to the sex-peptide. To achieve this scientific breakthrough, they attached the sex peptide pheromone, that normally circulates in the insects' blood, to the outside of neurons.

Now, if this cell-membrane-tethered sex-peptide is expressed in neurons that also express the receptor for the sex-peptide, it will induce post-mating behaviors. In this way, they were able to find where in the brain the neurons are that sense the sex-peptide. Their results are published in *eLife.*

To understand how the brain responds to the sex-peptide, the team explored the genetic framework of key genes involved in sex determination. These genes direct differentiation into male or female.

Unlike many other genes, sex determination genes are very complex. The research team, led by Dr. Matthias Soller, reasoned that the regulatory regions of these genes could be broken down to express in much fewer neurons.

In addition, the team found an additional genetic trick that allowed them to intersect two or even three expression patterns. Using this trick, they were able to direct expression of membrane-tethered sex-peptide to only a few neurons. Using this information, the team were able to map several distinct areas within the females' brain that triggered behavioral changes in the presence of the male sex-peptide.

Interestingly, the researchers found the neurons targeted by the sex-peptide belonged to a higher order group called "command neurons," which are essential for behavioral decision making. This contrasts with previous theories that the peptides influenced sensory neurons, which operate at a lower, reflexive level.

They also found that the peptide influenced more than one set of command neurons. The team identified at least five different sets of neurons implicated in the process, making it likely that the male sex-peptide interferes with female action selection at several different levels.

Lead author, Dr. Mohanakarthik Nallasivan, from the University of Birmingham's School of Biosciences, said, "This work will help us to understand how behavior is coded in the brain, and how sensory information is translated into action signals. Reproductive behaviors are hardwired in the brain, rather than learned behaviors, so if we can understand this behavioral pathway, we may be able to influence it, for example restricting the ability of mosquitoes to find hosts."

Lead-author Dr. Matthias Soller, from the University of Birmingham, added, "The Drosophila brain is the first where all neurons have been cataloged and synaptic connections have been mapped. We now have the resources available to unravel the neural basis of these behaviors. Like sequencing of the first genomes, Drosophila paved the way for getting the human genome sequenced, and here we have the same: research in Drosophila is instructing how we can get the architecture of the human brain.

"This pioneering work has implications for increasing our understanding of how our own brains work, particularly those behaviors that are 'hard wired,' or built into our neural circuitry."

But although the pathways through which the male sex peptide manipulates female behavior are now clearer, the female fruit fly can still override these behavioral instructions. For example, if she is not physically robust or if the environmental conditions are not right for egg laying, she will modify her behavior accordingly.

This research will serve as a prime paradigm, helping researchers to solve some of the most fundamental questions regarding brain architecture and function, including decision-making processes.

More information: Sex-peptide targets distinct higher order processing neurons in the brain to induce the female post-mating response, *eLife* (2024). DOI: 10.7554/eLife.98283.1. elifesciences.org/reviewed-preprints/98283

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