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How Sex Makes Fruitflies Hungry

Female fruitflies behave differently after mating. They become un-receptive to courtship attempts from new males, they increase their egg-laying, and, researchers now know, they eat more. Importantly, scientists have traced this complex behavioral change to the action of a single short protein, called "sex peptide," in the semen of males.

The finding, the researchers said, has broader implications than being just another oddity of fruitfly sex life. It offers scientists a new research model to explore how chemical signals passed between organisms can trigger complex behaviors. There are examples of parallel signaling in humans, they pointed out: substances called prostaglandins in human semen are known to influence the female immune response.

The research, performed by graduate student Gil Carvalho of the California Institute of Technology, was published online April 3, 2006, in the journal *Current Biology*. Carvalho worked in the laboratory of senior author Seymour Benzer, and the other senior author on the paper was Howard Hughes Medical Institute investigator David J. Anderson, also at Caltech. The other co-author was Pankaj Kapahi.

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According to Benzer, "This is a remarkable example of how a single, gene-derived peptide can essentially reprogram multiple components of behavior directed toward a common goal, in this case reproduction."

Anderson said that his involvement in the work arose from his interest in chemical triggers of innate behavior. And feeding represents an accessible, easily measurable behavior, he said.

“There have been indications in many organisms that pregnant females eat more, but the mechanisms that control that behavior were not understood in any detail. What was especially creative on Gil's part was to specifically look for a role for sex peptide in such behavior,” Anderson said.

Carvalho began by exploring whether female fruitflies consumed more food after mating. Using dye and radioactive tracers in their food, he found that the female flies did indeed, eat more after copulation.

Theorizing that the trigger for such eating could be a chemical in seminal fluid, he next genetically eliminated the “accessory gland” that produces these chemicals in males. After mating with these genetically altered males, females' appetites did not change. To determine whether the sex peptide - already known to trigger other postmating responses -- was the component of seminal fluid responsible for increased feeding, Carvalho used genetically altered males that lack the sex peptide, and those did not increase the females' food intake. Furthermore, expression of the sex peptide in virgin females did increase food intake.

“It was a case of both good scientific judgment and luck that Gil established this role for the sex peptide, since there are something like eighty different peptides transferred in male sperm to females upon copulation,” noted Anderson.

According to Anderson, the finding offers a rich pathway for further study. “I find it fascinating that one peptide injected into the female by the male coordinates at least three different behaviors of the female,” he said. “That suggests that sex peptide must be coordinating the activity of a number of different neural circuits that are programmed to control these different aspects of behavior.”

The most important next step in the research, he said, will be to identify the receptor molecule in brain cells that the sex peptide plugs into to alter behavior. “Through that receptor, it will be possible to identify the neurons and circuits that are being activated by the sex peptide, to understand how this one peptide can produce all these different effects.” In fact, said Anderson, it is not even known whether sex peptide acts directly on brain cells, or indirectly on other tissues that release regulatory chemicals that in turn affect the brain.

Carvalho is currently searching for the sex peptide receptor, and Anderson commented that he “has been the driving force behind this effort, and it has been a pleasure to work with him and Seymour as they have discovered this fascinating piece of biology.”

In a commentary in the same issue of *Current Biology*, Alex Wong and Mariana Wolfner of Cornell University note that the findings could lead to new ways to control disease-carrying mosquitoes - who must feed on blood to produce eggs. If mosquitoes are like fruitflies in that a male-derived peptide influences female feeding behavior, "it might help us to understand and possibly control the transmission of some vector-borne diseases," they wrote. Indeed, some studies have already shown that as in fruitflies, the behavior and physiology of female mosquitoes are influenced by mating.