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Fruit fly avoidance mechanism could lead to new ways to control pain in humans

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At first, fruit flies eat like horses. Hatching inside over-ripe fruit where they were laid, they feed wildly in the sugar-rich environment until nature sends them an offer they can't refuse. To survive, they must leave the fruit, wander off and burrow into the earth where they avoid food as if it were poison. Only then can the larvae grow and hatch into flies that will take wing to lay their own eggs.

Now, a team of researchers from the University of Georgia has discovered for the first time that the important developmental switch from food attraction to aversion in the fruit fly larva is controlled by a timing mechanism in the brain and its sensory system. The study shows how this important avoidance mechanism has been recruited into evolutionary processes to promote development and could one day lead to new methods of controlling pain in humans and other animals.

"The findings provide an intriguing glimpse into how an animal modulates its chemosensory properties and behaviors in coordination with development," said Ping Shen, an assistant professor in the department of cellular biology at UGA and a member of the Biomedical & Health Sciences Institute. The research was published today in the journal *Nature Neuroscience*.

"Fruit fly larvae are like tadpoles—they have to migrate from their first habitat to stay alive and flourish," said Shen. "What we found was that a molecular timing switch tells them when to quit eating and burrow into the earth. We also found that the same switch can trigger strong

cooperative behavior in the flies."

Authors of the paper in addition to Shen, all from the University of Georgia, are Andrew Sornborger of the Faculty of Engineering and the department of mathematics; Jie Xu, a doctoral student in Shen's laboratory; and Jennifer Lee, a former undergraduate and technician, also in Shen's lab.

Using cutting-edge imaging techniques developed by Sornborger and his colleagues, the researchers have imaged the fruit fly (Drosophila melanogaster) with unprecedented sensitivity.

"Analysis techniques have lagged behind image acquisition technology," said Sornborger. "This work addresses that gap. With our methods we have been able to image the inner workings of the nervous systems in real time amid massive amounts of data."

Fruit flies can't really stay in the rotting fruit where they are laid. Not only do they risk drowning in the ripening fluid, they are increasingly exposed to harmful microorganisms that can kill them. To escape, the larvae "wander" out and burrow into the ground.

One interesting finding is that the change from eating to non-eating is controlled by a timing mechanism that switches on a fructose sensor and involves a channel protein called PAIN, known to respond to noxious stimuli such as heat and horseradish.

While all this may seem extremely specialized since it involves fruit flies, that's far from the case, Shen and Sornborger said. The molecules at work in this system have counterparts in mammalian models that have been implicated in many psychological processes and behaviors such as the response to food and alcohol and the suppression of anxiety and pain.

Understanding the system in the fly could therefore lead to the development of new pain relievers that might do far less harm to the organism involved while shutting down pain at its most basic level. And that would be quite a gift from a fly.

Source: University of Georgia