Social Status Sculpts Activity of Crayfish Neurons

Like rival gunslingers in the Old West, two male crayfish living in the same territory are compelled to fight it out to determine who's the boss. First they circle and size each other up. Then their well-choreographed skirmish escalates into violent combat as they try to tear each other limb from limb. The winner of that clash becomes dominant, strutting his stuff confidently through the territory, while the loser skulks about, trying to stay out of his rival's way.\

Once those social lines have been drawn, the behavior of the two crayfish is so different that researchers suspected that the animals' experience must somehow change their nervous systems. Now, neurobiologist Donald Edwards of Georgia State University and his colleagues Shih-Rung Yeh and Russell Fricke provide the first direct evidence for that idea. On page *366,* they report that they have found a neuron in crayfish whose response to the neurotransmitter serotonin differs dramatically depending on the animal's social status. In dominant animals, serotonin makes the neuron more likely to fire, while in subordinate animals serotonin suppresses firing.

The finding's implications go beyond crayfish. For example, it complements work from Stanford University neurobiologist Russ Femald and his colleagues, who showed several years ago that a change to dominant social status alters the brains of male cichlid fish, causing the enlargement of neurons that release hormones that stimulate the sexual organs. But the Edwards group's finding is "the first time that one has been able to link a social phenomenon to a change in a particular identified synapse," says neuroscientist Allen Selverston of the University of California, San Diego. And that is something researchers have suspected might occur throughout higher animals, but have never seen. "Even though you are seeing something that in a sense you always knew had to be there," says Brandeis University neuroscientist Eve Marder, "it is incredibly powerful to actually see it."

Face off. Crayfish in combat. (Inset)

What's more, the activity change that the Edwards team has linked to social status takes place in a very well-studied neural circuit—a set of nerve cells that controls the escape reflex called the tail-flip. As a result, the team is in an ideal position to unravel the molecular and cellular events by which the change occurs, as well as to ask how changes in this neuron and others combine to alter the animal's behavior. "There are going to be a constellation of [nervous systeml changes that go along with this change in social status, each of which will endow the animal with different new abilities and serve it in some situation," says Fernald. "One way to think about it is that the animal in some sense has a different brain for different circumstances."

The present work grew out of a set of findings made 15 years ago by Harvard University neuroscientist Edward Kravitz and his then-student Margaret Livingstone. They found that serotonin injections caused lobsters and crayfish to assume the aggressive postures characteristic of dominant animals. That finding spurred researchers in several labs to study serotonin's effects on behaviors like the tail-flip reflex, which the animals use in both fighting and escaping.

In 1985, one of those researchers, Russell Fricke, then an assistant professor at Emory University, got a perplexing result. When he injected serotonin into young crayfish, it inhibited the tail-flip reflex in some animals, while enhancing it in others. As he tried to make sense of this, Fricke realized that the crayfish in which the reflex was enhanced had either been raised alone or were the biggest in their cage. That suggested the animals' social status might have been influencing his results.

Before going further in the work, however, Fricke left Emory to become a physician, and his observation "lay there for a long time," says Edwards. Then, in 1994, Yeh, a graduate student with Edwards, decided to pursue it. Yeh paired crayfish in cages, allowing them to fight and settle who was dominant. He then dissected the animals, and, in a culture dish, tested the effect of serotonin on the lateral giant neuron, which triggers the tail-flip reflex. He found that serotonin enhanced the excitability of the giant neurons from dominant animals, while it suppressed the activity of the neurons from subordinate animals.

Edwards and Yeh wondered what might be happening inside the lateral giant neuron to switch its response so dramatically. One possibility was that there was some sort of change in the receptors through which serotonin exerts its effects. There are three known types of serotonin receptors in crustaceans, which can exert different effects even within an individual cell.

The researchers' hunch proved correct. By using different compounds that activate different classes of serotonin receptors, Yeh and Edwards found that activation of one type of serotonin receptor makes the lateral giant neuron less excitable, while a second receptor type boosts its excitability. Neurons from subordinate and dominant crayfish respond differently to serotonin, says Edwards, because the subordinates seem to have "more, or more effective," receptors of the former type, while in dominants, the latter type prevails.

That state of affairs isn't permanent, however. Just as social status can change in the course of an animal's lifetime, the responsiveness of the lateral giant neuron can change as well. When Yeh placed two previously subordinate crayfish together, one would become dominant. Two weeks later when he tested the dominant animals' lateral giant neurons, the neurons' responsiveness was enhanced rather than inhibited by serotonin.

Dominant animals, in contrast, let go of their dominant physiology much more slowly, perhaps because of the advantages that dominant animals enjoy in access to food and mates. When Yeh paired dominant crayfish with each other, forcing one of each pair to become subordinate, the new subordinates continued to be truculent, provoking fights and getting themselves killed by their rivals at an unusually high rate. When he tested their lateral giant neurons more than a month after the new pairing, serotonin still enhanced their firing, as if "the animals are reluctant to go from being dominant to being subordinate," Edwards says. Fernald's group sees similar results with their male cichlid fish. Dominant males, even when forced to become subordinate, are very slow to give up their dominant physiology.

One question that's still unanswered is how the change in the lateral giant neuron might help explain the aggressive behavior of dominant males. Harvard's Kravitz offers a possible explanation. In lobsters, his group has found that the lateral giant neuron not only triggers the tail-flip reflex, but also activates other neurons that squirt out a burst of serotonin. And serotonin is the substance Kravitz and Livingstone had linked to aggressive behavior in lobsters and crayfish 15 years ago.

Edwards's group doesn't know yet whether the neuron also triggers a serotonin burst in crayfish, but they suspect that it might. If it does, then a "feed-forward loop" would operate in dominant animals, says Kravitz, in which triggering the lateral giant neuron would cause a burst of serotonin, which would make the neuron even more likely to be triggered again, causing more serotonin to be released. All that serotonin would pump up the animals' aggressive behavior. In contrast, subordinate crayfish are better served by not acting truculent and inviting a fight they are likely to lose, so it is adaptive for them to put the brakes on that cycle, which is what happens when the burst of serotonin caused by the lateral giant's firing makes the neuron less likely to fire again and trigger the release of more serotonmn.

Despite the appeal of that explanation, Kravitz and others point out that the lateral giant neuron alone is unlikely to be the full explanation for the behavioral changes. "You can't say this particular [neuron] ... is causally responsible for any behavioral changes," says Brandeis's Marder. "It is probably only a piece of the story."

To fill out the remaining pieces of that story, Edwards and others are eager to learn what other neurons may be influenced by the switch in social status, and whether some of those neurons show a change in serotonin receptors, or in receptors for other molecules. One target for study is the neurotransmitter octopamine, which Kravitz's group has shown to have the opposite effect to serotonin, producing submissive rather than aggressive behavior.

In addition, the researchers plan to take a closer look at the lateral giant neuron itself, focusing on the specific pathways through which social position gets translated into cellular and molecular changes in the neuron. With all these possibilities for future work, says Kravitz, the Edwards group has opened "a potentially incredibly exciting area of investigation.

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