Scientists discover mirror neurons in mice and find they're tuned to aggression

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Credit: AI-generated image (disclaimer)

In nature, when two animals fight, they are seldom without an audience. Pull back the camera on a pair of clashing lions and you'll see their peers looking on.

Stanford Medicine researchers wanted to know how the animals on the

sidelines perceive these aggressive interactions. In a new study in mice, they discovered that some neurons in a part of the brain known as the "rage center" fire both when a mouse is fighting and when it watches others fight. Such neurons are known as mirror neurons—they are active when an animal is doing the behavior and when it's watching another animal do that same behavior.

The study is the first to find mirror neurons in mice and in the hypothalamus—an evolutionarily ancient part of the brain—hinting at a more primal origin for mirror neurons than previously thought.

The study was published Feb. 15 in the journal *Cell*.

Assessing aggression

"Aggression in the wild is rarely a private affair," said Nirao Shah, MBBS, Ph.D., professor of psychiatry and behavioral sciences and senior author of the study. "Aggression is usually not only to defeat the other animal, but also to tell others in the vicinity, 'Hey, I'm the boss.' It's a public display."

Previous work in Shah's lab traced aggression in male mice to a cluster of brain cells in a part of the ventromedial hypothalamus. (In female mice, the same neurons do not trigger aggression.) Dubbed the "rage center," these neurons could activate aggression, but also seemed sensitive to a mouse's socialization—communally housed mice were less aggressive. "That study made us think, 'What else are these neurons sensitive to?'" Shah said.

Taehong Yang, Ph.D., a postdoctoral fellow in Shah's lab and the study's first author, proposed that these neurons might be sensitive to aggression between other mice.

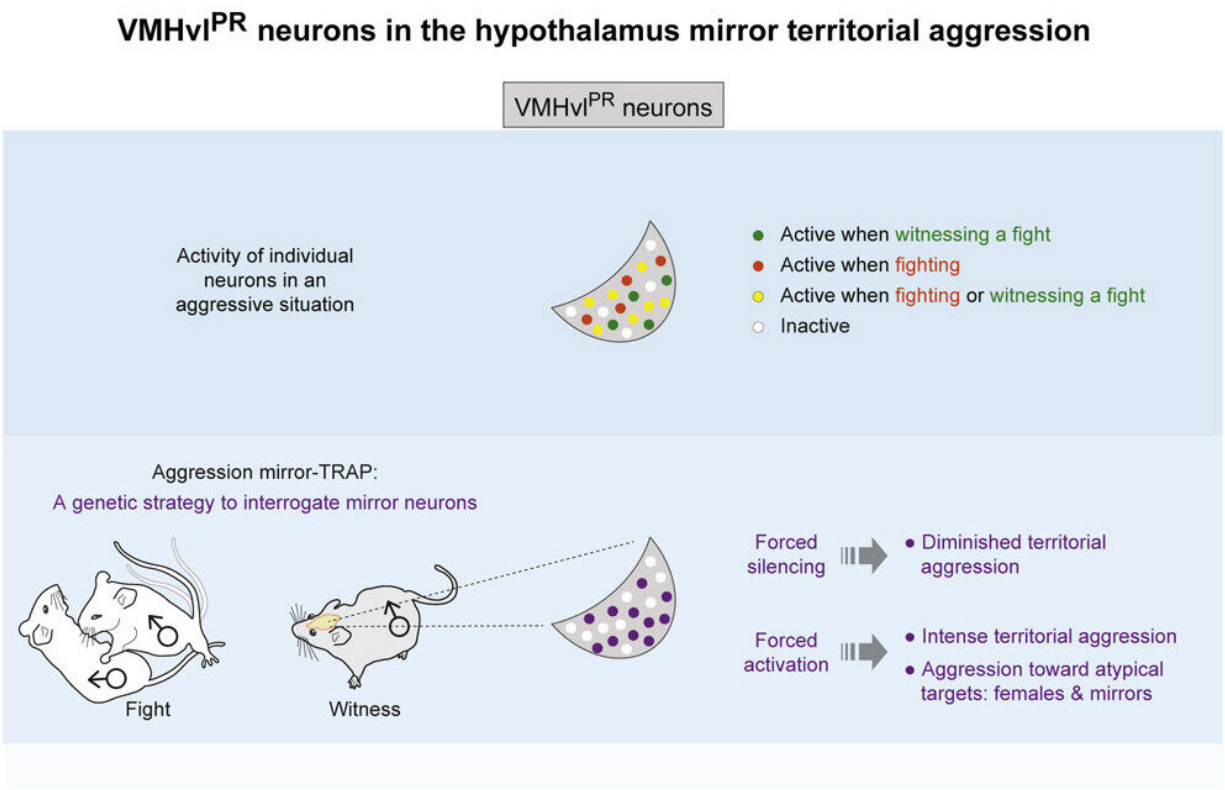
"And that turned out to be the case: They're mirroring aggression by other animals," Shah said. "These neurons are actually assessing, 'What kind of aggressive situation am I in?'"

Mirrors of rage

Using precise imaging techniques, the researchers recorded activity in the rage center of male mice engaged in a brawl and those witnessing a fight.

Sparking a fight between male mice is simple—the researchers had only to introduce a male mouse into another's cage. The resident mouse would attack the intruder and display threatening behavior, like tail-rattling. To set up a witness, the researchers allowed a lone mouse to observe these fights through a transparent divider.

They found that a nearly identical set of neurons in the rage center were active in both fighters and observers—qualifying them as mirror neurons.



Graphical abstract. Credit: *Cell* (2023). DOI: 10.1016/j.cell.2023.01.022

Finding mirror neurons in mice was "pretty shocking," Shah said. Most research on mirror neurons has focused on ones found in primates, in the cortex, the most evolutionarily advanced part of the brain.

Another surprise was that in an observer, aggression-mirroring neurons were triggered by sight, whereas in fighting mice, they are triggered by the smell of pheromones. Video recordings revealed that mirror neurons fired only in the moments when the observer was facing the fighters, not when it was turned away. And when the researchers turned off the lights, the observer's mirror neurons were entirely unresponsive to the fracas next door.

The researchers found also that these mirror neurons seemed innately tuned to aggression, even in mice that had never witnessed or engaged in aggressive behavior. They did not fire when mice watched other behaviors, like sniffing, grooming or running on a wheel.

Essential to the fight

Next, in a series of experiments, the researchers demonstrated that the aggression-mirroring neurons not only sensed aggression but enabled it. When they selectively inhibited these neurons, mice were less irked by a male intruder—and initiated only a third as many attacks or tail-rattles as normal mice.

Inversely, when the mirror neurons were switched on, the mice became indiscriminately aggressive. Not only did they initiate three times more attacks on male intruders than usual, they attacked even female visitors, who normally would have prompted frisky coupling behavior. Needless to say, they were less successful in mating. The male mice were so riled up they even tail-rattled at their own mirror reflection.

"It tells you that the activity of these neurons is sufficient for aggression, even when there's no provocation," Shah said.

Since they were discovered in the 1990s, mirror neurons have generated much interest in popular culture—and unfounded speculation that they might underlie our ability to mimic, to empathize, to develop culture, even to appreciate art. Yet their true function has remained a mystery, in part because it's difficult to study them in primates.

The new study in mice provides the first evidence that mirror neurons not only respond to a behavior—in this case, aggression—but also control it.

From mice to men?

The fact that aggression-mirroring neurons exist in such a primitive part of the brain indicates they may have been conserved across evolution, from mouse to human, Shah said.

"It suggests that we might have the same neurons, and maybe they encode some qualities of aggression in ourselves," he said.

The researchers did not investigate how observing aggressive behavior affected the observers, but they offer their own speculation—perhaps, like boxers studying videos of their opponent's moves, the mice on the sidelines learn to be better fighters.

More information: Taehong Yang et al, Hypothalamic neurons that mirror aggression, *Cell* (2023). DOI: 10.1016/j.cell.2023.01.022

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