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BIOLOGY OF BEHAVIOR

The Mr. Mom Switch

In the mouse world, virgin male mice are not known as nurturers. They're aggressive and infanticidal, regularly injuring or killing newborn mice fathered by other males. But research led by Catherine Dulac, Higgins professor of molecular and cellular biology, reveals that these murderous mice can be turned into doting dads simply by stimulating a set of neurons, shared by both males and females, that appears to drive parental behavior.

Dulac examines control of instinctive behavior in animal brains, particularly social actions such as courtship and parenting. Previous work in her lab revealed that mouse brains hold circuits that determine whether the animals adopt stereotypical male or female behavior: Dulac discovered that the vomeronasal organ (VNO), a set of chemical-sensing receptors in the nasal septa of mice, dictates which of the two circuits is activated. (Female mice lacking a functional VNO engaged in "very bizarre male-like behaviors," Dulac reports, emitting ultrasonic vocalizations normally sung by males to attract mates.)

In the most recent research, first described in the journal *Nature* last year, the investigators set out to learn if male mice had a similar capacity to match females' parenting abilities. A female mouse that has never encountered a male or babies will nonetheless spring into action if pups are placed in her cage. "She will immediately build a nest, retrieve the pups, groom them, and crouch around them," Dulac explains. "This is very robust, stereotyped behavior. If you do the same experiment with virgin males, they will immediately attack the pups." Yet when the researchers removed the VNO of virgin male mice, changing the way they sensed the pups, the normally hostile males became "perfect dads," Dulac reports. The infanticidal instinct vanished; the males built nests and placed the pups in them, groomed the pups, and huddled by them protectively. These findings, she says, suggest that there are "circuits in the male brain that underlie parental behavior," but those behaviors are "normally repressed."

Previous research at another lab identified one brief period in which male mice do seem driven to care for pups: beginning exactly three weeks after mating. Dulac replicated those findings and noted that it makes sense for infanticidal behavior to switch off in males at a point when their own progeny might be

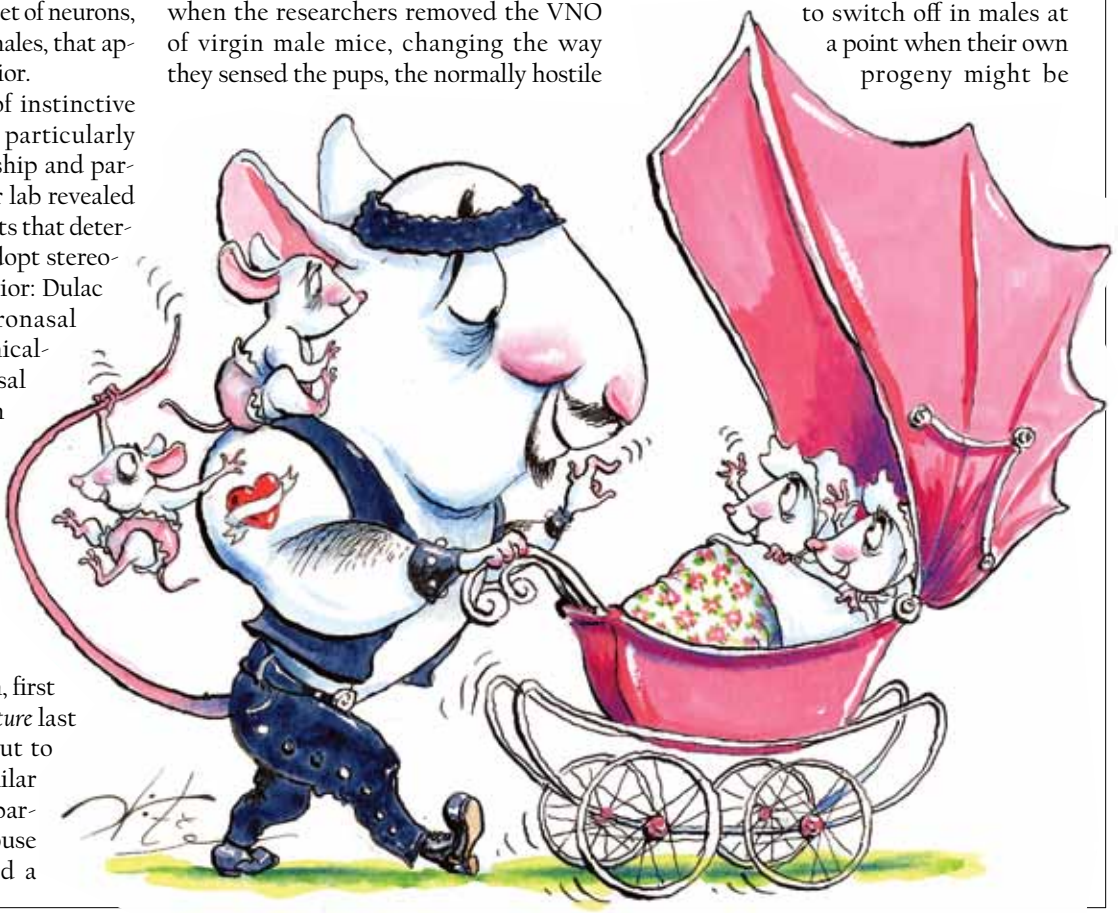

Illustration by Michael Witte

born. The males remain protective until the pups reach typical weaning age, about three weeks after birth; then the infanticidal instinct returns.

Seeking the specific brain structures that underlie parenting instincts, Dulac's team focused on the medial preoptic area of the hypothalamus (known to influence maternal behavior), and identified neurons that express a neuropeptide known as galanin. When the scientists destroyed the galanin neurons in mouse brains, the nurturing instinct disappeared in both males and females. "The effect is very striking," Dulac points out: previously mated males and females were largely indifferent to pups, and virgin females became as infanticidal as virgin males. This suggests, she explains, "that there are two groups of neurons—one that drives parental behavior and one [still unidentified] that drives infanticidal behavior—and somehow they inhibit each other."

Her team then employed optogenetic technology, using light to activate galanin neurons in the brains of virgin male mice—and the stimulation made previously infanticidal males behave like fathers. Their findings point to "these few hundred" galanin-expressing neurons as "the command neurons that drive parental behavior," Dulac says. She suspects humans possess similar circuits; neurons that express neuropeptides such as galanin are found in an area of the hypothalamus that scientists know controls instinctive behaviors such as sleeping, eating, reproduction, and aggression. "Each time these neurons have been discovered in animals, their equivalent has been found in humans, with similar functions and generating similar behavioral disorders when absent or impaired," she notes. If galanin neurons in the medial preoptic area do have a human analogue, she believes the discovery could lead to possible treatments for postpartum depression, which can make a mother indifferent to her newborn.

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These findings are particularly compelling in an era when human parents often feel they must consult books and blogs to do their jobs properly. "In fact," Dulac says, "it seems like all you have to do is push the right button in the brain in both males and females and animals know how to take care of their young." Male colleagues with children, she adds, "are happy to know that, at least from what is seen in mice, the male brain is also designed to care for the young."

—ERIN O'DONNELL

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