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RESEARCH NEWS

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Disabling a Sensory Organ Prompts Female Mice to Act Like Male Mice

By short-circuiting the sensory organ that detects the chemical cues mice use to attract mates, a team of Howard Hughes Medical Institute (HHMI) researchers has prompted female mice to behave like male mice in the throes of courtship.

The finding, reported August 5, 2007, in the journal *Nature*, suggests that the neural circuits that govern gender-specific behaviors, such as aggression and courtship, are similar in the male and female brain. According to the new study, the sexual behaviors of female mice, at least, are ruled by a pheromone-detecting organ that engages a neural circuit that determines whether a mouse shows its feminine side or acts like a male.

> "The female behaves exactly like the male. In the big picture, it suggests that the female brain has a perfectly functional male behavioral circuit."
> **— Catherine Dulac**

Biologists have long searched for the root causes of sexually dimorphic behaviors—those that differ between the sexes. The new findings promise to redirect that quest.

"From a developmental standpoint, the finding is very satisfactory," said Catherine Dulac, an HHMI investigator and Harvard University professor of molecular and cellular biology who led the new study. "It means you only have to build one brain in a species and that the one brain is built, more or less, the same in the male and the female."

Dulac's team, composed of first author Tali Kimchi, a postdoctoral fellow, and collaborator Jennings Xu, a Harvard undergraduate student, plumbed the neural depths of sexually dimorphic mouse behavior by engineering females to have functionally deficient vomeronasal organs. Also known as Jacobson's organ, the vomeronasal organ is a pocket in the nasal cavity of many animals that is packed with receptor cells. It is the key detector of pheromones, chemical signals that elicit specific behavioral responses in certain animals,

including mice.

The researchers found that female mice whose vomeronasal organs were genetically disabled behaved like males in the throes of courtship, exhibiting behaviors such as mounting, pelvic thrusts, solicitation and the complex ultrasonic vocalization characteristic of the male mouse. Correspondingly, female traits such as nursing behaviors and maternal aggression were diminished.

The findings provide strong evidence that male sexual behavior is hard wired into the female mouse brain and suggests, more broadly, that male and female courtship behaviors exist in the brains of both sexes and are switched on or off by the chemical cues mice use to initiate sex.

"The female behaves exactly like the male," said Dulac. "In the big picture, it suggests that the female brain has a perfectly functional male behavioral circuit."

"People who observe animal behavior have been struck by the fact that the biggest differences in behavior between animals of a given species are gender based," Dulac explained, but little is known about the underlying differences in the brain that govern the characteristic patterns of gender-based behavior.

Scientists have explored many avenues to explain sexually dimorphic behavior. To try and ferret out its cause, they've looked at everything from the influences of hormones such as testosterone to anatomy, positing that there may be a region of the brain that organizes gender-based behavior.

The sensory-controlled neural switch that governs the circuit is most likely different in male and female mice, Dulac noted, but that may be the extent of gender differences in the brain.

The work of Dulac and her colleagues promises to open a new window to the neural mechanisms that underlie gender-based behavior in animals by bringing the senses and an animal's ability to process what it sees, hears, and smells into the equation.

What occurs in humans and other animals may be quite different, Dulac noted, because the mouse depends largely on pheromones and its sense of smell, while humans and many other animals respond more to visual cues or a combination of sensory cues.

Scientists have been studying the vomeronasal organ for a century and know its role as a detector of pheromones well. While it is known that the organ is wired to the parts of the brain that govern reproductive behavior, its influence on gender-based behaviors was obscured in past studies because the surgical techniques used to ablate the organ flooded the nasal cavity with blood, disabling the olfactory system. To compare results from mice engineered to have a disabled vomeronasal organ, Dulac's group surgically removed the organ and ensured the nasal cavity was clear and the olfactory system operational.

"When we removed the vomeronasal organ surgically, we found the animal had the same phenotype" as the engineered mice, Dulac explained.

The new insight into the mechanisms that govern sexual behavior in animals gives science a new avenue to explore the molecular and physiological pathways that lead to differences in sexual behavior, according to Dulac. "Now we can really approach things from a mechanistic point of view," she said. "We can trace signaling events in the brain and see how brain areas controlling sex-specific behaviors are connected to each other."