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Scientists discover a tangle of neurons that control aggression

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(PhysOrg.com) -- In a tiny region buried deep in the brain, neurons that control two disparate behaviors – aggression and mating – are closely intertwined, Howard Hughes Medical Institute researchers have revealed. The study, conducted in mice, suggests that the association between these two classes of neurons may help to suppress aggressive behaviors during mating.

Scientists have long known that stimulating a particular region of the brain could trigger aggressive behavior. But the methods used in those studies, which date back to the 1920s, were far cruder than the sophisticated tools available to neuroscientists today, and they left scientists uncertain as to precisely where the neurons that control aggression are located in the brain, says Howard Hughes Medical Institute (HHMI) investigator David Anderson.

In a study reported February 10, 2011, in the journal Nature, Anderson and his colleagues decided to see if they could answer those questions using more modern approaches. They focused their efforts on a region of the brain's hypothalamus called the ventromedial nucleus. Both mating and fighting appeared to activate neurons in the very deepest part of this region, in a tiny area about 300 microns in diameter, called VMHv1.

To record activity in this region, the researchers inserted tiny bundles of electrodes into the brains of 30 male mice. Because the VMHv1 region is so tiny and buried so deeply within the brain, getting the electrodes

positioned correctly was exceedingly difficult. But Dayu Lin, a postdoctoral fellow in Anderson's lab who is now a professor at New York University, managed to hit the target (and only the target) in five of the mice. The electrodes enabled the researchers to record the activity of 104 individual neurons as the mice fought and mated, over a period of several months.

While a male mouse was alone in its cage, these neurons remained quiet. But mice are territorial, so when the researchers put a strange male into the cage, the mouse already in the cage attacked, thrashing its head and biting. Whenever this behavior occurred, the researchers observed that a subset of the cells near the implanted electrodes began firing. While some neurons began firing the moment a male entered the cage, others fired only once the mouse attacked.

When researchers placed a female mouse into the cage instead of a second male, the male mouse became amorous. Researchers could see that neurons in VMHv1 fired in this situation, too – but they were not the same neurons that became active in the presence of another male. As the mice began mating, the activity of neurons in the VMHv1 waned. Surprisingly, "many of the neurons that were activated during a male-male encounter became actively suppressed, as if beauty calmed the savage beast," says Anderson, a neurobiologist at the California Institute of Technology in Pasadena.

That experiment didn't prove that the neurons in VMHv1were causally involved in the mating or aggression, however. To prove that, the researchers needed to show that they could control mating or aggression by stimulating or suppressing the activity of those neurons.

So they used a virus to insert a gene into the neurons that encoded an ion channel that could be controlled using light. Once the virus had infected the neurons and inserted its genetic cargo, the researchers used a fiber

optic cable to light up this region of the brain. Turning the light on caused the neurons to fire. The mice attacked not just males, but also females and inanimate objects, including an inflated latex glove. “The light goes on and the animal attacks the glove. The light goes off and the animal stops attacking,” Anderson says. “That result is pretty remarkable.”

Anderson and his colleagues then used a similar method to prevent the neurons from firing. When the researchers turned neurons in VMHv1 off, the mice refused to fight, even in the presence of a strange male. “That indicated that neurons in that part of the brain are not only sufficient to produce an attack, but they’re also necessary for normal aggressive behavior,” Anderson says. “That finding moves the research from correlation to causation,” he says. The results suggest that aggressive behaviors are localized to this particular region of the brain, and not as broadly distributed in the hypothalamus as previous studies suggested.

Neither stimulating nor inhibiting the neurons appeared to have much of an impact on mating. However, mating did influence aggression. When the researchers allowed the male mice to mount a female before turning the light on, they failed to provoke an attack. Only when the mice had finished mating could the researchers again trigger aggression.

One possibility, says Anderson, is that the neurons in VMHv1 that are activated by a female inhibit fighting rather than promoting mating. The neurons might be intermingled for a reason. “The animal should not be trying to mate with an enemy when it’s supposed to attack it,” Anderson says, “and it should not be trying to attack a female when it’s supposed to be mating.”

The next step will be to determine which neurons in VMHv1 control which behavior. The hypothalamus is the most evolutionarily ancient

part of brain. So the neural connections that exist in mice likely exist in a wide variety of other species as well, including humans, Anderson says.

More information: *Nature* paper online: www.nature.com/nature/journal/ … ull/nature09736.html

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