Steroids in female mouse urine light up nose nerves of male mice

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A group of steroids found in female mouse urine goes straight to the male mouse's head, according to researchers at Washington University School of Medicine in St. Louis. They found the compounds activate nerve cells in the male mouse's nose with unprecedented effectiveness.

"These particular steroids, known as glucocorticoids (GCCs), are involved in energy metabolism, stress and immune function," says senior author Timothy E. Holy, Ph.D., assistant professor of neurobiology and anatomy. "They control many important aspects of the mouse's physiology and theoretically could give any mouse that sniffs them a detailed insider's view of the health of the animal they came from."

Holy plans further research to see if activating the nerves in the male mouse's nose leads to particular behavioral responses. He probes the male mouse's reaction to chemical signals from female mice to advance understanding of pattern recognition and learning in the much more complex human brain. In 2005, he found that female mice or their odors cause male mice to sing. He doesn't know yet if the GCC steroids' effects on the male mouse nose help to trigger this behavior.

Science has long recognized that urine, sweat and other bodily fluids contain chemical communication signals called pheromones that can influence the biology or behavior of others. Most mammals use the information in these signals for social purposes, such as establishing territory or dominance, or in courtship and mating. In many cases, though, the specific chemical identities of the signals are unknown.

The new study, published in *The Journal of Neuroscience* and led by graduate student Francesco Nodari, identified compounds that are unusually potent stimulators of the mouse nose. The pheromones activate nerve cells 30 times as often as all the other pheromones previously identified in female mouse urine combined. In addition, several of the new signals activate specific nerve cells. This may mean the male mouse's brain can assess different aspects of female mouse health by selectively analyzing individual pheromones.

Stressing female mice led to a threefold increase in the levels of GCCs in their urine, directly linking the female mouse's health and the GCC pheromones.

The GCC pheromones that Nodari identified were sulfated, which means they had a chemical attachment comprised of sulfur and oxygen atoms. This attachment is added to deactivate the steroids prior to excretion in the urine. When Nodari used an enzyme to remove these attachments, the GCCs lost their ability to activate nerves, further suggesting that the link between the sulfated GCCs and the nerve cells is a channel fine-tuned by evolution to carry information from female mice to male mice.

The nerves researchers studied in the male mouse nose are located in an area known as the accessory olfactory system. Humans and many closely related apes don't have an accessory olfactory system, but most other mammals and some reptiles do. The system, found in a structure called the vomeronasal organ, sends its outputs to a different part of the brain than the main olfactory system. Like the main olfactory system, it's dedicated to detecting airborne particles. But researchers believe the accessory olfactory system focuses on compounds from sources that are physically very close to or touching the animal.

According to Holy, this focus on scents from nearby sources makes the

accessory olfactory system "halfway between a taste system and a sense of smell." He believes the GCC pheromones account for approximately 75 percent of the signals detected in female urine by the male accessory olfactory system.

"Because these new pheromones are so good at activating the accessory olfactory system, they will be very helpful in efforts to better understand what this system does," he says. "That high degree of activation likely also means they have much potential for advancing the general study of pheromones."

Source: Washington University