

Flow of potassium ions in brain cells is key to sexual arousal

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When it comes to sex, a female rat knows how to avoid a communication breakdown. To announce her sexual readiness, she will automatically arch her back, deflect her tail and stand rigid to allow an aroused male to mount. Now, Rockefeller University researchers have figured out the precise chemical and physical mechanism in a group of brain cells that controls this swayback posture, a reflex called lordosis that signals one of life's most complex yet primitive instincts — the need for sex.

The group of cells that generates lordosis behavior resides deep in the brain in a structure called the hypothalamus. When an aroused male touches the flanks of a female, these cells determine whether the female will present her rump. “By way of these cells, the female controls sexual reproduction,” says lead researcher Donald Pfaff, head of the Laboratory of Neurobiology and Behavior. “That’s why these cells are so important.”

In past years, Pfaff and his colleagues have teased apart the neural circuitry and hormonal regulation of lordosis. “The struggle now,” he says, “is to understand it intimately at the cellular level, to bring it down to as fine a degree of chemical and physical knowledge as we possibly can.”

All neurons, whether they reside in the hypothalamus or elsewhere, maintain a constant flux of charged ions across their cell membranes via donut-shaped proteins called ion channels. The rise and fall of different brain chemicals can affect the flow of these ions into and out of the cell by opening or closing the channels. Although the Pfaff lab had long

known that norepinephrine, a brain chemical that heightens alertness and mediates stress, excites these cells in the hypothalamus, the question was which ions it affects and how.

Using a technique called whole cell patch clamp, Anna W.J. Lee, a postdoc in the Pfaff lab, found that norepinephrine prevents the exit of potassium ions from these cells, called ventromedial hypothalamic neurons, a block that activates them. (Specifically, norepinephrine reduces the fast-acting A-type potassium current.) With potassium ions locked inside the cells, the cells fire pulses of electrical activity, which then trigger the rest of the lordosis circuit to operate.

But that's not all. The team found that when female rats are treated with the sex hormone estradiol before the experiment, the number of cells that respond to norepinephrine soar, making the impulse to mate stronger. It turns out that the sex hormone turns on a set of genes, those for the receptor onto which norepinephrine binds — a self-fulfilling biological prophecy in the name of female reproduction.

Besides activating these cells in the hypothalamus, Pfaff and his colleagues believe that norepinephrine plays a much broader role in stimulating sexual behavior. “Female rats not only become generally aroused and alert but also sexually aroused,” says Pfaff. “The action of norepinephrine on these hypothalamic cells is a way in which generalized arousal force facilitates sexual arousal, which, in turn, fosters sex behavior, without which reproduction cannot occur.”

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