

# Learning from lab-rat love

## A libido-booster for female sexual dysfunction?

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**W**hat's a woman to do when sexual encounters become difficult or less satisfying?

- Vascularly directed sexual dysfunction treatments for men are not the answer; phosphodiesterase inhibitors such as sildenafil did no better than placebo among 800 women with various sexual problems.<sup>1</sup>

- The testosterone patch increases sexual interest for some women but failed to win FDA approval because of long-term safety concerns.

Even more frustrating, libido loss is a common side effect with some widely prescribed psychotropics—such as selective serotonin reuptake inhibitors. But an agent shown to boost libido in female rats may give women with sexual dysfunction a pharmaceutical option.

### FROM SUNSCREEN TO APHRODISIAC

Approximately 10 years ago, University of Arizona researchers studied a melanocortin-stimulating hor-



**Flirting rodents?** Behaviors such as meeting head to head with males then abruptly fleeing may suggest increased sexual desire in female rats, researchers say.

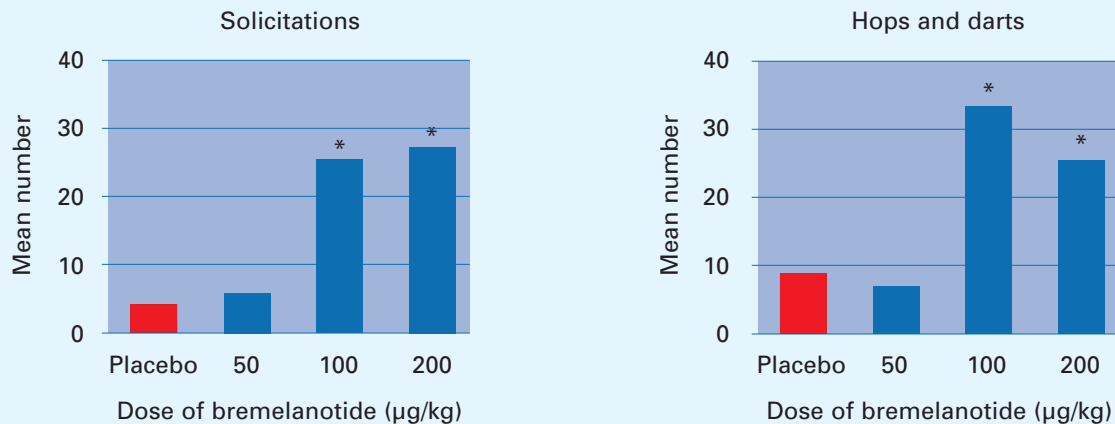
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mone analogue while trying to develop a product to allow light-skinned persons to tan without ultraviolet ray exposure. The product indeed darkened skin, but it also triggered spontaneous erections in all 3 men in the pilot study.<sup>2</sup> A modified version of the erection-inducing peptide—now called bremelanotide—is being tested in phase 3 clinical trials as a prospective erectile dysfunction treatment.<sup>3</sup>

Unlike its predecessors, bremelanotide works directly on neural pathways that control sexual function, rather than on the vascular system. But its

Figure

### Bremelanotide increases sexually solicitous behaviors in female rats



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highest-interest feature may be its effect on female sexual desire—at least in rats.

Behavioral neurologist James Pfau, PhD, identified behaviors female rats use to arouse males—what might be called the rodent equivalent of flirtation. These behaviors include solicitations (meeting head to head with males, then abruptly fleeing), pacing, hops, and darts.

His group then tested the effect of various doses of subcutaneous bremelanotide on 40 ovariectomized female rats primed with estradiol and progesterone.<sup>4</sup> Researchers paired each female with a male for 30 minutes and recorded their behaviors. Compared with females who received placebo or low-dose bremelanotide, high-dose bremelanotide females performed significantly more “flirtatious” behaviors (*Figure*). The researchers attributed this difference to increased sexual desire.

The drug’s mechanism of action remains in question, but it appears to act centrally. Injecting it directly into female rats’ ventricles produced similar behaviors when they were paired with receptive males. Also, markers of neuronal activ-

ity have been found in the anterior aspect of the hypothalamus and nucleus accumbens—areas associated with sexual activity and pleasure.

#### PILOT STUDY IN WOMEN

A randomized, double-blind, placebo-controlled, crossover trial suggests that bremelanotide as a nasal spray might increase desire in women with female sexual dysfunction (FSD).<sup>5</sup> When 18 perimenopausal women with FSD were given bremelanotide or placebo, the bremelanotide group reported greater sexual desire and genital arousal while watching a sexually explicit video.

Specifically, this pilot study—part of the drug’s phase 2 trials in women—found that:

- 72% of women who took bremelanotide reported feelings of genital arousal, compared with 39% in the placebo group
- 67% of treated women experienced sexual desire versus 22% of controls.

#### IS FSD A PATHOLOGY?

Some clinicians worry that FSD is a “disease” made up by pharmaceutical industry marketers.

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They argue that hypoactive sexual desire is not a disorder but an adaptive response to physical changes or relationship difficulties.<sup>6</sup>

On the other hand, a national survey of 1,749 women and 1,410 men ages 18 to 59 found sexual difficulties to be more prevalent in women than in men:<sup>7</sup>

- 43% of women reported sexual dysfunction, compared with 31% of men.
- 26% of women reported inability to achieve orgasm compared with 8% of men.

An effective and safe medication targeted at improving women's sexual desire might help some patients, such as peri- or postmenopausal women, in otherwise healthy relationships.

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