

## When brain metabolism dips, desire goes up in monkeys on 'female Viagra'

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Cuddling and grooming are important activities for common marmosets such as these at the Wisconsin National Primate Research Center. Cuddling, and especially grooming, strengthen pair bonding, physical intimacy and successful mating. A new study that used PET scans of marmoset brains reveals the effects on brain activity of a new drug just hitting the market for women with hypoactive sexual desire disorder. Credit: J. Lenon/Wisconsin National Primate Research Center, University of Wisconsin-Madison



As the drug touted as "the female Viagra" comes to market, researchers at the University of Wisconsin-Madison are learning more about how the drug, called flibanserin, affects the brain.

Inhibited <u>sexual desire</u>, known as hypoactive <u>sexual desire disorder</u>, affects premenopausal women, but no biological cause is known. In people, it can make physical intimacy difficult or impossible.

David Abbott, a professor of obstetrics and gynecology in the UW School of Medicine and Public Health, and Alexander Converse, associate scientist at UW-Madison's Waisman Center, studied the effects of flibanserin in the common marmoset, a monkey for which pair bonding is instrumental to mating success and family life.

In a new study now online in the *Journal of Sexual Medicine*, Abbott and Converse linked flibanserin-initiated decreases in female metabolism in the parts of the <u>brain</u> associated with executive function with increased <u>pair bonding</u>. Although both males and females in the study initiated more grooming, the behavior was more pronounced in the males, even though only females received the drug.

The researchers say that despite the increased intimate attention inspired by the drug, there is much room for improvement with flibanserin and related drugs. For example, it works in only about 10 percent of patients, according to FDA data. And unlike Viagra, where one pill does the trick, flibanserin, sold under the brand name Addyi, must be taken over time to have an effect. Side effects can be serious and include severely low blood pressure and potential loss of consciousness. Alcohol consumption, certain medicines and liver impairment can exacerbate the risks.

"More research is needed on the underlying mechanisms of how this new drug works, so that the treatment and safety can be improved," Abbott



says.

To begin to explore the mechanism of action, Abbott and Converse compared flibanserin-treated monkeys to untreated monkeys using noninvasive PET scanning on live common marmosets at the Wisconsin National Primate Research Center.

Marmosets and humans have similar hormonal signaling activity and mating behaviors, especially in response to sexual cues such as touch and scent. "The female marmosets in our study provided effective, unparalleled, controlled models, allowing us to determine how flibanserin acts in the primate brain," Abbott explains.

After mapping the animals' brains with MRI scans, Converse used PET imaging to correlate changes in brain chemistry, particularly the use of glucose at specific locations with flibanserin-induced behavioral changes. Together with colleague Yves Aubert, Converse and Abbott found that glucose metabolism declined in the medial preoptic area of the hypothalamus, a brain center long linked to intimate grooming and solicitation of sex in both marmosets and rodents.

The amount of metabolic decline correlated directly with an increase in grooming by a male partner. In short, the bigger the metabolic dip in brain activity, the more grooming.

"Metabolism in the prefrontal cortex, a brain area involved in assessing events and deciding on actions, was also reduced in females receiving flibanserin," Abbott notes. "The amount of decline predicted increased mutual grooming."

The research by the Wisconsin group was funded by the pharmaceutical company Boehringer Ingelheim, which developed flibanserin until 2011 when Sprout Pharmaceuticals took over development of the drug. Sprout



earned FDA approval for the drug earlier this year.

Although the female marmosets did not have <u>hypoactive sexual desire</u> disorder,

Abbott says the study nonetheless shows that flibanserin, by altering metabolic brain activity, prompts increased female behavior responses to grooming, a form of intimate, gentle touching from males. That, says Abbott, "offers the first insight into how the drug may be working in the brains of women."

## Provided by University of Wisconsin-Madison

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