Behavior is the ultimate arbiter: An alternative explanation for the inhibitory effect of fluoxetine on the ovulatory homolog model of orgasm in rabbits

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Pavlicev et al. (1) offer an experimental test of the ovulatory homolog model of female orgasm in rabbits. While we appreciate the importance of designing animal models of such elusive phenomena, there are several issues we would like to address.

Pavlicev et al. tested whether a daily dose of the selective serotonin reuptake inhibitor (SSRI) would have a dose-dependent effect on the number of contact ovulations in the female rabbit. Upon finding no such effect, the groups were pooled together. This yielded a statistically significant reduction in contact ovulations but also results in several issues. First, the experimental and control groups were small and unbalanced, which reduces power and gives inaccurate estimates of true effects (2). Second, we do not see the rationale behind using 2 separate control groups when 1 could have sufficed. Finally, the decision to pool both groups is concerning. If the authors hypothesized that there would be a dose-dependent effect of fluoxetine on contact ovulations, then the groups should not have been pooled. Thus, we suspect that decision was an a posteriori attempt to surpass the significant α level. This form of "researcher degree of freedom" in analyses can result in "*P*-hacking," which leads to statistical false positives and overestimated true effects (3, 4).

SSRIs delay or abolish orgasm in humans and do the same to orgasm-like responses in other animals (5). The lack of consummatory pleasure or reward is associated with a decline in sexual behaviors in animals, such as solicitations in female rats, that reflect appetitive sexual motivation (6). As female solicitations decrease, so do male responses to the females, and thus a decreased amount of clitoral and vaginocervical stimulation (VCS) (7). In rats, VCS is critical for the induction of nightly prolactin surges that maintain progesterone secretion from the corpora lutea (8) and is thus critical for successful pregnancy. Moreover, when fully receptive females can control (i.e., pace) the rate of intercourse, more will display a progestational state relative to females that receive the same number of intromissions (9). In turn, such paced copulation leads to the formation of conditioned preferences in female rats (6, 10). Thus, in the female rat, there exists a positive relationship between behaviors that achieve optimal sexual pleasure and the potentiation of reproduction. Unfortunately, Pavlicev et al. report no measures of copulatory behavior for either the females or male that might be indicative of a sexual reward state. This makes it impossible to know whether the animals experienced any decrease in sexual reward with fluoxetine treatment that might have led to a decrease in receptivity or appetitive responses, and a concomitant decrease in the strength of copulatory stimulation provided by the male. In female rats, SSRIs like fluoxetine consistently reduce the frequency of solicitations made toward a male, and thus decrease the number of penile intromissions and ejaculations received. If contact ovulations in rabbits are dependent on the strength and/or timing of copulatory stimulation, then it is possible that fluoxetine decreased contact ovulations by disrupting both appetitive and consummatory sexual behaviors.

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