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Male experimenters make female rats uneasy

Study shows the sex of the experimenter is a critical variable in rodent models

Researchers at the University of Lethbridge's Canadian Centre for Behavioural Neuroscience (CCBN) have shown that the sex of an experimenter, a factor typically not accounted for in preclinical studies using rodents, could have an effect on study results. Their findings were recently published in <u>Frontiers in Neuroscience</u>.

Dr. Gerlinde Metz, along with Drs. Mirela Ambeskovic, Jamshid Faraji and others, compared the effects of male and female experimenters on male and female rats. In some situations, the experimenter was physically present and in others, unwashed T-shirts worn by the experimenters were placed in the room. Animals were handled by their male or female experimenters for five minutes a day for 10 days before any experimental manipulations were done to ensure the rats were used to the experimenters.



"We watched a lot of different variables and compared how the animals responded to a male and a female experimenter working with them," says Metz. "We saw that the presence of a human makes a huge difference and we saw again that the rats responded to the Tshirt. It's not only visual interaction the rats responded to, but also some olfactory cues that influenced their behaviour."

Researchers measured the rats' stress levels before and after they were subjected to a mildly stressful situation. Infrared thermography was used to detect skin temperature and blood samples were taken to determine the levels of hormones involved in the stress response (corticosterone and oxytocin). Female rats in the presence of a male experimenter or T-shirt worn by a male experimenter showed higher levels of corticosterone and lower levels of oxytocin, the so-called bonding hormone. They also responded to the presence of a male experimenter by displaying more anxiety-like behaviour, such as spending more time near the walls of their enclosure, and had higher body surface temperatures.

"An interesting finding is that female rats display these heightened stress responses even after frequent exposure to male experimenters," says Faraji. "We call it the male observer effect."

"It's really a very important finding because it will affect how we design experiments," says Metz. "I don't mean we should only have female experimenters work with rats or any laboratory animals, but we need to report it and have better standards of how we pursue research with laboratory animals. We also need to be aware that our presence and our handling affects them."

The findings may help explain the replication crisis, which occurs when the same experiments done at different labs produce different results. When a study's results can't be replicated from one lab to another, the credibility of the findings can be in doubt.

"All scientists are concerned about controlling unwanted factors when they are manipulating experimental variables," says Faraji. "These results address this concern and reveal one of these factors in the field."

Given the study results, Metz says it would be better to have a series of observations or tests and then take an average or, as Faraji suggests might be possible in the future, to eliminate the variable by using robotics. The ultimate goal is to ensure results obtained in the preclinical stages are reliable and will lead to successful clinical trials in humans. Rodents are often used in preclinical studies, which take place before any testing in humans is done, to determine if a drug, treatment or procedure might be useful.

"Because experimenter sex in animal studies is not commonly reported, improved standards should require researchers to report the sex of experimenters," says Metz. "We cannot avoid the presence of a human experimenter or handling the animals in many situations, but we need to be aware of these variables and maybe include appropriate control situations in an experiment to be sure about the results."

Perhaps the study results aren't surprising to pet owners, who can attest to the bonds they have with their pets. One study, referred to in an article in <u>Smithsonian Magazine</u>, explored the bond between humans and their dog companions and found that dogs and humans gazing into each other's eyes caused both to secrete oxytocin.

This news release can be found online — <u>Male experimenters make female rats uneasy</u>.

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