

Study: Estrogen helps females respond better to stress

By Melissa Pandika, Los Angeles Times

In the battle of the sexes, a new study places females in the lead – concluding that they respond better to repeated stress thanks to estrogen.

“It’s kind of a popular view that males and females respond differently to stress,” said University at Buffalo neuroscientist and study co-author Zhen Yan. “Our study offers the molecular mechanism.”

Yan’s group found that young female rats stressed out by a week of periodic physical restraint showed no impairment in their ability to remember and recognize objects they had been shown a few hours earlier. Young males exposed to the same stress conditions fared worse on the short-term memory test.

But when the researchers manipulated estrogen levels in the brain, female rats respond to stress like males and vice-versa.

The study, published Tuesday in the journal *Molecular Psychiatry*, focused on a region of the brain known as the prefrontal cortex, which is “like a CEO,” Yan explained, controlling high-level executive functions such as memory, planning and decision-making.

The team looked at the activity of receptors in the prefrontal cortex that bind with an amino acid called glutamate, which is involved in the completion of memory and planning tasks. Glutamate receptors comprise the majority of receptors in that part of the brain, Yan said.

In 2012, the team reported that male rats exposed to repeated

stress lost glutamate receptors in their prefrontal cortex region, resulting in impaired performance on a number of memory tasks.

When the researchers later examined female rats as a control, they saw that females exposed to the same stress showed enhanced cognition and memory. Other animal studies have produced similar results.

Yan's group suspected that the female sex hormone estrogen might have a protective effect against stress. It "was kind of an intuitive guess," she said.

For the current study, the scientists physically restrained young male and female rats, placing them in a small cylindrical compartment for two hours a day over a roughly one-week period. The experiment was intended to mimic the challenging – but not dangerous or life-threatening – stress that humans face day-to-day, Yan said.

As expected, the prefrontal cortex of young males exposed to restraint stress showed a loss of glutamate receptors. In contrast, the prefrontal cortex of young females exposed to the same stress showed no change in glutamate receptor numbers.

To test the animals' short-term memory, the researchers showed the rats two identical objects, followed by a second pair an hour later. Three hours later, they presented the rats with one object from each pair. Spending more time exploring the object from the first pair indicated that the animal remembered it from four hours prior. A preference for the more novel object from the second pair signified impaired short-term memory.

Female rats performed better on the memory test than their male counterparts. But when male rats were injected with the female hormone estradiol, they showed increased glutamate transmission, and the restraint stress had no effect on their

ability to recognize objects. And when the researchers suppressed one type of estrogen receptor in the female rats' brains, their performance suffered.

It's still not clear exactly how estrogen protects against stress – for example, whether estrogen is affecting stress hormone release or directly affecting the glutamate receptor. Yan said her group plans to pursue this question in future research.

The study offers a scientific explanation for what has been mainly anecdotal evidence of women being better able to cope with stress than their male counterparts, Yan said.

"It's not that there's no reason," she said, adding that the study might also shed light on sex differences in mental disorders.

Yan cautioned that her group's results are based on rat studies. Still, the findings may hold relevance for humans since many cellular functions are conserved between the two species, she said.