PRESS RELEASE

By Ron Hartung
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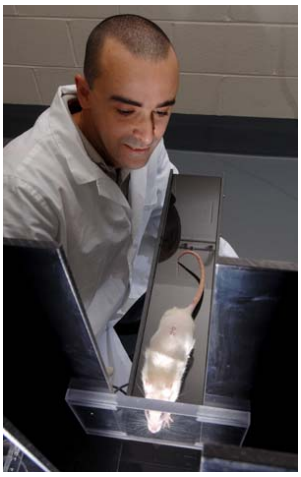
Researcher wins $1.8M grant to find out why anxiety targets women


Mohamed Kabbaj

Anxiety disorders afflict women twice as often as men, but estrogen might not be the reason. Testosterone, though, could be.

That is one of the preliminary findings in the lab of Florida State University researcher Mohamed Kabbaj, associate professor in the College of Medicine. He recently was awarded a five-year, $1.8 million grant from the National Institute of Mental Health to investigate the sex differences in anxiety. His research team also is working to identify the role of a gene called zif268.

"It's a very important molecule," Kabbaj said. "So far, zif268 plays a major role in learning, memory and drug addiction. I think our work shows for the first time that it's also implicated in anxiety."

Years from now, the result may be drugs that can reduce anxiety more effectively.

In their lab, Kabbaj and his team exposed male and female rats to situations that provoked anxiety. They knew stress would activate the zif268 gene, so they explored the brains of the rats to see how the gene had expressed itself. Kabbaj called it "a fishing expedition."

The results surprised them. Only one part of the brain showed a difference in gene expression between males and females: the medial prefrontal cortex, the part of the brain that allows humans to experience emotions and the meaning of things.

"We were not expecting to see that," Kabbaj said, "so we wanted to follow up with functional studies to see if this difference between males and females has any significance in terms of anxiety and difference in social interaction."

Males have more zif268 in their prefrontal cortex than females do. Males also are less anxious. So the researchers reduced the expression of zif268 in the prefrontal cortex of the males. Result: The males became as anxious as the females.

"One of the questions you have to ask," Kabbaj said, "is why males have more zif than females. We think it's because of testosterone. Testosterone is keeping that level of zif very high.

"Our recent findings show that the hormone estrogen is not implicated in sex differences in anxiety. However, our preliminary data show the male hormone testosterone may be protecting male rats from developing anxiety. The fact that females do not have a lot of testosterone may put them at risk of developing anxiety disorders."

Kabbaj and his team think testosterone activates receptors in the prefrontal cortex, which in turn activate various molecules, and those molecules lead to the increased expression of zif, which then activates a series of other molecules. Their project also involves determining the exact molecular targets of zif268 that are relevant to sex differences in anxiety. They refer to these as the gene's downstream targets.

"If we could demonstrate the role of zif in anxiety, then we could design drugs that affect either its upstream or downstream targets to hopefully reduce anxiety in women," Kabbaj said. "If we increase zif expression in men who have some level of depression or anxiety, maybe we can help them, too."