Researcher awarded $1.8 million to study gender differences in antidepressant effects

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Mohamed Kabbaj, professor of biomedical sciences at Florida State.

In low doses, the general anesthetic drug ketamine works as an antidepressant, and for females the boost in mood is easier to achieve.

A Florida State University College of Medicine researcher is learning more about why this drug, used as an antidepressant for the last decade, requires a higher dosage to improve depression in males.

Mohamed Kabbaj, a professor in the Department of Biomedical Sciences at the College of Medicine, received a $1.8 million grant from the National Institute of Mental Health to support his research.

“The first purpose is to show the molecular mechanism behind the hormones estrogen and progesterone that are enhancing the effect of ketamine in females,” Kabbaj said. “The other purpose of the grant is to determine whether males will respond to estrogen and progesterone in addition to ketamine administered at a low dose.”

Researchers are interested in looking for ways around giving higher doses of ketamine to males because of the drug’s side effects.

“At medium and high doses, ketamine can create dissociation from one’s surroundings,” Kabbaj said. “It’s also an addictive drug, and you cannot give it chronically.”

Administering ketamine with a combination of estrogen and progesterone, which are more abundant in females, may diminish some of these side effects. Kabbaj and his team continue investigating ketamine despite its side effects because of its quick antidepressant response time.

“Ketamine is used as an antidepressant in clinics now because it takes effect acutely,” Kabbaj said. “Two hours after one low dose, patients feel better. The classic antidepressants take two to three weeks to work.”

This quick, low-dose effect can be a lifesaver for suicidal patients whose repeated thoughts of harming themselves make time a precious commodity. It is also used as an alternative to electroconvulsive shock therapy, which depressive patients sometimes refuse.

But Kabbaj's research has shown that gender differences must be considered.

"Even with classic antidepressants there are studies showing that men and women respond differently to different classes of antidepressant drugs," Kabbaj said. "Their brains are different, so we need to find out if there are treatments that work better in women and treatments that work better in men."

Kabbaj wants to know whether striking the right balance between ketamine, progesterone and estrogen in both genders will allow for safer use of ketamine as an ongoing treatment for depression, so that it can treat those in need of immediate relief from depression without the secondary effects.

By Julie Jordan