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Men and women have opposite genetic alterations in depression

A study in Biological Psychiatry examines the sex-specific molecular changes in major depressive disorder

Philadelphia, March 13, 2018 – Men and women with major depressive disorder (MDD) have opposite changes in the expression of the same genes, according to a new postmortem brain [study](#) by researchers at the University of Pittsburgh and Centre for Addiction and Mental Health (CAMH), Toronto, Canada. The findings, published in [Biological Psychiatry](#), indicate distinct pathology, and suggest that men and women may need different types of treatment for depression.

“This important paper highlights the divergent molecular mechanisms contributing to depression in men and women. It challenges the assumption that a similar diagnosis across people has the same biology,” said John Krystal, MD, Editor of *Biological Psychiatry*.

This is the first time that this unique opposing pathology has been reported. “While researchers have been examining the brains of depressed subjects for decades, many of these studies included only men,” said lead author Marianne Seney, PhD, of University of Pittsburgh. This is despite the differences in MDD between men and women—women are twice as likely to be diagnosed with MDD, and report greater illness severity and different types of symptoms than men.

The study combined eight published datasets (four in men and four in women) in a meta-analysis. Senior author Etienne Sibille, PhD, of CAMH, and colleagues analyzed gene expression levels, which indicate how much protein a gene is producing, in postmortem brain tissue of 50 people with MDD (26 men and 24 women) and the same number of unaffected men and women for comparison.

Most of the genes that had altered expression were changed in only men or only women. However, genes that were altered in both men and women were changed in opposite directions. Women had increased expression of genes affecting synapse function, whereas men had decreased expression of the same genes. Women had decreases in genes affecting immune function, whereas men had increased expression of these genes. Additionally, the researchers applied their methods to data from a different set of subjects and replicated the opposing changes.

The analysis included three different brain regions that regulate mood—the anterior cingulate cortex, dorsolateral prefrontal cortex, and amygdala—and that are dysfunctional in MDD. The opposite changes in gene expression were specific to the different brain regions. So if women had increased expression of a particular gene in one region and decreased in another, men showed just the opposite.

Because the study used postmortem brain tissue, the effect of the opposite molecular signatures on how MDD affects men and women differently could not be studied. But the findings support sex-specific pathology in the disorder.

“These results have significant implications for development of potential novel treatments and suggest that these treatments should be developed separately for men and women,” said Dr. Seney. For example, in the paper the authors suggest that new treatments targeting the sex-specific pathology in MDD might suppress immune function in men, or boost its function in women.

Notes for editors

The article is "Opposite molecular signatures of depression in men and women," by Marianne L. Seney, Zhiguang Huo, Kelly Cahill, Leon French, Rachel Puralewski, Joyce Zhang, Ryan W. Logan, George Tseng, David A. Lewis, and Etienne Sibille (<https://doi.org/10.1016/j.biopsych.2018.01.017>). It appears in *Biological Psychiatry*, published by [Elsevier](#).

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at Biol.Psych@UTSouthwestern.edu or +1 214 648 0880. Journalists wishing to interview the authors may contact Ashley Trentrock at trentrockar@upmc.edu or +1 412 529 9092, or Sean O'Malley at sean.omalley@camh.ca or +416 970 8243.

The authors' affiliations and disclosures of financial and conflicts of interests are available in the article.

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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