

Sex differences seen in response to common antidepressant

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Women with depression may be much more likely than men to get relief from a commonly used, inexpensive antidepressant drug, a new national study finds. But many members of both sexes may find that it helps ease their depression symptoms.

The persistence of a gender difference in response to the drug — even after the researchers accounted for many complicating factors — suggests that there's a real biological difference in the way the medication affects women compared with men. The reasons for that difference are still unclear, but further studies are now examining hormonal variations that may play a role.

The study involved citalopram, a commonly used antidepressant that is available both as a generic drug and under the brand name Celexa.

Researchers from the University of Michigan Depression Center and their colleagues from around the country tested the drug's ability to help depression patients achieve remission, or total relief from their symptoms, in a multi-year study called STAR*D.

The gender differences emerged from a detailed analysis of data from 2,876 men and women who had a clear diagnosis of major depression, and took citalopram over a number of weeks, with the doses increasing over time.

In the end, women were 33 percent more likely to achieve a full

remission of their depression, despite the fact that women in the study were more severely depressed than the men when the study began.

The study showed no differences between men and women in side effects, the amount of time that patients stuck to taking the drug, or the amount of time it took for them to achieve remission of their symptoms.

The new findings, which represent the largest and most rigorous analysis ever of gender differences in response to an antidepressant, are published online in the Journal of Psychiatric Research.

Elizabeth Young, M.D., a professor and associate chair of psychiatry at the U-M Medical School and member of the Depression Center, is the study's lead author. "Other studies have suggested that there are differences between men and women in response to different antidepressants, but the evidence has been conflicting," she says. "This study is large enough, and we were able to control for enough complicating factors, that we feel confident there is a true difference. These results have clear implications for the clinical treatment of depression."

Young and her colleagues, including Susan Kornstein, M.D., of Virginia Commonwealth University, and John Rush, M.D., formerly of the University of Texas Southwestern Medical Center at Dallas, conducted the analysis of data from men and women between the ages of 18 and 75, many of whom were being treated by primary care physicians and not psychiatrists. All of the patients had been experiencing depression for years, with the average length of experience around 12 years.

The study was funded by the National Institute of Mental Health. Unlike many previous industry-sponsored studies of antidepressants, it included a "real world" sample of people with major depression, and did not exclude people who had a history of suicidal thinking. The study did not

include people with bipolar disorder. Participants in the study could continue with psychotherapy that they had been undergoing before the start of the study, but could take no other antidepressants.

Citalopram is one of a class of medicines known as SSRIs, or selective serotonin reuptake inhibitors. In earlier decades, gender differences had been seen in studies of patients taking an older generation of drugs called tricyclics, with men tending to respond better to such medications. But for more than 15 years, SSRIs have been the first choice for treating depression.

Although the current study didn't look at hormonal variations between men and women that might account for the difference in response to citalopram, Young and her colleagues note that animal studies have shown that estrogen modifies the brain systems involved in the activity of serotonin, a key brain chemical.

Kornstein is leading further analysis of the STAR*D results to look for possible differences among women according to their menopausal status and their use of hormone replacement therapy. Meanwhile, Young's research as a member of the U-M Molecular & Behavioral Neuroscience Institute focuses on the interactions of sex hormones and stress response in depression and other mood disorders.

Overall, women are more affected by depression than men, with about 12 percent of women suffering from some form of depression in a given year compared with 6 percent of men. Depression and other mood disorders are the leading cause of disability among women under the age of 45.

But the study's authors are quick to caution that their findings don't mean that citalopram should only be used in women. Raw data from the study show that 24 percent of men achieved remission with the drug,

compared with 29 percent of women. The difference in remission rates grew larger once the researchers adjusted for other factors, but the fact remains that many men were helped.

Rather, they note that STAR*D and other studies have shown that many people with depression need to try several treatments to find the one that's right for them and will produce lasting results.

That's why a new study called CO-MED has begun. Young and colleagues from U-M and around the country are now enrolling people with depression for this study that will assess the impact of combinations of medications. One of the medications in that study is escitalopram, a cousin of citalopram, but it also includes other common SSRI antidepressants.

Source: University of Michigan Health System

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