

Genetic variation alters efficacy of antidepressant

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Having a different form of a gene that regulates the brain chemical noradrenaline influences how well men remember negative memories after taking the antidepressant drug reboxetine, according to a study published in the October 23 issue of *The Journal of Neuroscience*. The findings demonstrate how genes can influence antidepressant response.

While it is normal for our strongest memories to be associated with emotional experiences, previous studies suggest the heightened recall of negative events may be linked to depression and anxiety disorders. Research also shows that reboxetine, which exclusively affects brain levels of noradrenaline, reduces the tendency of people with depression to recall [negative memories](#).

In the current study, Ayana Gibbs, MD, PhD, Theodora Duka, MD, PhD, and others at the University of Sussex examined how reboxetine influences emotional memories in healthy men with a variant form of the α -2B adrenoceptor gene (ADRA2B), which contains the instructions for a type of noradrenaline receptor. The researchers found that while reboxetine weakened aversive memory in people with the common form of ADRA2B, the drug did not change aversive memory in people with the variant gene form.

"Researchers are increasingly interested in how antidepressants like reboxetine affect the way emotional information is processed and how this information could be used to predict the drugs that are most likely to be successful antidepressants," Gibbs said. "Our study suggests genetic

makeup is another important piece of the puzzle."

More than 100 healthy white men participated in the University of Sussex study, where they received a genetic test to see if they had the ADRA2B variant (30 percent of whites do). They were then randomly assigned to receive a single dose of reboxetine or a sugar (placebo) pill. After waiting a couple of hours for the drug to be absorbed into the bloodstream, the men viewed a series of positive, negative, and neutral images on a computer screen. Such images included pictures of children riding a rollercoaster ride, the scene of an accident, and a man looking out of a window. Thirty minutes later, they were asked to write descriptions of as many pictures as they could remember.

While all participants remembered the positive and negative pictures better than the neutral ones, the participants with the ADRA2B variant recalled more negative pictures—an effect that remained even in those who received the reboxetine treatment.

"This study is good news for the scientific community, which has struggled for decades to identify factors influencing the admittedly moderate efficacy of antidepressants," explained Andreas Papassotiropoulos, MD, who studies how genes influence memory at the University of Basel and was not involved with this study. "This study elegantly demonstrates the importance of the concept of aversive memory in psychiatric disease and paves the way for further experiments dealing with the molecular underpinnings of antidepressant efficacy," he added.

According to Gibbs, future studies will explore whether the ADRA2B variant influences the effectiveness of reboxetine in other groups, including women, and establish whether similar effects are observed in patients with depression or [anxiety disorders](#).

Provided by Society for Neuroscience

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