

Common gene variants explain 42% of antidepressant response

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Antidepressants are commonly prescribed for the treatment of depression, but many individuals do not experience symptom relief from treatment. The National Institute of Mental Health's STAR*D study, the largest and longest study ever conducted to evaluate depression treatment, found that only approximately one-third of patients responded within their initial medication trial and approximately one-third of patients did not have an adequate clinical response after being treated with several different medications. Thus, identifying predictors of antidepressant response could help to guide the treatment of this disorder.

A new study published in *Biological Psychiatry* now shares progress in identifying genomic predictors of antidepressant response.

Many previous studies have searched for genetic markers that may predict antidepressant response, but have done so despite not knowing the contribution of genetic factors. Dr. Katherine Tansey of Institute of Psychiatry at King's College London and colleagues resolved to answer that question.

"Our study quantified, for the first time, how much is response to antidepressant medication influenced by an individual's genetic makeup," said Tansey.

To perform this work, the researchers estimated the magnitude of the influence of common genetic variants on antidepressant response using a



sample of 2,799 antidepressant-treated subjects with <u>major depressive</u> <u>disorder</u> and genome-wide genotyping data.

They found that genetic variants explain 42% of individual differences, and therefore, significantly influence antidepressant response.

"While we know that there are no genetic markers with strong effect, this means that there are many genetic markers involved. While each specific genetic marker may have a small effect, they may add up to make a meaningful prediction," Tansey added.

"We have a very long way to go to identify genetic markers that can usefully guide the treatment of depression. There are two critical challenges to this process," said Dr. John Krystal, Editor of Biological Psychiatry. "First, we need to have genomic markers that strongly predict response or non-response to available treatments. Second, markers for non-response to available treatments also need to predict response to an alternative treatment. Both of these conditions need to be present for markers of non-response to guide personalized treatments of depression."

"Although the Tansey et al. study represents progress, it is clear that we face enormous challenges with regards to both objectives," he added. "For example, it does not yet appear that having a less favorable genomic profile is a sufficiently strong negative predictor of response to justify withholding antidepressant treatment. Similarly, there is lack of clarity as to how to optimally treat patients who might have less favorable genomic profile.."

Additional research is certainly required, but scientists hope that one day, results such as these can lead to personalized treatment for depression.



More information: "Contribution of Common Genetic Variants to Antidepressant Response" by Katherine E. Tansey, Michel Guipponi, Xiaolan Hu, Enrico Domenici, Glyn Lewis, Alain Malafosse, Jens R. Wendland, Cathryn M. Lewis, Peter McGuffin, and Rudolf Uher, doi: 10.1016/j.biopsych.2012.10.030, *Biological Psychiatry*, Volume 73, Issue 7 (April 1, 2013)

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