Current genetic tests unlikely to improve antidepressant treatment, study finds

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(Medical Xpress)—Genetic markers cannot predict which patients with major depression will respond to anti-depressant drugs, according to a large collaborative study led by researchers at King's College London's Institute of Psychiatry.

Published in *PLOS Medicine*, the study is the largest to date to look at the link between genetic markers and antidepressant response and suggests that genetic tests will not meaningfully improve the treatment of depression with antidepressants.

Professor Peter McGuffin, from King's College London's Institute of Psychiatry and co-author of the paper says: 'The results demonstrate that it is extremely unlikely that any previously reported or novel common genetic variant could be used to inform antidepressant prescription.'

Dr Rudolf Uher, also from King's College London's Institute of Psychiatry, and senior author of the paper says: 'The large samples we used makes this a definitive study in the field. We found that no single genetic variant, or combination of genetic variants, could predict response to antidepressant treatment. This study stands out against the background of numerous claims from commercial companies that genetic tests could help doctors decide which antidepressant to choose based on the results.'

The authors add that future studies will need to draw on a much broader base of clinical, genetic, epigenetic, transcriptomic, and proteomic information to obtain a clinically meaningful prediction of how an individual with major depression will respond to antidepressant treatment.

Major depressive disorder, also known as clinical depression, is one of the top ranking diseases in terms of lost productivity, absence of work and health care costs world-wide. Prescription of antidepressants is the most common treatment, but upon being given their first antidepressant, less than 50% of patients see their symptoms improving. This has led experts to investigate whether genetic information could be used to personalise treatment.

The researchers from the NEWMEDS consortium, an international academic–industry collaboration, drew on information from several NEWMEDS research studies. They studied 1,790 individuals with major depression who had been given two types of common anti-depressant drugs—serotonin-reuptake inhibitors (SRI) and noradrenaline-reuptake inhibitors (NRI). The researchers knew which patients had responded well to the drugs and had information on the genetic make-up of each patient, as each patient had been tested for over 500,000 genetic variants.

The researchers carried out four genome-wide analyses. The first searched for genetic markers to predict response to both types of antidepressants in the whole sample of 1,790 individuals. The second and third searched for predictors of response to SRI (1,222 individuals) and NRI (568 individuals). A fourth analysis searched for genetic variants which could predict a different response to SRI or NRI.

In each case, the researchers found that no single genetic variant, or combination of genetic variants, could significantly predict response to treatment. Response to treatment was measured as a difference in at least 3 points in the reduction of depression symptoms severity on the Hamilton Rating Scale for Depression (HRSD-17).

Finally, the researchers compared the results from NEWMEDS with data from another large-scale study – the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) where all participants with major depression were treated with an SRI. The combined data on 2,897 individuals and 1.4 million genetic variants also confirmed that no common genetic variant could predict antidepressant treatment response.

More information: Tansey, K. et al. 'Genetic Predictors of Response to Serotonergic and Noradrenergic Antidepressants in Major Depressive Disorder: a Genome-wide Analysis of Individual-level Data and a Meta-Analysis' *PLOS Medicine* (16th October 2012) doi:10.1371/journal.pmed.1001326

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