Scientists present first genetic evidence for why placebos work

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usually mere sugar pills designed to represent "no treatment" in a clinical treatment study. The effectiveness of the actual medication is compared with the placebo to determine if the medication works.

And yet, for some people, the placebo works nearly as well as the medication. How well placebos work varies widely among individuals. Why that is so, and why they work at all, remains a mystery, thought to be based on some combination of biological and psychological factors.

Now, researchers at UCLA have found a new explanation: genetics. Dr. Andrew Leuchter, a professor of psychiatry at the UCLA Semel Institute for Neuroscience and Human Behavior, and colleagues report that in people suffering from major depressive disorder, or MDD, genes that influence the brain's reward pathways may modulate the response to placebos. The research appears in the August edition of the Journal of Clinical Psychopharmacology (currently available online by subscription).

Placebos are thought to act by stimulating the brain's central reward pathways by releasing a class of neurotransmitters called monoamines, specifically dopamine and norepinephrine. These are the brain chemicals that make us "feel good." Because the chemical signaling done by monoamines is under strong genetic control, the scientists reasoned that common genetic variations between individuals — called genetic polymorphisms — could influence the placebo response.

Researchers took blood samples from 84 people diagnosed with MDD; 32 were given medication and 52 a placebo. The researchers looked at the polymorphisms in genes that coded for two enzymes that regulate monoamine levels: catechol-O-methyltransferase (COMT) and monoamine oxidase A (MAO-A). Subjects with the highest enzyme activity within the MAO-A polymorphism had a significantly lower placebo response than those with other genotypes. With respect to COMT, those with lower enzyme activity within this polymorphism had a lower placebo response.

"Our findings suggest that patients with MDD who have specific MAO-A and COMT genotypes may be biologically advantaged or disadvantaged in mounting a placebo response, because of the activity of these two enzymes," said Leuchter, who directs the Laboratory of Brain, Behavior and Pharmacology at the UCLA Semel Institute.

"To our knowledge, this is the first study to examine the association between MAO-A and COMT polymorphisms and a response to placebo in people who suffer from major depressive disorder," he said.

Leuchter noted that this is not the sole explanation for a response to a placebo, which is likely to be caused by many factors, both biological and psychosocial. "But the data suggests that individual differences in response to placebo are significantly influenced by individual genotypes," he said.

Including the influence of genotype in the design of clinical trials could facilitate more powerful testing of future treatments, Leuchter said.

Source: University of California - Los Angeles