

# Genes determine whether sugar pills work

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It is a well-known fact in drug trials that individuals can respond just as well to placebos, sugar pills, as to the active drug. On the other hand, it is difficult to explain why only certain people get better from placebos. A team of researchers from Uppsala University and Gothenburg University have now found gene variants that can impact the placebo effect and a mechanism in the brain that characterizes those who respond to placebos.

The study, published in *Journal of Neuroscience*, examined 108 individuals suffering from social phobia using a brain camera (PET, positron emission tomography). The individuals were participating in a treatment study looking into how anxiety-moderating drugs affect brain activity. Just under one fourth of the subjects were given a placebo instead of a drug. This was a double-blind study, meaning that neither the subjects nor the research team know who was taking the drug or the sugar pill.

Before and after an eight-week period of treatment, the participants were asked to give a stressful oral presentation while their brain activity was monitored. When all the metering was finished and the study was decoded, it turned out that 40 percent of the placebo group had received the same degree of anxiety relief from the sugar pill as other groups got from a drug.

Those who responded well to the placebo had a significant reduction in activity in the amygdala in the temporal lobe, while this reduction was not found in the others. In previous research the amygdala has stood out

as a key structure for emotional reactions. Both serotonin-active drugs (SSRI preparations) and cognitive behavioral therapy moderate activity in this area.

"Thus, successful placebo treatment works through the same mechanism in the brain," says Tomas Furmark at the Uppsala University Department of Psychology, who directed the study.

The study also analyzed two genes that influence the reabsorption and synthesis of serotonin in the brain (the serotonin transporter gene and the tryptophan hydroxylase-2 gene). The findings showed that only individuals who had certain variants, alleles, of these genes had a moderation of activity in the amygdala. Above all, the tryptophan hydroxylase-2 genes variants could predict the degree of relief from anxiety achieved by the placebo pill as well as the moderation of the amygdala.

Statistical analyses showed that it is a genetic effect on the activity in the amygdala that influences the propensity to respond to a placebo, that is, a path from the gene, via the brain, to behavior.

The study shows for the first time that genes influence the placebo effect by regulating the propensity to react in an area of the brain that is important for our feelings.

This could have significant consequences for all drug testing and other treatment studies that use a placebo.

"The findings show that the possibilities of demonstrating that an active treatment functions better than a placebo can be affected by the gene variants in the trial subjects. It is also possible that genes can explain why certain people respond well or poorly to anxiety-moderating drugs and psychotherapy respectively," says Tomas Furmark.

Source: Uppsala University

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