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Genes may influence placebo effect

Response to sham treatment depends on certain DNA details, analysis suggests

By ASHLEY YEAGER 1:46PM, APRIL 14, 2015

REAL EFFECTS Tweaks to certain genes may make some people more likely to experience the placebo effect, a new study finds.

People who get a feel-good boost from sham medical treatments may have their genes to thank.

Researchers reviewing studies of individuals' genetics and placebos have identified 11 genes that appear to play a role in people's response to the sham treatments. Establishing a link between certain genes and the placebo effect is in its infancy, the researchers say online April 13 in *Trends in Molecular Medicine*. But if confirmed, such a connection could change the way scientists analyze clinical drug trials and how doctors treat patients, the researchers note.

“We don’t actually know how big of a role genetics play in the placebo effect,” says study coauthor Kathryn Hall, a molecular biologist at Beth Israel Deaconess Medical Center in Boston. Studies suggesting a link between the placebo effect and a set of specific genes —what the team calls the placebome —have been popping up over the last few years, Hall says. She and colleagues reviewed recently published data on the placebome, hoping the results would get more scientists thinking about how genes, placebos and drugs interact.

“The placebome approach is very interesting, but we must be aware that genetics is only a part of the whole placebo phenomenon,” says Fabrizio Benedetti, a neurophysiologist at the University of Turin Medical School in Italy.

In the placebo effect, patients given a nonmedically active substance, such as a sugar pill, report improvement in their condition because they think they’ve been given something that will help. Whether the placebo effect was real or a figment of patients’ imaginations was questioned until a little over 20 years ago, says study coauthor Ted Kaptchuk, also of Beth Israel Deaconess. At that time, scientists showed that the body’s pain system and response to placebo pain medication could be manipulated to dull the ache of a pulled tooth. Researchers then showed that brain regions involved in pain suppression were activated in patients expecting to get pain medicine (*SN: 12/20/08, p. 26*; *SN: 9/3/05, p. 157*). Those brain scan results showed that the placebo effect really existed, Kaptchuk says. Finding genetic influences on the effect is moving placebo science to an even more basic level, he says.

Among the genes that appear to mediate the placebo effect, five are associated with the chemical messenger dopamine and four are linked with the chemical messenger serotonin. A gene related to opioids and one associated with endocannabinoids, which play a role in producing the feeling of getting high from pot, are also implicated in the placebome. Variations in these genes may change the way the body makes and uses the chemicals and molecules, the scientists say.

Molecule	Gene name	Gene symbol
Dopamine	Catechol-O-methyltransferase	*COMT*
	Monoamine oxidase	*MAO-A*
	Dopamine B hydroxylase	*DBH*
	Dopamine receptor 3	*DRD3*
	Brain-derived neurotropic factor	*BDNF*
Serotonin	Tryptophan hydroxylase-2	*TPH2*
	5-Hydroxytryptamine transporter	*SLC6A4*
	5-Hydroxytryptamine receptor 2A	*HTR2A*
	Serotonin transporter gene-linked polymorphic region	*5-HTTLPR*
Opioid	Opioid receptor	*OPRM1*
Endocannabinoid	Fatty acid amide hydrolase	*FAAH*

SHORT LIST Based on a review of previous studies, scientists have shown that variants of 11 genes associated with dopamine, serotonin, opioids and endocannabinoids may be involved in the placebo effect. *K.T. Hall et al/Trends in Molecular Medicine 2015*

Large-scale genome studies run in conjunction with clinical drug trials could help fill in the gaps in understanding which genes are involved and what role they play in boosting the placebo effect, in general and possibly within specific diseases. Another possibility is to include a no-treatment group in studies to control for the placebo effect, the researchers say. They note that screening participants in clinical drug trials and removing those who are genetically predisposed to show a placebo response might make clinical trials more efficient.

There’s a clinical rationale for identifying genes associated with larger placebo effects, too, says neuroscientist Luana Colloca of the University of Maryland School of Nursing in Baltimore. A doctor who knows that a patient responds positively or negatively to placebos can use that information to tailor personalized treatments, she says.

Colloca and the study authors note, however, that using the placebome in the clinic and in clinical trials has ethical implications. Designing drugs only for those who don’t respond to placebos or using placebo response to manipulate drug effects in clinical trials raise questions and concerns, the scientists say.

Still, it’s exciting to think that genes play a role in the placebo effect, Colloca says. “We do not know why we

evolved genetic variability in the placebo effect," she says. "Probably it provides us with an advantage in resilience and self-healing."

Citations

K.T. Hall, J. Loscalzo and T.J. Kaptchuk. Genetics and the placebo effect: the placebome. *Trends in Molecular Medicine*. Published online April 13, 2015. doi: 10.1016/j.molmed.2015.02.009.

Further Reading

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