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Java gene study links caffeine metabolism to coffee consumption behavior

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A new Northwestern Medicine caffeine study has found that a variant in a gene that has previously been linked with nicotine metabolism is also linked to caffeine metabolism. Credit: Northwestern University

Depending on a person's genetic make-up, he or she might be able to guzzle coffee right before bed or feel wired after just one cup, based on continuing research at Northwestern Medicine.

Studying how genes impact coffee consumption habits is nothing new. In previous work from Marilyn Cornelis, assistant professor in the department of Preventive Medicine at Northwestern University Feinberg School of Medicine, she identified genetic variants associated with coffee consumption behavior.

In a new Northwestern Medicine study, Cornelis applied similar methodology to study metabolites in the blood—or chemicals found in one's blood after consuming caffeine—instead of coffee consumption behavior. She found the same variants as in previous research, as well as an additional variant. Additionally, she discovered that a variant in the gene CYP2A6, which previously had been linked to smoking behavior and nicotine metabolism, is also linked to caffeine metabolism.

"Each of us could be potentially responding to caffeine differently, and it's possible that those differences can extend beyond that of caffeine," Cornelis said.

The study was recently published in *Human Molecular Genetics*.

The study's first and most important takeaway, Cornelis said, is that all but one of the genes linked to caffeine metabolites in the blood are biological candidates for caffeine metabolism: CYP1A2, AHR, POR, ABCG2 and CYP2A6. But Cornelis and her collaborators were surprised to find that the gene GCKR, which has been repeatedly linked to glucose and lipid metabolism in independent studies, may also play a role in metabolizing caffeine, according to this new research.

"How this gene relates to both caffeine metabolism and caffeine-seeking behavior is unclear but worthy of further study, given its link to several health outcomes," Cornelis said.

The second finding in Cornelis' research is that genetic variants linked to

lower levels of caffeine metabolites, which imply faster caffeine metabolism, are the same variants previously linked to higher coffee consumption.

"This makes sense, conceptually, but the genetic research confirms it and further re-emphasizes the notion that not everyone responds to a single cup of coffee (or other caffeinated beverage) in the same way," Cornelis said. "It's important to know, given coffee has been implicated in so many diseases."

And finally, many of the genes that she and her collaborators found to metabolize caffeine also coded for proteins that function in the metabolism of other clinically important drugs, such as those that treat insomnia, Parkinson's Disease, hypertension and more.

The findings support additional links between metabolism of caffeine, nicotine and possibly other pharmaceutical drugs. At this point, Cornelis said this is largely unknown but could have great implications for the field of precision medicine.

More information: Marilyn C. Cornelis et al, Genome-wide association study of caffeine metabolites provides new insights to caffeine metabolism and dietary caffeine-consumption behavior, *Human Molecular Genetics* (2016). DOI: 10.1093/hmg/ddw334

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