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## Migraine Sufferers Have More Nitrate-Reducing Microbes in their Mouths

Researchers at University of California San Diego School of Medicine have found that the mouths of migraine sufferers harbor significantly more microbes with the ability to modify nitrates than people who do not get migraine headaches. The study is published October 18 by *mSystems*.

“There is this idea out there that certain foods trigger migraines — chocolate, wine and especially foods containing nitrates,” said first author Antonio Gonzalez, a programmer analyst in the laboratory of Rob Knight, PhD, professor and director of the [Center for Microbiome Innovation](#) at UC San Diego and senior

author on the study. “We thought that perhaps there are connections between what people are eating, their microbiomes and their experiences with migraines.”

Many of the 38 million Americans who suffer from migraines report an association between consuming nitrates and their severe headaches. Nitrates, found in foods such as processed meats and green leafy vegetables and in certain medicines, can be reduced to nitrites by bacteria found in the mouth. When circulating in the blood, these nitrites can then be converted to nitric oxide under certain conditions. Nitric oxide can aid cardiovascular health by improving blood flow and reducing blood pressure. However, roughly four in five cardiac patients who take nitrate-containing drugs for chest pain or congestive heart failure report severe headaches as a side effect.

Using publicly available data from the [American Gut Project](#), a crowdfunded citizen science effort managed by the Knight lab, Gonzalez and colleague Embriette Hyde, PhD, sequenced bacteria found in 172 oral samples and 1,996 fecal samples from healthy participants. The participants had previously filled out surveys indicating whether they suffered from migraines.



*The mouths of migraine sufferers harbor significantly more microbes with the ability to modify nitrates than people who do not get migraine headaches. Photo courtesy of [Pixabay](#).*

The bacterial gene sequencing found that bacterial species were found in different abundances between people who get migraines (migraineurs) and non-migraineurs. In terms of bacterial community composition, the team did not find huge differences in either fecal or oral samples from migraineurs compared to non-migraineurs.

The team then used a bioinformatic tool called PICRUSt to analyze which genes were likely to be present in the two different sets of samples, given the bacterial species present. In fecal samples, they found a slight but statistically significant increase in the abundance of genes that encode nitrate, nitrite and nitric oxide-related enzymes in migraineurs. In oral samples, these genes were significantly more abundant in migraineurs.

“We know for a fact that nitrate-reducing bacteria are found in the oral cavity,” said Hyde, project manager for the American Gut Project and assistant project scientist in the Knight lab. “We definitely think this pathway is advantageous to cardiovascular health. We now also have a potential connection to migraines, though it remains to be seen whether these bacteria are a cause or result of migraines, or are indirectly linked in some other way.”

Gonzalez and Hyde said the next steps will be to look at more defined groups of patients, separated into the handful of different types of migraines. Researchers can then determine if their oral microbes really do express those nitrate-reducing genes, measure their levels of circulating nitric oxide and see how they correlate with migraine status.

Co-authors of this study include: Naseer Sangwan and Jack A. Gilbert, University of Chicago; and Erik Viirre, UC San Diego.

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