Medical Xpress

Mouse study reveals what happens in the gut after too much fructose

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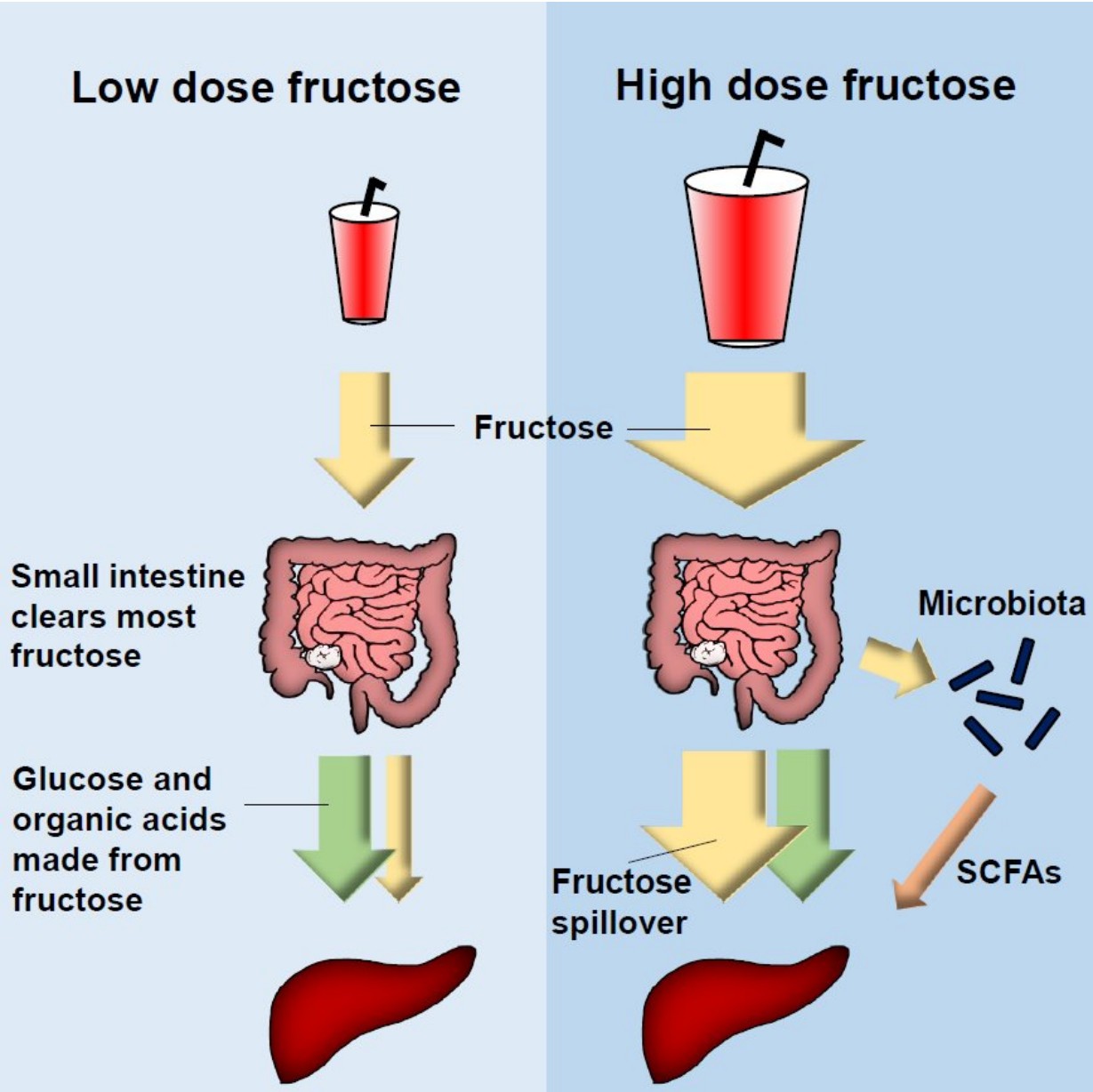

This graphical abstract depicts the findings of Jang et al., which show that it is actually the small intestine that clears most dietary fructose, and this is enhanced by feeding. High fructose doses spill over to the liver and to the colonic microbiota for metabolism. Credit: Jang et al./*Cell Metabolism* 2018

Princeton University researchers report that in mice, fructose, a sugar found in fruit, is processed mainly in the small intestine, not in the liver as had previously been suspected. Sugary drinks and processed high-sugar foods overwhelm the small intestine and spill into the liver for processing. Additionally, the authors learned that the ability of the small intestine to process fructose is higher after a meal. The work appears February 6 in the journal *Cell Metabolism*.

Evidence from previous animal and human studies has shown that excessive sugar ingestion can be harmful, especially to the liver. Chronic over-consumption can lead to obesity and foster insulin resistance that can progress to diabetes; it also can contribute to non-alcoholic fatty liver disease, which can lead to cirrhosis or liver cancer.

"There is a fundamental physiological difference in how smaller and larger amounts of sugar are processed in the body," explains Joshua D. Rabinowitz of the Lewis-Sigler Institute for Integrative Genomics at Princeton University, whose laboratory led the study. The prior view was that the liver processes all ingested sugar. But this study showed that more than 90 percent of the fructose was cleared by the small intestine in mice.

"We can offer some reassurance—at least from these animal studies—that fructose from moderate amounts of fruits will not reach the liver," he says. However, the small intestine probably starts to get overwhelmed with sugar halfway through a can of soda or large glass of

orange juice.

In the study, Rabinowitz and his colleagues studied the path of isotope-labeled fructose through the digestive systems of laboratory mice. The researchers observed that excess fructose that is not absorbed by the small intestine continues through the intestine into the colon. As a consequence, it also comes into contact with the natural microbiotic flora of the large intestine and colon, known as the microbiome.

"The microbiome is designed to never see sugar," Rabinowitz says. "One can eat an infinite amount of carbohydrates, and there will be nary a molecule of glucose that enters the microbiome. But as soon as you drink the soda or juice, the microbiome is seeing an extremely powerful nutrient that it was designed to never see."

While the study did not show that fructose influences the microbiome, the authors suggest an effect is likely and should be studied further to learn more about the biological consequences of high sugar intake.

The investigators also found that the small intestine clears fructose more efficiently after a meal. "We saw that feeding of the mice prior to the sugar exposure enhanced the small intestine's ability to process fructose," said Rabinowitz. "And that protected the liver and the microbiome from sugar exposure." The researchers theorize that in a fasting state, such as upon awakening or in the mid-afternoon, one is extra vulnerable to fructose due to a lessened ability to process it in the small intestine.

Although the study was conducted in mice, Rabinowitz encourages "the most old-fashioned advice in the world" for humans. Limit sweets to moderate quantities after meals, and do not have sweet drinks away from meal time.

More information: *Cell Metabolism*, Jang, C. et al: "The Small

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Intestine Converts Dietary Fructose into glucose and organic acids" www.cell.com/cell-metabolism/f … 1550-4131(17)30729-5 , DOI: 10.1016/j.cmet.2017.12.016

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