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Ghrelin receptor mediates HFCS-induced adipose inflammation and insulin resistance

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High fructose corn syrup (HFCS) is the most-used sweetener in US. While some studies suggest that HFCS consumption correlates with obesity and insulin resistance, other studies disagree. HFCS continues to be used as the primary sweetener in food supplies.

To investigate the metabolic effects of HFCS, we studied mice fed regular diet, high fat diet (HFD), or regular diet supplemented with 8% HFCS in drinking water (to mimic soft drinks). HFD-fed mice consumed the most total calories, and showed the most weight gain and fat deposition. Surprisingly, HFCS-fed mice exhibited the most severe insulin resistance; disproportionately greater in relation to their calorie intake and body fat. Adipose tissue macrophages (ATMs), consist of pro-inflammatory F4/80$^+$/CD11c$^+$ and anti-inflammatory F4/80$^+$/CD11c- macrophages, are closely linked to obesity and insulin resistance. HFCS feeding triggered robust increase of total ATMs similar to HFD, but intriguingly the ratio of anti-inflammatory ATMs was much lower, suggesting intensified adipose inflammation.

Orexigenic hormone ghrelin, via its receptor Growth Hormone Secretagogue Receptor (GHS-R), promotes adiposity and insulin resistance. To determine whether GHS-R mediates the effects of HFCS, we studied HFCS-fed *Ghsr*-null mice. The *Ghsr*-null mice exhibited lower pro-inflammatory ATMs and pro-inflammatory cytokine expression, but no difference in anti-inflammatory ATMs, in visceral fat. Moreover, the *Ghsr*-null mice showed attenuated liver steatosis and less-pronounced HFCS-induced insulin resistance.

In summary, HFCS has detrimental effects on adipose inflammation and insulin resistance, beyond the extra calories from HFCS; thus the safety of HFCS should be re-evaluated. GHS-R antagonists may represent novel drugs for ameliorating adipose inflammation and insulin resistance.

Biography

Yuxiang Sun received her MD from Beijing Medical University, P. R. China and PhD at the University of Manitoba, Canada. She subsequently received postdoctoral training at Baylor College of Medline. She is currently a principle investigator at Baylor College of Medicine. Her research interests are obesity, diabetes and metabolic regulation. He has published more than 40 peer reviewer papers many of which are in high ranking journals such as Cell Metabolism, JCI, PNAS, and Aging Cell. Currently, she serves as reviewer for a number of endocrine journals, and she is the Editorial Board Member of World Journal of Diabetes (WJD).

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