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GUT MICROBIOTA

Microbial metabolites feed into the gut–brain–gut circuit during host metabolism

New research published in *Cell* demonstrates a link between the gut microbiota and the gut–brain axis during host metabolism. Short-chain fatty acids (SCFAs) generated by the fermentation of soluble dietary fibre by the gut microbiota feed into a gut–brain neural circuit that ultimately affects host nutrient sensing.

The benefits of dietary fibre to human health are long-established, but the underlying mechanisms are poorly understood, although SCFAs are thought to play a part given that they are produced as a result of the breakdown of soluble fibre. Using gene expression analysis and radioactive tracers, Gilles Mithieux and colleagues tracked whether dietary fibre (fructo-oligosaccarides) and/or SCFAs (butyrate and propionate specifically) affected glucose production and energy homeostasis in rats fed different diets rich in these components.

The researchers found that diets rich in butyrate, propionate or fibre induced production of glucose in the gut. Moreover, butyrate and propionate both regulated the expression of genes involved in intestinal gluconeogenesis; butyrate through direct induction of these genes (via cAMP), and propionate via FFAR3 signalling from the periportal nervous system that fed into a gut–brain–gut neural circuit to affect gluconeogenesis in the gut. Ultimately, intestinal gluconeogenesis conferred beneficial effects on body weight (due to increased energy expenditure) and glucose control (insulin sensitivity), as well as protection against the development of obesity and diabetes upon feeding mice with a high-fat, high-sucrose diet.

"Our results suggest that one must focus on the effects of the metabolites produced by the [gut] microbiota on the metabolism of the host (under specific nutritional conditions), rather than simply on the changes in the [gut] microbiota composition," notes Mithieux. "Gut glucose metabolism ... is a powerful lever to positively modulate glucose and energy homeostasis and confer protection against obesity and type 2 diabetes," he concludes, which warrants further study.

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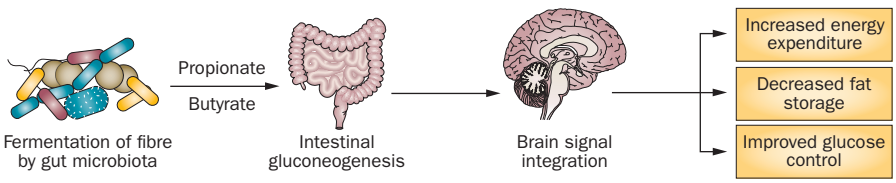

Original article De Vadder, F. *et al.* Microbiota-generated metabolites promote metabolic benefits via gut-brain neural circuits. *Cell* **156**, 84–96 (2014)