MedicalXpress

Altered microbiome burns fewer calories

December 14 2015

The link between the gut microbiome and obesity seems clear, but just how changes to gut bacteria can cause weight gain is not.

A new University of Iowa study in mice shows that drug-induced changes to the gut microbiome can cause obesity by reducing the resting metabolic rate - the calories burned while sleeping or resting. The findings, published in the journal *eBiomedicine*, highlight the critical role of gut microbes in energy balance and suggest that unhealthy microbiome shifts can lead to weight gain and obesity by altering resting metabolism.

"Our research leads to the conclusion that it is probably bacteria (in the gut) that are responsible for the calories you burn while you are asleep," says John Kirby, PhD, professor of microbiology and urology at the UI Carver College of Medicine.

Kirby and his colleagues focused on the effects of risperidone, an antipsychotic drug that causes significant weight gain in patients. Risperidone is used to treat various psychiatric disorders in adults and children, including autism, bipolar disorder, and schizophrenia, and prescribing rates for children have increased nearly eight-fold over the last two decades.

In an earlier study, Kirby and Chadi Calarge, a UI pediatric psychiatrist, compared patients taking risperidone long-term to patients who were not on the drug. They found that weight gain was correlated with a significant shift in the composition of the patients' gut microbiomes.

These results were published in Translational Psychiatry.

In the new *eBiomedicine* study, Kirby teamed up with Justin Grobe, UI assistant professor of pharmacology, to find out how this risperidone-induced microbiome shift causes weight gain. Mirroring the human studies, the researchers showed that risperidone causes weight gain in mice (an extra 2.5 grams, or approximately 10 percent of the total body mass, over two months compared to controls) and significantly alters the bacterial composition of the mouse microbiome. They then showed that the altered microbiome causes a reduction in resting metabolic rate that is entirely responsible for the excess weight gain.

"The control mice gain a little weight as they age and their microbiome undergoes a 'healthy shift' due to aging. With the risperidone, the mice become obese and exhibit an alternative, less healthy shift in their microbiome," Kirby says. "With this study, we now have a mechanism for how a shift in the microbiome contributes to weight gain, and it's to do with changes to the resting metabolic rate."

The team was able to investigate how the microbiome shift affected the animals' metabolism by using a novel piece of equipment - a total calorimetry machine - invented by Grobe. The apparatus allows precise measurements of energy intake, oxygen consumption and carbon dioxide output, and heat production in a single animal to determine the total energy change, or "delta G," of the mouse.

The researchers discovered there was no change in aerobic (oxygen-dependent) resting metabolic rate for mice fed risperidone compared to control mice, but there was a significant decrease in non-aerobic resting metabolic rate sufficient to account for the animals' weight gain

"It's about a 16 percent change in resting metabolic rate, which is enormous," Grobe says. "It would be 29 pounds of fat gained every year

for an average human."

"That is the equivalent of eating one additional cheeseburger every single day," adds Kirby.

To prove that it was the "shifted" microbiome that was responsible for this metabolic change and the weight gain, the researchers transferred the microbiome from risperidone-fed mice into control mice and saw the same effect: decreased resting metabolic rate and increased weight gain. Moreover, they found it wasn't just the bacteria that could produce this effect. Transferring just the bacteriophage (phage) - viruses that infect the microbiome bacteria—was sufficient to reduce resting metabolic rate and cause weight gain in control mice.

The results may suggest that manipulating resting metabolic rate, specifically by targeting the gut microbiome, could represent a new approach to treating obesity. Alternatively, preventing unhealthy changes to the microbiome may prove beneficial for patients undergoing risperidone treatment.

More information: Sarah M. Bahr et al. Risperidone-induced weight gain is mediated through shifts in the gut microbiome and suppression of energy expenditure, *EBioMedicine* (2015). DOI: 10.1016/j.ebiom.2015.10.018

Provided by University of Iowa