Medical Xpress

A gut check for PCOS-related obesity

March 8 2016, by Michael Price

Modifying gut bacteria could be a treatment option for some of the symptoms associated with the widespread disease polycystic ovary syndrome (PCOS), according to a recent study by San Diego State University researchers in collaboration with investigators from the University of California, San Diego. The study found that changes in gut bacteria are strongly associated with obesity and signs of diabetes in a mouse model that mimics PCOS.

PCOS affects approximately 10 percent of women worldwide, said SDSU biologist Scott Kelley, the study's lead author. PCOS is typically diagnosed in women that have increased levels of testosterone, menstrual cycle irregularity and cysts on the ovaries. In addition to a high incidence of infertility, women with PCOS have an increased risk of developing type-2 diabetes and heart disease.

Scientists have long known that gut bacteria aid in food digestion, make important vitamins and stimulate the immune system. Over the last decade, scientists have also discovered that people with obesity or diabetes have different bacteria in their guts than healthy people.

"What you see when you look at obesity," Kelley explained, "is large changes in specific groups of microorganisms that are involved in breaking down dietary fiber and regulating metabolism. We wondered if women with PCOS also have the same types of changes in their gut bacteria."

Testosterone boost

To answer this question in a controlled experiment, Kelley and his collaborator at UC San Diego, Varykina Thackray, turned to a mouse model of PCOS that is induced by giving mice the drug letrozole. This drug, which is used to treat certain types of breast cancer, blocks the conversion of testosterone into estrogen and results in a condition known as hyperandrogenism. About 80 percent of women with PCOS have hyperandrogenism.

"When you treat female mice with letrozole, you get similar symptoms to what you see in women with PCOS," Kelley said.

Half of the mice in the study were given letrozole and the other half received placebo. Both groups of mice ate the same diet. After five weeks, the letrozole group gained significantly more weight and were substantially fatter than the control group. They also had elevated blood glucose levels, which is associated with insulin resistance.

To look for changes in the gut bacteria, the researchers also collected fecal pellets from each mouse and analyzed the bacterial DNA in them. By comparing the fecal DNA to "barcodes" of known microbial DNA, Kelley was able to determine which gut bacteria were present in each mouse.

They found that the number of different bacterial species in the letrozole-treated mice was much smaller than in the control group. The results were published in January in the journal *PLOS ONE*.

Decreased diversity

"At first, things started out the same in the letrozole and control groups," Kelley said. "But rapidly, the gut bacterial communities as a whole diverged. In fact, the letrozole mice just stayed the same over the course

of the study. The diversity of the gut bacteria didn't go up with age, whereas the control mice got more and more diverse over time."

The researchers also saw an increase in certain types of bacteria that have been shown to change in mouse models of obesity, as well as in human obesity, suggesting that changes in the gut bacteria could contribute to the metabolic dysfunction associated with PCOS, he added.

It's unclear, though, whether these changes in the gut bacteria after letrozole treatment were the result of the weight gain or the cause of it. Kelley and his collaborators are currently delving into this question and early results seem to indicate that the microbes themselves may be responsible for the obesity. If that's the case, it suggests that by altering the microbial communities in the gut through probiotic treatment or other means, researchers might be able to help control the metabolic disorders associated with PCOS.

"The good part about this study is that we can increase our understanding not only of women's health but also our biology in general and how we might control the gut microbiome," Kelley said.

More information: Scott T. Kelley et al. The Gut Microbiome Is Altered in a Letrozole-Induced Mouse Model of Polycystic Ovary Syndrome, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0146509

Provided by San Diego State University