Scientists study links between obesity, age and body chemistry

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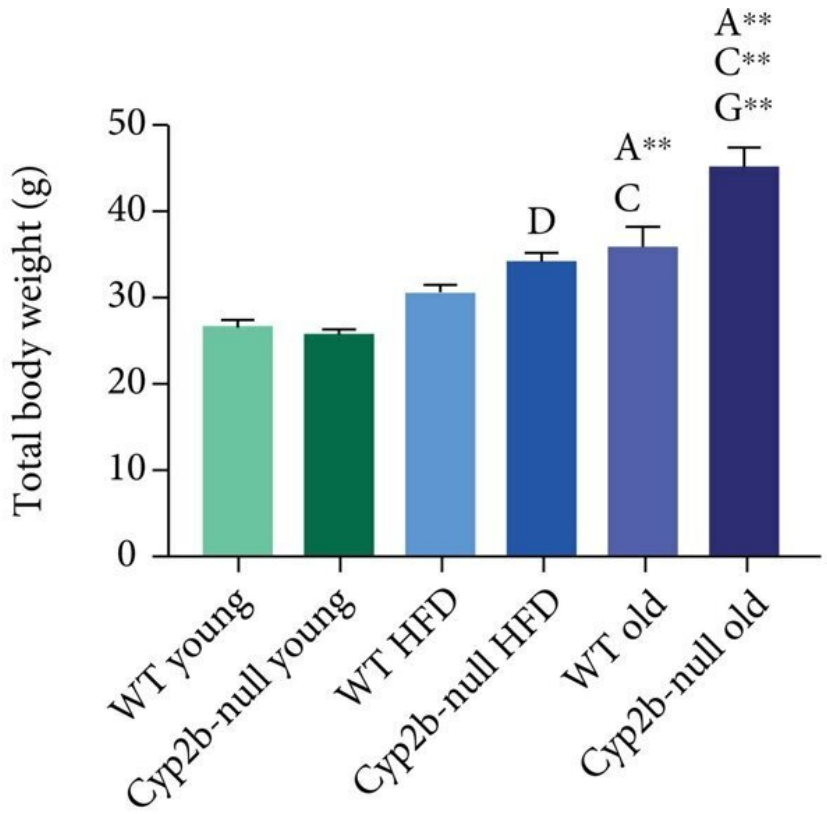

Comparison of total body, liver, and WAT weights between all treatment groups. Total body weight, liver weight, hepatic somatic index (HSI), WAT weight, and WAT somatic index (WSI) were measured for all treatment groups. Data are presented as . Statistical significance was determined by one-way ANOVA multiple comparison test with Tukey's multiple comparison test as the post hoc test (). "a" (age) indicates age difference between young (4.5 mo) and old (9 mo) mice within the same genotype and diet group, "c" (catch) indicates difference between HFD-fed young (4.5 mo) and ND-fed old (9 mo) mice within same

genotype, “d” (diet) indicates diet difference between ND-fed and HFD-fed mice within in same genotype and age, and “g” (genotype) indicates genotype difference between WT and Cyp2b-null mice within same diet and age group. No asterisk indicates a value Journal of Lipids (2022). DOI: 10.1155/2022/7122738

A team of Clemson University scientists is making inroads in understanding the relationship between certain enzymes that are normally produced in the body and their role in regulating obesity and controlling liver diseases.

According to Centers for Disease Control and Prevention (CDC) data collected in 2017-18, more than 42% of U.S. adults and 19% of U.S. youths are obese.

Three Clemson researchers and colleagues from the Emory University School of Medicine studied male mice that lacked the Cyp2b enzyme and how the lack of the enzyme affected the mice's metabolism.

William Baldwin, a professor and graduate program coordinator in Clemson's Department of Biological Sciences, said the research was triggered in part by a simple observation: male mice that lacked the Cyp2b enzyme were putting on weight. The same effect was not noticed in female Cyp2b-null mice.

"We noticed that our Cyp2b-null mice were heavier," said Baldwin, a professor in the department of biological sciences. "They are more prone to obesity—at least, diet-induced obesity—especially in males than are wild-type mice, and we were trying to find out why that is."

While the observation that tipped off the researchers was pretty

straightforward, it turned out that understanding the interactions behind the weight gain would be much more complex.

"It would be nice if there was a nice, simple answer," Baldwin said, "but there probably isn't a nice, simple answer."

Variety of roles

Baldwin noted the complexity of numerous chemical processes involving the CYP enzyme, part of a superfamily of enzymes that plays a variety of roles in humans. He said the Cyp2b enzymes help to metabolize certain toxicants and drugs to eliminate them from the body.

But those same CYP enzymes have other jobs, as well. "They metabolize bile acids; they metabolize steroid hormones; they metabolize polyunsaturated fats from our diet," Baldwin said. "This means that all these things can interact, too. If you have a diet that's full of fat, that might inhibit your drug metabolism. Of course… drugs might inhibit your fat metabolism, might affect your steroid metabolism, and so on."

The researchers also looked at the association between "perturbed lipid profiles" and disease.

Disease susceptibility and overall health is greatly affected by changes to the lipidome, the researchers noted. High-fat diets, such as the Western diet, cause obesity and drastically alter the hepatic lipidome, and perturbed lipid profiles are associated with specific liver diseases, such as nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH).

Impact of age and diet

Baldwin has led previous research into the relationship between diet and

environmental toxicants. The most recent study focused on the impact of age and diet on these metabolic processes.

"What does a poor diet do to us? What does age do to us? That's kind of the idea here," Baldwin said of the latest research. "We're looking at these enzymes; what might happen over time to our profiles in this mouse model compared to just a wild-type mouse. What might happen over time with a high-fat diet, what might happen as we age, and how does it differ between this one mouse model, which doesn't have these enzymes, compared to one that does have these enzymes."

Simply put, Baldwin said, "One of the things that we saw, and not surprisingly, is that getting older is bad. It's tougher for the mice to regulate body weight. They gain weight. The weight that they have is more white adipose tissue [connective tissue mainly comprising fat cells]. … And some of these things were a little bit worse in the mice that lacked the Cyp2b enzymes. They were a little bit heavier. They had a little more fat than their counterparts. Their livers were a little bit bigger and a little bit less healthy. So they had a lot of those things that we associate with age going on."

Diet also had an impact on the mice's health.

"Of course, diet didn't help, as well," Baldwin continued. "It's the same case: Eating a poor diet caused weight gain, and it was a little worse with these [Cyp2b-null] mice, probably because of poor metabolism."

He said the exact mechanism by which the Cyp2b enzyme works is not completely understood.

"You take away an enzyme that helps metabolize these, but I don't think its really important that it helps get rid of the fat, but that it lets the body know the fat is there. It probably produces signaling molecules that say,

'Hey, we need to decide what we're going to do with this fat; we need to distribute this fat.' That kind of information. That's just an educated guess at this time, but I think that's probably what's happening."

Differences in humans

Baldwin said his current research takes a closer look at the mechanisms that are in play and how they differ in a human model from the mouse studies. He said that research, which will be a part of an as-yet-unpublished paper, indicates that the mouse and the human enzymes probably don't work exactly the same. "The human enzyme seems to cause us to keep some of the fat in the liver, and the mouse enzyme seems to drive that to the white adipose tissue. There are hints here in this paper that that's the case," Baldwin said.

Findings from the study were published in the *Journal of Lipids* in a paper titled, "Age- and Diet-Dependent Changes in Hepatic Lipidomic Profiles of Phospholipids in Male Mice: Age Acceleration in Cyp2b-Null Mice."

More information: Melissa M. Heintz et al, Age- and Diet-Dependent Changes in Hepatic Lipidomic Profiles of Phospholipids in Male Mice: Age Acceleration in Cyp2b-Null Mice, *Journal of Lipids* (2022). DOI: 10.1155/2022/7122738

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