

Fatty livers are in overdrive

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When our livers become loaded with fat, it isn't because they are slacking. A new study of human patients in the December *Cell Metabolism* shows that fatty livers actually burn more fat, not less. All that "hard work" may be at the root of the organ damage that comes with nonalcoholic fatty liver disease (NAFLD), a condition associated with insulin resistance that affects about one in three in the U.S. population.

The findings represent a [paradigm shift](#) in the connection between metabolism and [fatty liver disease](#), as it was previously thought that fatty livers burned less fat.

"Our overwhelming goal is to try to understand what happens in those with fatty liver," says Jeffrey Browning of the University of Texas Southwestern Medical Center. "By understanding what leads to the onset and progression of the disease, we hope we can come up with therapies that actually work."

Most studies of people with [insulin resistance](#) have focused on the more accessible skeletal muscle. Those studies show that the mitochondria that power [skeletal muscle cells](#) work at a slower pace in the context of [metabolic syndrome](#), including insulin resistance and fatty liver. Browning and his colleague Shawn Burgess weren't so sure that muscle could tell you much about what might be happening in other organs, including the liver.

"Unless skeletal muscle is working, it doesn't have much of an energy requirement," Browning explained. "The liver is always working." The

liver breaks down fat and makes glucose and ketone bodies that fuel the rest of our bodies, including our hearts and our brains.

In the new study, the researchers used a special method that allowed them to trace metabolic inputs and outputs in the human liver in people with low and high levels of triglyceride fats in their livers. Those studies show that people with fatty livers are breaking down lipids 50 percent faster and producing glucose 30 percent faster in comparison to those with healthy livers.

That increased demand on the liver suggests a link between fatty liver, oxidative stress, and liver damage. Browning says that means therapies including antioxidants like vitamin E might help protect the liver.

The researchers now hope to explore how metabolism shifts over the course of the disease. One day the tracer technique they have developed might even help to identify those patients at the greatest risk of progressing to the point of liver transplantation.

"A third of the population has fatty liver, and it is difficult to look at them and tell anything without a liver biopsy," Browning says. The trouble is all those biopsies would simply overwhelm the health care system.

Perhaps most important, the findings show that researchers need to rethink what insulin resistance means for the functioning of mitochondria throughout the body. "Skeletal muscle is very different from the [liver](#)," he says.

Provided by Cell Press

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