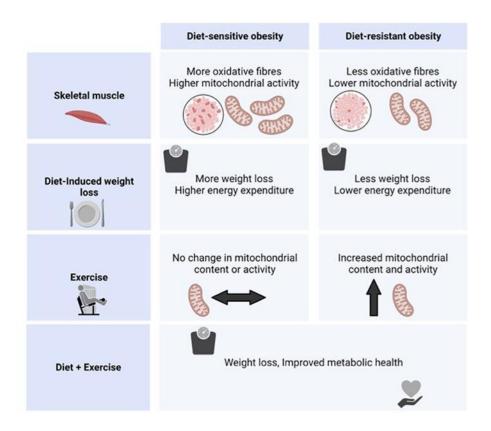


New insights on how some individuals with obesity can lose weight, and keep it off

August 15 2022, by David McFadden



Diet and exercise diagram for obesity phenotypes. Credit: University of Ottawa

For decades, there's been a persistent one-size-fits-all approach to treating obesity: Embrace a diet that's low in calories. Yet evidence shows that this diet-focused approach simply doesn't work for a subset



of adults with obesity who are adherent in a clinical weight management program.

Now, compelling new research published in the journal *eBioMedicine* challenges the deeply ingrained idea that diet alone should be adequate for everyone seeking to shed pounds.

The important conclusions could significantly improve <u>public health</u> by guiding the advent of personalized treatment plans that will help individuals with difficult-to-treat <u>obesity</u> lose weight—and keep it off.

"It's exciting and important work. These findings have clinical implications and reveal molecular mechanisms that will drive research for many years to come," says Dr. Mary-Ellen Harper, an award-winning professor and research chair in mitochondrial bioenergetics at the uOttawa Faculty of Medicine who was the study's senior author.

Understanding distinct obesity phenotypes is key to teasing out insights into individual variations in <u>weight loss</u>. And for "diet-resistant" obesity— patients in the bottom 20% for rate of weight loss following a low-calorie diet—<u>exercise training</u> should be prioritized, as it decreases fat mass and boosts <u>skeletal muscle</u> metabolism.

The research team mined clinical data from over 5,000 records. Ultimately, 228 files were reviewed and a subset of 20 women with obesity were identified to undergo a closely supervised exercise program made up of 18 progressive sessions using treadmills and weights done three times per week for six weeks.

Using bioinformatics and machine learning approaches to analyze skeletal muscle, the results indicate that exercise preferentially improves skeletal muscle metabolism and enhances weight loss capacity for individuals with obesity who are deemed diet resistant.



These are the type of patients with difficult-to-treat obesity who have often been accused of non-adherence when they have not lost weight with diet restriction.

"For those individuals who have obesity and who've had enormous difficulty losing weight, the message for them is: You are in a group of individuals for whom exercise is particularly important. And that's really going to help you lose weight," says Dr. Ruth McPherson, a leader in cardiovascular genetics who is a professor at the uOttawa Faculty of Medicine and director of the Ruddy Canadian Cardiovascular Genetics Centre, Atherogenomics Laboratory and the Lipid Clinic at the Ottawa Heart Institute.

The stakes are high: The number of people who are overweight or obese has grown to epidemic proportions globally and obesity is a risk factor in a slew of chronic diseases. In Canada, two out of every three adults are overweight or obese, according to Statistics Canada.

Dr. Robert Dent, founder of the Ottawa Hospital's weight management clinic and an endocrinologist at uOttawa, described the findings as the "crowning glory" of the research work done alongside Drs. Harper and McPherson over two decades. The three partners have collaborated on numerous projects over the years, helping to unlock mysteries of mitochondrial energetics and the genetic predictors of weight loss.

"If you look at a large group of people who are overweight and trying to lose weight, they don't respond to exercise very much. But now we've found that people in this [diet-resistant] obesity phenotype really do," Dr. Dent says. "What the findings are telling us is that when we see individuals with obesity who don't respond to dietary restriction, they should be shunted over to physical activity."

The study has the potential to help reshape the science of weight-loss



programs so they can be customized for individual patients. And since the study opens up various exciting research possibilities at the molecular level, the team is already recruiting for a study with a larger sample size.

"Exercise training enhances muscle mitochondrial metabolism in dietresistant obesity" is published in *eBioMedicine*.

More information: Chantal A. Pileggi et al, Exercise training enhances muscle mitochondrial metabolism in diet-resistant obesity, *eBioMedicine* (2022). DOI: 10.1016/j.ebiom.2022.104192

Provided by University of Ottawa

Citation: New insights on how some individuals with obesity can lose weight, and keep it off (2022, August 15) retrieved 7 May 2024 from https://medicalxpress.com/news/2022-08-insights-individuals-obesity-weight.html

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