

Females no longer neglected in obesity research

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One of the environmental factors that promote obesity, and the consequent health problems, are energy dense diets. Intense research is ongoing, looking for the mechanisms behind and ways to prevent this. But a recent review published in *Frontiers in Nutrition* shows that the typical male rat model used for investigating diet-induced obesity is too limited. The work discusses how the common neglect of sex differences can make the prediction and treatment of long-term obesity in females very difficult.

"There has been an over-reliance on male animals in preclinical research in the past, and as we have worked to study female specific physiological conditions, we became aware that even many aspects of our basic model of diet induced obesity are different in females," says Erin Giles, assistant professor at Texas A&M University and lead author of the study.

Formerly, different strains of rats were used in obesity research: a strain that was known for its leanness, and a strain known to become obese. To overcome the negative side-effects of having to use genetically different strains, scientists began selecting certain phenotypes in just one rat strain over 25 years ago. Generating and studying this wealth of phenotypes has given crucial information for understanding both the development of obesity, as well as the physiological changes that occur with weight loss and weight regain.

But work on a single strain has been male-centered, or too male-



centered, according to Giles. With her colleagues Paul MacLean and Matthew Jackman at the University of Colorado, Giles revise the work on males and points to how research on females is starting to give an idea on what the differences between the 2 sexes could mean.

Giles research team collected data of more than 300 animals to find the optimal time point to identify early in life an animal's predisposition to become obese. They found that in males, change in body weight in response to a high fat diet early in life is the strongest predictor of long term obesity. When looking at females, however, a completely opposite result was obtained.

"I think that even we were surprised when we looked at the data to see how poorly many of these measurements are at predicting long term adiposity in females, especially given that they are very reliable predicators in males. Percentage of body fat at a much later time point showed to be a better predictor for females."

The scientists also show that their rat model can give insight into the phenomenon of weight regain after <u>weight loss</u>. They observed that the rate of regain increased with time in weight maintenance.

In other words, keeping a reduced weight for a longer time makes one regain weight quicker once one starts to relapse to old and even higher weight, in males. The researchers are currently performing the same studies on females to also investigate the effect of menopause on this process.

"More research should be done on female rats. While our and other research groups are working to understand many of the differences between male and female physiology, we are still playing catch-up from years of studies that were conducted primarily in males," says Giles.



This need is now being recognized, and is starting to be addressed. "Funding agencies have recognized this limitation and are now encouraging and requiring study designs that address sex-differences across all disciplines; however, we still have a long way to go with the research," she concludes.

Giles sees many societal applications of the research. "The knowledge can be used to make people aware of the fact that they likely need to be more proactive in preventing weight regain in the future because they are competing against biology that is trying to promote weight gain in formerly obese individuals. Researchers can use this knowledge to develop lifestyle interventions to help make it easier for formerly obese individuals to maintain a lower weight," says the researcher.

As common to most scientists, Giles literally takes her research home. "There never seems to be quite enough time in the day to complete everything, so there are times when I work on grants, publications, and data analysis while at home. I also think that as a scientist who studies obesity, I try to keep a balanced lifestyle and stay active in the same way that I would recommend to anyone who asks about my research."

More information: Erin D. Giles et al, Modeling Diet-Induced Obesity with Obesity-Prone Rats: Implications for Studies in Females, *Frontiers in Nutrition* (2016). DOI: 10.3389/fnut.2016.00050

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