Revealing estrogen's secret role in obesity

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In a demonstration of estrogen's role in controlling body weight and fat distribution, these adult female rats both received surgery to induce post-menopausal conditions. The smaller one received estrogen supplements following surgery while the obese rat did not. Credit: Courtesy of Min Liu, University of Cincinnati Academic Health Center

New research on the effects of the female sex hormone estrogen in the brain lend credence to what many women have suspected about the hormonal changes that accompany aging: Menopause can make you fat.

Scientists long have sought to understand how changes in hormones during menopause could account for the increase in appetite and accompanying weight gain that often occurs among aging women.

In a series of animal experiments described today at the 234th national

meeting of the American Chemical Society, the world's largest scientific society, researchers showed how estrogen receptors located in the hypothalamus serve as a master switch to control food intake, energy expenditure and body fat distribution. When these receptors are destroyed, the animals immediately begin to eat more food, burn less energy and pack on pounds.

This research seems to support a link between estrogen and regulation of obesity, especially the dangerous accumulation of abdominal fat linked to heart disease, diabetes, and cancer, says Deborah J. Clegg, Ph. D., assistant professor of psychiatry at the University of Cincinnati Academic Health Center, who is directing the studies.

The findings may also help scientists develop more targeted hormone replacement therapies, capable of stimulating estrogen receptors in one part of the brain or body while dampening it in the next, Clegg says.

Estrogen receptors are located on cells throughout a woman's body. Previous studies have shown that one type of estrogen receptor, known as estrogen receptor alpha or ER-alpha, plays a role in regulating food intake and energy expenditure. But scientists have been unable to pinpoint exactly where these fat-regulating receptors reside or how they work to govern these behaviors.

To determine the effect of dwindling estrogen levels in the brain, Clegg and her colleagues are focusing on two ER-alpha rich regions located in the hypothalamus, an area of the brain that controls body temperature, hunger and thirst. The first region, called the ventromedial nucleus or VMN, is a key center for energy regulation.

Using a relatively new gene-silencing technique called RNA interference, the researchers in earlier research deactivated the alpha-receptors in the VMN. The estrogen receptors in other regions of the

brain maintained their normal capacity.

When estrogen levels in the VMN dipped, the animals' metabolic rate and energy levels also plummeted. The findings show the animals quickly developed an impaired tolerance to glucose and a sizable weight gain, even when their caloric intake remained the same. What's more, the excess weight went straight to their middle sections, creating an increase in visceral fat.

The findings suggested that the ER-alpha in this region plays an essential role in controlling energy balance, body fat distribution and normal body weight.

Clegg now plans to perform a similar experiment to deactivate ER-alpha in the arcuate nucleus region of the hypothalamus. This region contains two populations of neurons: one puts the brake on food intake and the other stimulates food intake. Clegg anticipates that a loss of estrogen in this region may create an increase in the animals' appetites as well as their weight.

Clegg says her studies address an area that is sorely needed given the incidence and impact of gender differences in obesity and its complications.

"The accumulation of abdominal fat puts both men and women at a heightened risk of cardiovascular disease, diabetes, and insulin resistance," she says. "Women are protected from these negative consequences as long as they carry their weight in their hips and saddlebags. But when they go through menopause and the body fat shifts to the abdomen, they have to start battling all of these medical complications."

By identifying the critical brain regions that determine where body fat is

distributed, Clegg says her findings may help scientists design hormone replacement therapies to better manage and manipulate estrogen levels.

“If we could target those critical regions and estrogen receptors associated with weight gain and energy expenditure, we could perhaps design therapies that help women sidestep many of the complications brought on by the onset of menopause,” she says.

Source: American Chemical Society

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