UT SOUTHWESTERN MEDICAL CENTER NEWS

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UT Southwestern study shows estrogen works in the brain to keep weight in check

DALLAS – Oct. 20, 2011 – A recent UT Southwestern Medical Center study found that estrogen regulates energy expenditure, appetite and body weight, while insufficient estrogen receptors in specific parts of the brain may lead to obesity.

"Estrogen has a profound effect on metabolism," said Dr. Deborah Clegg, associate professor of internal medicine and senior author of the study published Oct. 5 in *Cell Metabolism*. "We hadn't previously thought of sex hormones as being critical regulators of food intake and body weight."

The mouse study is the first to show that estrogen, acting through two hypothalamic neural centers in the brain, keeps female body weight in check by regulating hunger and energy expenditure. Female mice lacking estrogen receptor alpha – a molecule that sends estrogen signals to neurons – in those parts of the brain became obese and developed related diseases, such as diabetes and heart disease.

Similar results were not seen in male mice, although researchers suspect other unknown estrogen receptor sites in the brain play a similar role in regulating metabolism for males as well.

Estrogen receptors are located throughout the body, but researchers found two specific populations of estrogen receptors that appear to regulate energy balance for female mice.

The findings are potentially important for millions of postmenopausal women, many of whom have decided against hormonal replacement therapy. The study could lead to new hormonal replacement therapies in which estrogen is delivered to specific parts of the brain that regulate body weight, thereby avoiding the risks associated with full-body estrogen delivery, such as breast cancer and stroke.

Doctors stopped routinely recommending long-term estrogen therapy for menopausal women in 2002 when a Women's Health Initiative study showed the hormone also led to increased risk of cardiovascular disease.

"The role of estrogen in postmenopausal women continues to remain uncertain," Dr. Clegg said. "Current research is focused on the timing and the type of estrogen supplementation that would be most beneficial to women. Our findings further support a role for estrogens in

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regulating body weight and energy expenditure, suggesting a benefit of estrogen supplementation in postmenopausal women."

Other UT Southwestern researchers involved in the study included lead author Dr. Yong Xu, a former postdoctoral researcher in Dr. Clegg's lab; Dr. Carol Elias, assistant professor of internal medicine; and Dr. Joel Elmquist, professor of internal medicine.

The research was supported by grants from the National Institutes of Health, the American Heart Association and the American Diabetes Association.

Visit http://www.utsouthwestern.org/nutrition to learn more about clinical services in nutrition at UT Southwestern, including treatments for diabetes, kidney disease and obesity.

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