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Obesity leads to brain inflammation, and low testosterone makes it worse

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Low testosterone worsens the harmful effects of obesity in the nervous system, a new study in mice finds. The results will be presented Monday at The Endocrine Society's 95th Annual Meeting in San Francisco.

"Low testosterone and obesity are common in aging men, and each is associated with type 2 diabetes and Alzheimer's disease," said the study's lead investigator, Anusha Jayaraman, PhD, of the University of Southern California in Los Angeles. "Our new findings demonstrate that obesity and low testosterone combine to not only increase the risk of diabetes but also damage the brain."

The study – which was conducted in the laboratory of Christian J. Pike, PhD, Professor in the Davis School of Gerontology at USC and funded by the National Institutes of Health's National Institute on Aging – consisted of three groups of male mice that received a high-fat diet (60 percent of calories were from fat) to induce obesity. Each group had eight mice and varied by testosterone status. One group had normal testosterone levels, and the second group underwent surgical removal of the testes so that the mice had low testosterone levels. The third group also underwent castration but then received testosterone treatment through a capsule implanted beneath the skin.

The high-fat diet, Jayaraman reported, resulted in obesity and evidence of diabetes – abnormally high blood glucose (sugar) levels and poor glucose tolerance, which is the ability to clear glucose from the bloodstream. Compared with the group that had normal testosterone

levels, the testosterone-deficient mice had more body fat, higher blood sugar levels and poorer glucose tolerance, she said.

After blood testing, brain tissues from the mice underwent analysis for changes. The brains of obese mice showed substantial inflammation and were less able to support nerve cell growth and survival, according to Jayaraman. These damaging effects of diet-induced obesity were significantly worse in mice with low testosterone, she said, adding that control groups of mice fed a normal diet did not show these changes.

"Our findings suggest that low testosterone and obesity interact to regulate inflammation of the nervous system, which may increase the risk of disorders such as type 2 diabetes and Alzheimer's disease," she said.

Because many of the negative outcomes of the high-fat diet were eased in the group of mice that received testosterone therapy, Jayaraman said that "testosterone treatment may be useful in reducing the harmful effects of obesity and low testosterone on the nervous system."

Provided by The Endocrine Society