

## Researchers identify site in brain where leptin may trigger puberty

December 22 2010

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UT Southwestern Medical Center researchers have pinpointed a tiny site in the brain where the hormone leptin may help trigger the onset of puberty.

The findings in mice indicate that a site within the hypothalamus called the ventral premammillary nucleus, or PMV, is the target where the hormone leptin effectively kick starts puberty in females.

Researchers have known that puberty starts when individuals have enough energy stores or fat to meet the demands of reproduction, and that leptin – a hormone produced by fat cells – acts in the brain to mediate this process, but the precise locale in the brain where leptin exerts this effect remained unclear.

"We found that the PMV is a key site of leptin action on puberty. This may not be the only site, considering the importance of the reproductive function for species survival, but the role played by PMV neurons has not been recognized before," said Dr. Carol Elias, assistant professor of internal medicine at UT Southwestern and senior author of the article available online and in the Jan. 4, 2011, print issue of the *Journal of Clinical Investigation*. "Our findings show that leptin action only in the PMV is sufficient to induce puberty in female mice."

Prior research has shown that in mice and humans lacking leptin, puberty grinds to a screeching halt at the prepubescent level, and the animals are infertile. Studies also have shown that reintroducing leptin to

leptin-deficient people causes puberty to resume. Partly because of this, some researchers speculate that obese children may begin puberty earlier due to the higher levels of leptin produced by their fat tissues.

"We are witnessing an alarming situation in which the increasing incidence of childhood obesity may be inducing an advance in the onset of puberty in girls," Dr. Elias said. "The main obstacle for researchers in the field has been identifying the cell population involved in this event."

In this study, the researchers wanted to determine where leptin plays its role. To do this, they developed transgenic mouse models in which the mice had functional leptin receptors only in the PMV. Because of the lack of leptin signaling everywhere else in the body, the mice were obese but showed pubertal development and were able to get pregnant.

"One result that surprised us was that leptin acting only in the PMV was sufficient to induce puberty and improve fertility in females, but not in males," Dr. Elias said. "We're now trying to understand what's going on with males and whether leptin acts in different brain sites to induce puberty and fertility in males."

The next step, Dr. Elias said, will be to determine the molecular mechanism behind leptin's effects on puberty and reproductive control.

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Provided by UT Southwestern Medical Center

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