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Why underweight babies become obese: Study says disrupted hypothalamus is to blame

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It seems improbable that a baby born underweight would be prone to obesity, but it is well documented that these children tend to put on weight in youth if they're allowed free access to calories. Now, researchers believe they understand why this happens.

A new animal model study at UCLA has found that in low–birth-weight babies whose growth was restricted in the womb, the level of appetite-producing neuropeptides in the brain's hypothalamus — the central control of the appetite — is higher, resulting in a natural tendency among these children to consume more calories.

"Other studies have shown that neuronal processes that signal the brain to eat were wired differently in the hypothalamus if a hormonal gene, such as leptin, was missing," said the study's lead author, Dr. Sherin Devaskar, professor of pediatrics and executive chair of the department of pediatrics at Mattel Children's Hospital UCLA. "What we found is that appetite-producing genes in the hypothalamus are completely programmed toward eating more to make up for the relative decrease in nutrition while in the womb. So the natural tendency for a child born with low birth weight is to eat more and try to catch up in growth. But if this is not curbed, it can result in childhood obesity."

The findings appear in the June issue of the *Journal of Neuroscience Research* and are currently available online.

The study was undertaken in rodent models that mimicked small human babies. This was accomplished by reducing rodent mothers' intake of calories, which in turn led to the birth of small, low–birth-weight and growth-restricted babies. The rodent babies were then examined at an early age to see how much milk they consumed and to monitor their energy expenditure. In addition, the researchers examined the effect that being growth-restricted in the womb had on hypothalamic neuropeptides that control appetite when the babies were weaned.

The researchers observed that those neuropeptides that bring increased appetite with decreased energy expenditure were increased in the hypothalamus, while the neuropeptides that reduce appetite and increase energy expenditure were decreased. Therefore, the homeostatic balance of appetite-controlling neuropeptides was disrupted. The hypothalamus was poised to consume as many calories as were available, with no sense of satisfaction.

These findings expand on recent research published by Devaskar and colleagues in the June issue of the journal *Diabetes*, which found that if small babies are placed on a diet of moderately regulated calories during infancy, their propensity to become obese decreases. Because this was an early animal study, the UCLA researchers do not recommend that mothers of low–birth-weight infants start restricting their children's nutrition and suggest they consult with a pediatrician regarding any feeding questions.

About 10 percent of babies in the United States are born "small" — defined as less than the 10th percentile by weight for a given gestation period. Some organizations define low birth weight as less than 2,500 grams — or 5 pounds, 5 ounces — at term.

Low birth weight can be caused by malnutrition due to a mother's homelessness or hunger or her desire not to gain too much weight during

pregnancy. Additional causes include illness or infection, a reduction in placental blood, smoking, or use of alcohol or drugs during pregnancy.

Growth restriction before birth may cause lasting changes in genes in certain insulin-sensitive organs like the pancreas, liver and skeletal muscle. Before birth, these changes may help the malnourished fetus use all available nutrients. After birth, however, these changes may contribute to health problems such as obesity and diabetes.

Devaskar said the next phase of research will look at an intervention to reverse the hypothalamic neuropeptide changes that cause the central control of appetite to be set too high.

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