Maternal stress during pregnancy may affect child's obesity

April 12 2011

There is increasing evidence from human and animal studies that offspring of parents who were physically or psychologically stressed are at higher risk of developing obesity, and that these offspring may in turn "transmit" that increased risk to the next generation. Now research conducted at the University of Minnesota and Georgetown University suggests that a mother's nutritional or psychological stress during pregnancy and lactation may create a signature on her child's genes that put the child at increased risk for obesity later in life, especially if the child is female.

Ruijun Han at the University of Minnesota Medical School's Department of Integrative Biology and Physiology will discuss the team's findings at the at the Experimental Biology meeting (EB 2011), being held April 9-13, 2011 at the Walter E. Washington Convention Center, Washington, DC. The title of his presentation is "Stress-induced Epigenetic Programming for Adipogenesis: Role of Neuropeptide Y and Adipose Stem Cells."

Two-Tiered Research

The Minnesota team focused on the behavior of neuropeptide Y (NPY), a neurotransmitter found in the brain and autonomic nervous system that is associated with appetite stimulation and the storage of energy as fat. Building on prior research in the field, the team undertook two studies, one involving mice and the other involving mouse embryonic stem cells.

In the first study, the researchers sought to determine if prenatal and postnatal stress exerted long-term effects on the activation of NPY and its Y2 receptor (Y2R) that would result in the creation of fat cells and the promotion of obesity. First, they exposed pregnant mice to stress by feeding them a low-protein diet. The team found that this diet caused low birth weight in the offspring. Female offspring of the mice stressed during pregnancy and lactation grew faster after weaning when they were fed a high-fat diet, and within 2 months, they developed abdominal fat, prediabetes (impaired glucose tolerance) and increased upregulation of Y2R in their fat tissue. Although male offspring of stressed mothers also had low birth weight, they did not develop obesity and they had lower Y2R expression and better metabolic health, even when fed a high-fat diet.

"This indicates that maternal stress during pregnancy and lactation could induce gender-specific abdominal obesity and impaired glucose metabolism associated with increased plasma NPY and fat Y2R," says Dr. Han.

Stress may affect NPY and Y2R in several ways, says Dr. Zofia Zukowska, professor of physiology and the senior researcher of the study. "It could be that the mother's poor nutrition or other type of stress can affect fetal development by depriving the fetus of necessary nutrients or exposing it to levels of stress hormones such as cortisol, norepinephrine and epinephrine [adrenaline], which in turn up-regulate the NPY-Y2R system to affect metabolism and fat growth of the offspring."

The team sought to tease out these effects in the second study by observing how mice embryonic stem cells behave when over-exposed to stress hormones at a critical point in their differentiation. Embryonic stem cells that have been treated with insulin and dexamathasone (synthetic glucocorticoid) will differentiate into fat cells. The team

exposed such cells with epinephrine in a test dish and saw that the cells increased fat-cell formation and NPY expression. The cells also decreased DNA methylation in the NPY promoter region, through an epigenetic (non-genetic) process that alters expression of this peptide in cells so that the cells "remember" their type (i.e., stem cells will remain committed to fat cell lineage and give rise to fat cells, instead of becoming or giving rise to another kind of cell).

"All of this data suggests that stress may induce epigenetic changes in NPY and its receptor genes and program [the offspring's DNA] for the future development of abdominal obesity and metabolic syndrome," says Dr. Han.

Implications

Although mice are not people, the Minnesota team's research has implications for tackling human obesity because it sheds light on the process by which fat cell volume and the number of fat cells are derived, says Dr. Han. "Adipocyte number before adolescence is a major determinant [of a person's risk of obesity], so intervention during pregnancy and childhood might be an efficient way to prevent adult obesity."

Provided by Federation of American Societies for Experimental Biology