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Study shows offspring response to maternal diet and male hormone

March 22 2018

A novel study published online in *The FASEB Journal* identifies sex-specific responses to maternal diet and androgen (male hormone) excess among male and female animal offspring.

Using mice, the study revealed sex-specific, anxiety-like behavior in the offspring of both normal-weight and obese pregnant mice exposed to the androgen dihydrotestosterone. Independent of the mothers' other diet components, female offspring exposed to maternal androgens in utero developed an anxiety-like behavior. Male offspring, on the other hand, were unaffected by the elevated maternal androgen levels, but displayed anxiety-like behavior in response to a maternal high-fat-high-sucrose (HFHS) diet. The findings could have important clinical implications for women with polycystic ovary syndrome (PCOS), a condition that is associated with androgen excess and closely linked to obesity.

To conduct the experiment, doctoral student Maria Manti and Elisabet Stener-Victorin, PhD, professor of Physiology and Pharmacology, Reproductive Endocrinology and Metabolism, at the Karolinska Institute in Stockholm, Sweden, and colleagues investigated 16 groups of female and male mice offspring. During fetal life, the mice were exposed to both diet-induced obesity and male hormone in the mother. After birth, half of the mice were exposed to HFHS diet-induced obesity to also investigate the effect of diet in the offspring.

The researchers conducted anxiety-like behavior tests to assess if these environmental factors affected the mice's behavior, and if so, how these

factors interacted with each other. They next assessed whether these behavior changes were related to gene expression changes within the brain.

The research team found that a number of genes implicated in anxiety were dysregulated in the amygdala and hypothalamus in a sex-specific manner. They also showed that consumption of a HFHS diet in the offspring led to gene expression changes within the brain and may have a role in the deterioration of anxiety symptoms.

"The novelty of our study is the multifactorial approach, which made it possible to distinguish between factors including diet-induced obesity and exposure to male hormones during pregnancy; diet-induced obesity in the offspring; and sex-specific differences," Stener-Victorin said.

"This insightful analysis highlights the interplay of maternal diet and androgen levels in effecting a transgenerational physiological consequence," said Thoru Pederson, PhD, Editor-in-Chief of *The FASEB Journal*.

Provided by Federation of American Societies for Experimental Biology