







Article

Early Caffeine Exposure Causes Metabolic and Hormonal Changes Differently According to the Window of Exposure (Gestation or Lactation), Sex, and Age in a Rat Model

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Abstract

Background/Objectives: Many women report restrictions on caffeine intake during gestation, but some of these restrictions are withdrawn during the lactation period. Given that both periods have elevated epigenetic plasticity, our aim was to compare the effects of caffeine exposure during each isolated period on offspring metabolism and susceptibility to obesity in response to metabolic overload. **Methods:** Pregnant Wistar rats received orogastric caffeine (CAF) (25 mg/kg/day) or vehicle during gestation (CAF G) or lactation (CAF L) periods. We evaluated the body mass, adiposity, hormone levels, and food behavior of offspring of both sexes at different ages. Adult animals were subjected to metabolic overload, with fructose solution (10%) offered for ten days. **Results/Discussion:** CAF G and CAF L dams presented lower T3 levels (−70 and −52%) because of reduced TSH activity in the thyroid gland (−28 and −29%), despite unchanged gland morphology. At weaning, CAF G and CAF L males presented lower T3 levels (−75 and −80%), as did CAF L females (−85%). At puberty, females in the CAF L group showed glucose intolerance. In adulthood, CAF G males exhibited a greater preference for palatable food. In addition, CAF G and CAF L males showed increased feed efficiency, suggesting a greater susceptibility to obesity development. To test this susceptibility, the animals were subjected to fructose overload. Indeed, we observed that despite the absence of a fructose effect in the control group, male CAF G and female CAF L animals showed greater adiposity in response to fructose overload (+43% and +37%, respectively). **Conclusions:** Caffeine exposure during lactation increases the risk of obesity development among female offspring. However, for male offspring, gestation seems more critical.

Keywords: maternal caffeine; lactation; gestation; DOHaD; obesity development; fructose overload

1. Introduction

Early life is a critical period of development in which intense epigenetic plasticity exists, susceptible to environmental factors [1]. Therefore, inadequate maternal diet or



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