“Neonatal overfeeding permanently programs late onset obesity and diabetic phenotype across multiple generations”

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Abstract

Epidemiological and clinical studies show that rapid weight gain in early life is strongly associated with several components of the metabolic syndrome several years later. Even more, accelerated neonatal growth rate may influence diabetes risk in subsequent generations.

In order to determine which events, occurring during early life, may determine the adverse metabolic consequences in adulthood, we have developed a mouse model of accelerated growth rate by neonatal overnutrition in males (ON). As it happens in humans, we show that ON mice exhibited accelerated growth and by age 4 months developed many features of the metabolic syndrome, including obesity, impaired glucose tolerance and insulin resistance. Importantly, many abnormalities (obesity, tissue-specific insulin resistance) are already detectable by weaning, before whole body metabolism is altered.

Strikingly, early programmed diabetic phenotypes are inherited into the following generation offspring, F2, through the paternal lineage. This effect occurred even though mice from F2 have not been exposed to nutritional challenges during development. This type of, environmentally-induced paternal effects strongly implicates the role of epigenetic mechanisms in mediating both long-term and transgenerational effects in ON mice.