

Is the detrimental metabolic programming of low birth weight individuals caused by dysregulated fatty acid oxidation and lipotoxicity?

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Low birth weight (LBW) individuals have an increased risk of developing insulin resistance and type 2 diabetes later in life, compared with normal birth weight (NBW) individuals, when exposed to an affluent life style such as overfeeding. Nevertheless, the underlying or exacerbating mechanisms behind the type 2 diabetes susceptible phenotype of LBW individuals are not clear.

In the present project, we hypothesised that an increased, incomplete fatty acid beta-oxidation in mitochondria could be part of the adverse metabolic events leading to insulin resistance in LBW individuals. Accordingly, we have recently analysed fasting plasma levels of acylcarnitines, as markers of incomplete beta-oxidation, in young, apparently healthy LBW (0th-10th percentile) and NBW (50th-90th percentile) men before and after a short-term high-fat overfeeding intervention. Furthermore, we hypothesised that an accumulation of lipotoxic lipid species in non-adipose tissue could induce insulin resistance in LBW individuals. Therefore, we are currently in the process of determining plasma levels of ceramides in the LBW and NBW men.