Interactions between fetal programming and postnatal diet: implications for development of the metabolic syndrome

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Epidemiological studies indicate that several adult-onset pathologies, including cardiovascular and metabolic diseases, are influenced by the fetal environment. Thus, increased frequencies of hypertension, obesity, dyslipidemia and type 2 diabetes, collectively referred to as the 'Metabolic Syndrome', have been linked to intrauterine growth retardation. Fetal glucocorticoid excess is a key programming signal that leads to various adverse outcomes in adults including components of the metabolic syndrome. While fetal programming by glucocorticoids likely reflects direct actions in fetal tissues, it also appears to be mediated *via* effects on the placenta. Specifically, maternal glucocorticoid treatment stimulates placental apoptosis and reduces expression of placental gene products that are pro-angiogenic, including PPARγ and VEGF. These changes are specific to the region of maternal-fetal exchange and are associated with a marked reduction in placental vascularity. This would be expected to compromise fetal nutrient supply, an effect likely to exert additional adverse programming effects. Subsequent, long-term effects of fetal programming can either be amplified or attenuated by the postnatal environment. For example, adverse programming outcomes are exacerbated by a high-energy diet in postnatal life, whereas we have shown that 'programmed' hypertension, hyperleptinemia and hyperinsulinemia are all prevented by a postnatal diet enriched with omega-3 fatty acids. These effects are mediated by the prevention of 'programmed' changes in gene expression in the kidney (11B-HSD2 and Na/K-ATPase) and adipose tissue (leptin). In summary, fetal programming by glucocorticoids appears to be mediated, in part, *via* detrimental effects on placental vascularity. Postnatally, programming outcomes can be modified by dietary manipulations, thus raising the possibility of preventative, therapeutic interventions.