Plenary Session / EC – US Workshop: Early life programming of obesity

Lecture 2: Programming the central energy balance regulatory system

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Abstract

Extremes of birth weight are associated with increased risk of obesity in later life, indicative of fetal programming, yet the underlying mechanisms remain unresolved. Body weight and energy balance are normally regulated within the hypothalamic region of the brain in response to metabolic feedback from the periphery, but the system is defective in obesity. It is hypothesised that programming of obesity could be due to an inappropriate nutrient supply causing sustained changes in the developing hypothalamic energy balance regulatory system in the fetus. The singleton-bearing sheep is a particularly good model for the human, with similar size, adiposity and brain maturity at birth. Using sheep models of intra-uterine growth retardation and altered gestational glycaemia, we have demonstrated changes in hypothalamic gene expression for leptin receptor and key energy balance regulatory neuropeptides. Such changes provide a potential mechanism whereby the prenatal environment may programme subsequent predisposition to obesity.