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Influence of intrauterine growth restriction and gender on body composition and metabolism throughout the life-course

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Intrauterine growth restriction (IUGR) is a risk factor for adverse metabolic health and obesity, particularly when offspring are born into an unrestricted nutritional environment. Using our established ovine model of placental growth restriction[1], we assessed the impact of poor prenatal nutrient supply followed by postnatal nutrient abundance on body composition and metabolism at key stages spanning juvenile to adult life.

Singleton-bearing adolescent dams were fed control (C) or high (2·25 × C) nutrient intakes during pregnancy to induce normal or growth-restricted pregnancies, respectively[1]. The resulting normal (N; 12 male [M], 12 female [F]) or IUGR (9 M, 16 F) lambs suckled their *ad libitum*-fed mothers until weaning at 11 weeks of age. Thereafter offspring were individually housed and had *ad libitum* access to the same nutrient-dense complete diet. Body composition was determined by dual energy X-ray absorptiometry (DEXA) at 11, 36, 56 and 100 weeks; fasting blood samples were collected and intravenous glucose tolerance tests (GTT) performed at 7, 28, 55, 76 and 99 weeks, before necropsy at 103 weeks (mid-adulthood).

IUGR lambs were 36% lighter at birth than N lambs and had reduced height and girth (all $P < 0{\cdot}001$, no effect of gender). Fractional growth rate from birth to adulthood was greater in IUGR *vs* N groups, ($P < 0{\cdot}001$), was highest in IUGR males ($P = 0{\cdot}006$) and was inversely correlated with birth weight ($r = -0{\cdot}818$, $P < 0{\cdot}001$). Nevertheless absolute catch-up growth was not complete and IUGR offspring of both sexes had modestly reduced stature and weight at necropsy ($P = 0{\cdot}056$–$0{\cdot}018$). DEXA revealed reduced bone mineral density in IUGR compared with N lambs at all 4 stages examined ($P = 0{\cdot}02 - < 0{\cdot}001$) and an effect of gender (M>F, $P < 0{\cdot}001$) at 36, 56 and 100 weeks. Total body fat percentage was higher in F *vs* M throughout ($P = 0{\cdot}01 - < 0{\cdot}001$) and in IUGR *vs* N at weaning and in mid-adulthood ($P < 0{\cdot}001$), but not during intervening adolescence or early adult life.

At 7 to 55 weeks of age, fasting plasma insulin, glucose and glycerol concentrations, and insulin and glycerol secretion after GTT were higher in IUGR *vs* N lambs ($P = 0{\cdot}05 - < 0{\cdot}001$) but by mid-adulthood the effect of gender dominated (M>F for insulin, M<F for glucose and glycerol; $P = 0{\cdot}012 - < 0{\cdot}001$). In contrast the glucose area under the curve after GTT was independent of prenatal growth at 7 weeks but higher in IUGR *vs* N thereafter ($P = 0{\cdot}023$–$0{\cdot}001$) indicative of persistent glucose intolerance. Both fasting NEFA levels and post glucose NEFA responses were variously influenced by prenatal growth status (IUGR>N) and/or gender (M<F) from 7 to 76 weeks of age. By mid-adulthood NEFA concentrations were robustly higher in IUGR lambs ($P < 0{\cdot}001$, no effect of gender).

Thus in our animal model, prenatal growth restriction has negative consequences for body composition and metabolism throughout the life course. The ontogeny of these effects may be dependent on gender-specific differences in postnatal growth rate and body composition. Clearly, both gender and prenatal growth status are important predictors of postnatal metabolic health.

1. Wallace *et al.* (2006) *Placenta* **27** Suppl A, S61–68.