Metabolic phenotypes of infants with normal birth weight, small-for-gestational-age, or after maternal gestational diabetes mellitus

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Summary

Numerous studies have associated both under- and overnutrition during early life with long-term metabolic outcomes. Those conditions are typically represented by two groups of infants in animal and human studies: infants born small-for-gestational-age (SGA; reflecting intrauterine undernutrition) and offspring of mothers with gestational diabetes mellitus (OGDM; reflecting intrauterine overnutrition and hyperglycaemia). However, the underlying mechanism behind this phenomenon is still unknown: how these distinct groups can end up with similar metabolic risks, despite having opposite *in utero* nutritional conditions.

This thesis aims to characterise biological similarities and differences across SGA, OGDM, and a control population from the Cambridge Baby Growth Study (CBGS). The CBGS, set up in 2001, is an ongoing longitudinal cohort aiming to examine the ante- and postnatal determinants of infant growth and body composition, including genetic and environmental factors.

While SGA infants in CBGS showed typical rapid postnatal growth patterns, the contemporary OGDM cohort showed a distinct trend to that in earlier cohorts, with normal birth weights but reduced adiposity, which was sustained from birth to 24 months. Preliminary analyses of infant capillary blood spot profiles suggested that pre- and postnatal exposures reflected in SGA and OGDM may share common hormonal and lipidomic signatures during early infancy, independent of feeding practice and other confounding factors. In a CBGS breastmilk (BM) study, higher BM intake volume at 6 weeks conferred protection against subsequent rapid weight gain. Analyses of BM macronutrients also suggested that carbohydrate and protein intakes may have functional relevance to later infant growth and adiposity.

This work has characterised in detail the effects of antenatal and postnatal nutritional factors on infant growth, body composition and biochemical profiles. The early infancy metabolic signatures identified here may reflect the continuum of early programming from pre- to early postnatal and might be potentially linked to future metabolic risks.