Metabolic Regulation of Pre- and Postnatal Growth

Berthold Koletzko, Franca F. Kirchberg, Christian Hellmuth, Martina Weber, Veit Grote, Hans Demmelmaier, Marie Standl, Joachim Heinrich, Elisabeth Thiering, and Olaf Uhl

Growth characteristics during periods of early developmental plasticity are closely linked with later health outcomes, including physical and cognitive performance, and with disease risks. Evidence is particularly convincing for early growth modulation of later risks of obesity, adiposity, and associated noncommunicable diseases, e.g., type 2 diabetes, hypertension, cardiovascular diseases, and asthma. Infant growth is modulated by genetic, epigenetic, inflammatory, endocrine, nutritional, and metabolic factors. Improved nutrition offers major opportunities for disease prevention. High protein intakes in infancy can induce excessive early weight gain [1, 2] and increased later obesity [3]. Targeted metabolomic profiling of small molecules (<1.5 kDa) in biological samples, i.e., substrates, intermediates, and products of biological processes, offers insights into underlying mechanisms. Using high-performance liquid chromatography coupled to triple quadrupole mass spectrometry (LC-MS/MS), we are able to precisely quantify several hundreds of molecules in small volumes of 10–50 µl plasma. These analyses show that high protein supplies with conventional infant formulae markedly increase infant plasma concentrations of indispensable amino acids (AA), particularly of branched-chain AA which can upregulate the mTOR pathway and thereby induce protein and lipid synthesis, as well as excessive growth [4]. With conventional protein intakes, the infant’s capacity of branched-chain AA breakdown via branched-chain α-keto acid dehydrogenase is exceeded, while the initiation of fatty acid β-oxidation is suppressed, which may enhance body fat deposition [4]. High protein supplies also induce increased tyrosine concentrations, which predict insulin resistance in obese children [5]. They also enhance the secretion of the growth factors insulin and IGF-1 [6]. A path model analysis shows a stronger response of insulin to AA and very different effects of individual AA [7]. Moreover, the energetic efficiency of infant formulae for weight and length gain depends particularly on the
protein quality provided [8]. Together, these results lead us to conclude that improving both the quantity and quality of protein intakes may be of considerable importance for achieving optimal infant growth.

Acknowledgments

The authors’ work is financially supported by the European Commission, project EarlyNutrition (FP7–289346), MeDALL (FP7–261357), DynaHEALTH (H2020–633595), and LifeCycle (H2020–SC1–2016–RTD), and the European Research Council Advanced Grant META-GROWTH (ERC-2012–AdG 322605). Additional support from the German Ministry of Education and Research (No. 01 GI 0825), the German Research Council (Ko 912/12–1), and the Helmholtz Association is gratefully acknowledged.

References