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In This Issue

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This issue of J DOHaD contains three review articles, eleven original papers and one brief report. Two of the original papers examine the effects of prenatal androgen excess. Silva *et al.* demonstrated adverse effects of hepatic development and lipid metabolism in rat offspring, while the results Lew *et al.* suggest a potential impact on cognitive function in human offspring.

Review articles

COVID-19 age-dependent immunology and clinical outcomes: Implications for vaccines. Sarfraz and co-authors review information on immunologic responses to COVID-19 in relation to DOHaD hypotheses. Specifically, the authors propose that immunological responses may explain sociogeographic differences in the morbidity and mortality impacts of COVID.

Birth weight and adult earnings: A systematic review and meta-analysis. Lambiris and colleagues examine 15 studies from mostly high-income countries. The authors demonstrate that an increase in birth weight was associated with an increase in annual earnings, though there was no statistically significant association between being born low birth weight and earnings. The authors suggest that interventions that improve birth weight may provide beneficial effects on adult economic outcomes.

The role of genetics in fetal programming of adult cardiometabolic disease. Sanchez-Soriano *et al.* provide an insightful review of the contribution of genetics to birth weight and ultimately cardiometabolic programming. The authors note that through genome-wide association analyses of 190 different loci have been associated with birth weight, the role of many of these loci is not yet understood. The authors emphasize the importance of the understanding of genetic determinants of birth weight and the interactions between maternal, paternal and offspring genotype.

Original articles

Fetal programming by androgen excess impairs liver lipid content and PPARg expression in adult rats. Silva and co-authors examine the offspring of pregnant rats hyperandrogenized with free testosterone during late pregnancy. Offspring of the hyperandrogenized dams demonstrated altered ovulatory function, hepatic lipid profiles and fatty acid metabolism. These findings indicate that prenatal hyperandrogenization may have a negative impact on offspring hepatic development and lipid metabolism.

Developmental variation in testosterone:cortisol ratio alters cortical- and amygdala-based cognitive processes. Lew *et al.* examined a healthy cohort of 4- to 22-year-olds for the association between testosterone-cortical ratio and brain structure. Greater testosterone-cortical ratio was associated with growth of specific brain structures and lower verbal executive function and higher spatial working memory. These findings indicate that testosterone-cortical profiles may be associated with cognitive strengths and weaknesses.

Early childhood BMI trajectories in relation to preclinical cardiovascular measurements in adolescence. Montazeri *et al.* assess childhood BMI growth trajectories in a Spanish birth cohort of 11-year-old adolescents in relation to cardiovascular measurements of macro- and micro-vascular function. Children with lower or higher birth size and accelerated BMI gain had increased systolic blood pressure. These findings emphasize the importance of early childhood BMI gain trajectories on long-term cardiovascular function.

Early life disease environment and adult height in historical populations. Casal and colleagues examine the impact of disease environment during early life among populations in Spain born in the early 20th century. The authors found that disease burden in early life had a significant negative effect on adult stature.

Leptin and the adiponectin concentrations in infants with low birth weight: Relationship with maternal health and postnatal growth. Santana-Meneses and co-authors examine a cross-sectional study of low birth weight infants aged 9 to 12 months. Nearly all of the infants' energy intake was above recommendations, and 15% were overweight. SGA infants showed faster recovery and higher leptin. The authors concluded that LBW infants showed early changes in leptin influenced by maternal intrauterine and postnatal weight gain.

Placental insufficiency induces a sexually dimorphic response in the expression of cardiac growth and metabolic signaling molecules upon exposure to a postnatal Western diet in guinea pigs. Darby *et al.* induced placental insufficiency in pregnant guinea pigs with uterine artery ablation. When compared to normal birth weight offspring weaned onto a controlled diet, low birth weight male, but not female, offspring fed a Western diet demonstrated altered mRNA

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expression in the myocardium. The authors conclude that low birth weight offspring exposed to a postnatal Western diet may demonstrate sexually dimorphic cardiac pathology.

DNA methylation profile of liver in mice conceived by *in vitro* fertilization. Lira-Albarran and co-authors examine the effects of IVF on DNA methylation changes in the liver of adult mice (30 weeks of age). IVF mating was associated with epigenetic changes in genes related to hepatic fibrosis, cellular metabolic processes and insulin receptor signaling, providing a potential mechanism for the predisposition to chronic diseases in IVF offspring.

The effect of season of birth on brain epigenome-wide DNA methylation of older adults. Didikoglu *et al.* examine the association between season of birth and epigenome-wide DNA methylation of two post-mortem human brain regions (hypothalamus and temporal cortex). The authors identified areas of differential methylation associated with circadian rhythm, entrainment, cholinergic transmission and neurodevelopment, suggesting a tissue-specific programming impact of perinatal light exposure.

Altered neurodevelopmental DNA methylation status after fetal growth restriction with brain sparing. Richter and colleagues performed a follow-up study of fetal growth restricted (FGR) children, examining the prenatal cerebral-placental ratio (CPR). FGR children with fetal brain sparing demonstrated a trend toward hypermethylation of select genes, with hypermethylation of *VEGFA* associated with poorer performance IQ. The authors suggest that early oxygen-dependent epigenetic alternations may be associated with altered neurodevelopmental outcome.

Metformin in obese pregnancy has no adverse effects on cardiovascular risk in early childhood. Yang *et al.* performed a follow-up study of children born to obese mothers who participated in a randomized study of metformin versus placebo during pregnancy. The findings suggest no evidence of increased cardiovascular risk in children born to obese mothers who took metformin during pregnancy. These results provide reassuring data for the continued use of metformin during prenatal care.

Advanced maternal age perturbs mouse embryo development and alters the phenotype of derived embryonic stem cells. Khurana and colleagues examine preimplantation embryos from young and old female mice mated with young males. Advanced maternal age was associated with developmental retardation in blastocyst morphogenesis, increased incidence of aneuploidy and an altered pattern of pluripotency markers. These findings provide insight into the impact of advanced maternal age on developmental consequences.

Brief report

Early postnatal overnutrition impairs VO2max gains with moderate exercise and increased post-exercise muscle damage in adult male rats. Almeida and colleagues examine the effect of exercise on male rats exposed to postnatal over-feeding. Although moderate exercise counteracted obesity in sedentary rats, early-life over-nutrition restricted fitness gains resulting from exercise.

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