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NRP Endocrine Disruptors

Final Summary

Role of environmental endocrine disruptors including smoking-derived toxicants, in the aetiology of intrauterine growth retardation and its later consequences such as disorders in brain development and adult-onset obesity
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Endocrine Disruptors and the foetal origin of adult diseases

Exposure to Endocrine Disruptors Chemicals (EDCs) may lead to reversible adverse effects in adult individuals. In contrast, exposure of foetus or very young infants might induce irreversible damages with altered growth and development and sequelae later in life. Such an occurrence could be due to EDCs that pregnant/lactating women might absorb.

Research questions

Adverse events during gestation represent a major concern for the developing fetus. Exposure to EDCs from the environment has been recognized only recently as potential health hazards. Concomitantly, increased incidence of obesity or altered cognitive development in the pediatric population is a new concern in public health. It is therefore quite timely to evaluate the relationship between exposure to toxic compounds such as EDCs during gestation and the recent increase of "civilisation diseases". Nicotine from cigarette smoking and Bishphenol A from plastics could be considered a "domestic" health hazard for foetuses, with the potential of being in part responsible for the childhood obesity outbreak. The effects of exposure during gestation to Nicotine and Bisphenol A were therefore studied in rodent models.

Results

As expected, calorie restriction or exposure of the foetus to glucocorticoids resulted in delays in growth and development, and in adolescent age obesity and poor control of glucose metabolism. Interestingly, development of obesity and loss of glucose control was also quite striking in pups born from nicotine-treated dams, as such a new finding. The profile of adipocyte differentiation at weaning of rats born from dams that received Bisphenol A was altered with though fewer consequences at the adult age. Effects of adverse foetal environment on brain development during gestation were studied with Magnetic Resonance technology at the EPFL as well as

histopathology. The changes in the neurochemical profile of the hippocampus and the cortex were very similar for the glucocorticoid exposure or malnutrition models. Nicotine exposure during gestation had a distinct effect on the neurochemistry, consistent with a different mechanism, likely reflecting altered glutamate neurotransmission. Studying the effect of Bisphenol A on brain development indicated altered neurochemical profile in a manner consistent with altered malate-aspartate shuttle activity, which we propose to reflect impaired mitochondrial function. It was expected that malnutrition and glucocorticoids would induce structural damages; it is interesting to see that both nicotine and Bisphenol A produced significant alteration of structural brain development in the offspring.

Perspectives

With the help of Nestlé-Nutrition, we will evaluate the benefit of nutritional interventions during the perinatal period meant to prevent or repair the damages encountered during foetal life due to exposure to EDC's. Nutritional interventions may represent an acceptable mean to correct these damages.