

Sex-specific effects of programming: how your gender plays a role in determining your disease risk

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It is now well-established that the environment to which individuals are exposed before birth and/or in early infancy plays a critical role in determining their susceptibility to a range of diseases in child and adult life. This early life programming of disease risk is thought to be due to the ability of environmental perturbations during critical windows of development to alter the developmental trajectory of key organs and regulatory systems, leading to permanent deficits in their structure and/or function. While programming occurs in both males and females, it is becoming increasingly clear that the same environmental exposure at the same time in development often has very different effects on male and female offspring. By extension, the impact of a specific environmental insult on male offspring cannot be assumed to be the same in females, and there are a number of examples of studies in which one sex exhibits a pronounced phenotype in response to an intrauterine exposure which appears entirely absent in the other. While the sex-specific nature of programming is well-described, the mechanisms underlying this remain poorly understood. What is clear, however, that there are physiological differences between males and females well before puberty, and at least some of these are present from the time of conception. In addition, there is accumulating evidence that there are key differences between the male and female placenta, which may account at least in part for sex differences in the response to intrauterine insults. This also has important implications for translation, since it implies that the optimal conditions for fetal/neonatal developmental, and therefore the advice provided to pregnant and lactating women, may differ according to the sex of their offspring.