

Neuroendocrine

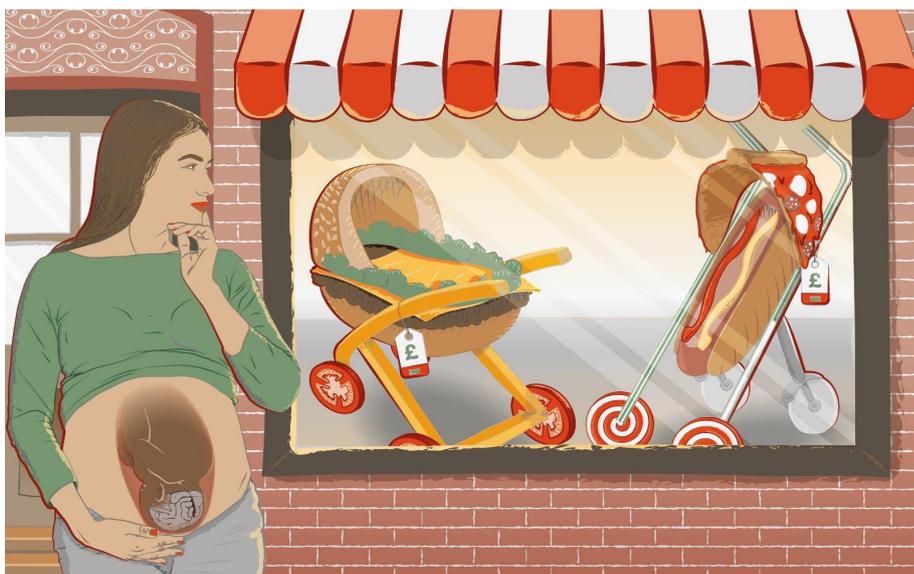
BRIEFING

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SUMMARY

A woman's food choices in pregnancy can leave a lasting effect on her child's brain. Changes in behavior in the child are correlated with disruptions to the baby's brain connectivity. Through mapping how nutrition can cause these changes, we can find the primary culprits and perhaps even intervene to help secure a healthier metabolic future for the next generation.

Eating for two?



'You are what you eat' is the old saying, but maybe we are a product of what our mothers ate. The rise in overweight and obese pregnant women is enlightening us to the consequences of the food choices during pregnancy. Indeed, energy-dense, hard-to-resist food is so easily accessible in Western culture and, taken together with the 'eating for two' mentality, it is understandable that mothers-to-be eat more than they need.

Statistically, half of all women in Western culture put on more weight than recommended by the USA's Institute of Medicine guidelines. Shockingly, the UK's National Institute for Health and Care Excellence does not provide any recommendations on weight gain during pregnancy. The lack of weight management and comprehensive nutrition advice is likely a contributing factor in the prevalence of overweight and obese pregnant women in the UK.

Unfortunately, the numbers of overweight and obese children are also steadily rising. A third of all European children are overweight, with an extremely high risk of continuing this into adulthood.

The mirroring between maternal obesity and childhood obesity is no coincidence: maternal overnutrition can affect the health and development of the baby, but what exactly are the consequences?

'I got it from my momma!'

The early phases of development, and specifically brain development, are sensitive to insults. Any disruptions in this environment put that child at risk for onset of disease later in life. Most would agree that this is true when it comes to drugs of abuse, smoking and even stress, but what about food, specifically those high-fat and energy dense foods that are the hallmark of our diet today? Research suggests that maternal obesity correlates with adverse neurodevelopmental, behavioural, and metabolic effects in children. There is an increased risk of diabetes and obesity, but perhaps even more troublesome are the links to augmented ADHD symptomology, risk of anxiety/depression, and increased prevalence of eating disorders such as binge-eating. Animal studies using overnutrition in rodent

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mothers recapitulate the observations from humans and allow for the deciphering of the complex molecular changes occurring within the brain. In animals, as in humans, high-fat diet consumption during the perinatal phase results in increased hyperactivity, anxiety/depression-like behaviour, substance abuse and rewarding food overconsumption. Thus, an unhealthy maternal diet during pregnancy can be detrimental to a child's health, but how this occurs, remains a mystery.

Overriding the system: how the brain controls food intake and what goes wrong in development

Food intake is controlled by two main neuronal systems in the brain, traditionally studied via the hypothalamus and more recently via the basal ganglia. Circulating hormones ghrelin and leptin signal via the hypothalamus to tell us, in broad terms, when we're hungry and full, respectively. These hormones work in synchrony to regulate food intake and maintain energy homeostasis.

Aside from hunger cues, one of the most potent drivers of feeding, specifically with foods high in sugar and fat, is its rewarding nature. We eat because we enjoy it. Eating palatable food results in more dopamine release in the brain within areas of the brain referred to as the 'reward system', making the experience of eating pleasurable. Indeed, when presented with a buffet of highly enticing foods, the majority of humans or other mammals will eat more than they actually need. This is often referred to as 'hedonic feeding'.

In a healthy person these two systems integrate feeding cues that are optimal for survival and longevity. When the system becomes dysfunctional, adverse effects on food intake and appetite follow quickly behind. Scientific backing links excessive food intake to dysregulation of neuronal

connections and dysfunction in the reward system.

Interestingly, studies in humans and mice have shown that these systems, both in the hypothalamus and in the basal ganglia, and the behaviours they control are negatively affected by maternal overnutrition, further fuelling the link between maternal diet and negative metabolic outcomes in children. In rodent models of maternal overnutrition, offspring develop impaired neuronal circuitry in hypothalamic circuits, ultimately predisposing offspring to overeating and obesity. However, we are now beginning to realise that these effects spread beyond the hypothalamus to other brain networks, leading to impaired neuronal activity and release of neurotransmitters therein. This culminates in a multitude of altered behaviours in offspring: from locomotion, to memory, to response to rewarding food.

Can the cycle be broken?

The field of foetal reprogramming is relatively young, and the role of maternal overnutrition in driving changes to multiple aspects of brain function is in its infancy. There is much to learn about not only the neuronal systems that govern our food intake, but also how these neurons and their connections are affected by maternal nutrition. In the meantime, it is imperative that awareness of the effects that maternal obesity and unhealthy diet can have on foetal neurodevelopment is spread and a collective guideline for what 'healthy' nutrition during pregnancy looks like, in a broad and easily accepted manner, is developed. Maybe then we can finally break the negative metabolic cycle.



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