How maternal flavor education may prevent childhood obesity?

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ABSTRACT

Childhood obesity has been associated with a number of perinatal factors, in particular a specific maternal phenotype characterized by nutritional and metabolic imbalance that increases the supply of nutrients to the feto-placental unit and leads to excessive fetal growth and fat mass deposition. A varied and balanced maternal diet could, through prenatal flavor education, play a role in preventing obesity in later life. Factors predisposing individuals to make dietary choices that may be antithetical to health, are: 1) innate flavor preferences, driven by evolution, and 2) harmful consequences of not being exposed to the flavors of healthy foods at the beginning of life. We focus on scientific evidence that suggests how early experience of flavors can influence the future food choices of infants.

KEYWORDS

Epigenetics, flavor, diet, pregnancy, breastfeeding, obesity, food, healthy food.

Introduction

Adequate nutrition during pregnancy and lactation is essential to prevent excessive maternal weight gain and promote good blood sugar control and correct distribution of caloric intake between carbohydrates, proteins and fat [1]. In addition, adequate micronutrient intake during pregnancy plays a fundamental role in mediating long-term outcomes, most likely through epigenetic mechanisms [2].

Maternal diet could also influence a predisposition to obesity in the offspring by modulating the development of flavor preferences, and thus contributing to unhealthy nutrition in the infant. This review focuses on how an unhealthy dietary attitude in the mother may contribute to the development of long-term obesity, also through perinatal development of flavor perception.

The importance of maternal nutrition in the programming of obesity

Due to the worldwide epidemic of obesity, there has been an increase in the number of women entering pregnancy with a body mass index that places them in the overweight or obese category. A high risk of short-term clinical complications, including neonatal hypoglycemia, jaundice, shoulder dystocia, and unexplained neonatal death has been shown in infants born to these women [3]. Moreover, maternal overweight and obesity are also associated with a significant increase in the risk of obesity and diabetes in both childhood and adulthood, as well as cardiovascular disease in adults [4,5]. Therefore, an intergenerational cycle of obesity and metabolic disease is established, whereby heavier infants, born to heavier mothers, go on to be fatter and less metabolically healthy in later life.

During pregnancy the maternal circulation carries nutrients to the developing fetus, and the maternal diet plays an essential role in determining the short- and long-term developmental outcomes of the offspring. Studies of infants of diabetic mothers have shown the effects of maternal overnutrition on the human fetus and neonate [6,7]. Glucose is transferred through the placenta by passive transfer following a concentration gradient [8], therefore high concentrations of glucose in the maternal circulation lead to increased exposure of the fetus to glucose [9,10]. In obese women, an inflammatory environment has been described, associated with increased oxidative stress and placental malfunction [11]. The "fuel-mediated teratogenesis" model, developed by Metzger, explains that fetal hyperglycemia results in fetal hyperinsulinemia due to increased release of insulin by the fetal pancreas [12]. Fetal hyperinsulinemia causes increased uptake of glucose, amino acids and fatty acids into insulin-sensitive tissues such as the adipose tissue, leading to excess accumulation of fat mass and fetal overgrowth that is frequently observed at delivery in infants of diabetic mothers. Furthermore, these infants are also at a greater risk of obesity later in life [6,7]. In the absence of overt maternal diabetes, even mild impairments of maternal glucose tolerance or maternal insulin resistance are also associated with increased fat mass in

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the neonate and an increased risk of obesity and diabetes in the child. In fact, a significant correlation between glucose concentrations in the umbilical cord blood at delivery and neonatal fat mass has been described, with glucose found to play a key role in excess intrauterine fat deposition [13].

Several animal studies have shown that increased total caloric intake or specific increases in the consumption of sugar and/or saturated fat are related to significant increases in the incidence of insulin resistance and obesity in the offspring after weaning [14]. These animal studies have supported clinical and epidemiological findings and have allowed researchers to understand the biological mechanisms that explain the relationship between exposure to an elevated nutrient supply before birth and a predisposition to obesity later in life.

These studies have led to the hypothesis that exposure of the fetus/neonate to an elevated nutrient supply, in the form of either global caloric excess or an elevated supply of fat or glucose, during critical developmental windows leads to potential alterations in the methylation pattern of several genes with permanent alterations in the function and structure of key systems involved in the regulation of metabolism [14,15]. In one study, the DNA methylation pattern of human fetal tissue at birth was analyzed and perinatal DNA methylation was found to be associated with the adiposity of children evaluated at 9 years of age [16].

It has been documented that the fat cell, or adipocyte, is implicated as a key target of developmental programming. Programming of the adipocyte is the primary event that drives the early-life (prenatal) programming of obesity in offspring exposed to an increased nutrient supply. Studies on small and large animal models have documented that during critical periods in the development of adipose depots exposure to an increased supply of lipids and glucose is associated with precocial upregulation of lipogenic genes within fat depots [17,18]. This leads to a greater susceptibility to fat deposition in postnatal life because there is an increase in the ability of adipocytes to store fat [15].

Development of flavor perception

The first experience with flavors occurs before birth when the flavor of the amniotic fluid changes according to the mother's diet. Flavor is the product of several sensory systems, mainly taste and smell [19]. The development of olfactory and taste receptors begins at 7-8 weeks of gestation [20]. The olfactory receptors are mature by the 24th week and the taste receptors by the 17th week of gestation. Fetal swallowing begins around the 12th week, and by the 24th week the amniotic fluid is also inhaled [21].

The fetus can react to different flavors, linked to the mother's diet, with changes in mimicry and behavior. Furthermore, de Snoo found that injecting a sweet-tasting stimulus into amniotic fluid stimulates fetal swallowing [22], while Liley found that injecting a bitter stimulus inhibits fetal swallowing [23]. In premature infants, exposure to glucose or sucrose solutions, as opposed to water, causes stronger and more frequent sucking; in addition, when a sweet solution is placed in the oral cavity, children relax their faces and sometimes smile [24]. On the contrary, quinine (a bitter stimulus) delays sucking [25]. These reactions have been interpreted as an innate taste preference, driven by evolution: specifically, a preference for sweet-tasting foods rich in calories and immediate energy (sugars), which were once rare. This is echoed by a rejection of potentially toxic food that has a bitter taste. This evidence could partly justify the great epidemic of childhood obesity, in the face of the wide availability of junk food.

The maternal diet, through repeated exposure of the offspring to the flavors of healthy foods during pregnancy (through the amniotic fluid) and subsequently during breastfeeding (through breast milk), could counteract this innate preference and contribute to correct flavor education of the infant.

Perception of salty tastes appears to develop later, perhaps at 2-6 months [26]. A salty preference is more complex, less understood and apparently more moldable than a sweet preference [27]. Babies born to women with moderate or severe morning sickness showed significantly more saline intake at 4 months than babies whose mothers reported having had no more than mild morning sickness [28]. Teens and young adults preferred higher concentrations of salt in a soup and reported significantly higher daily salt use if they had suffered from childhood vomiting or diarrhea or if their mothers had suffered from morning sickness [27].

Pregnancy: the flavor of amniotic fluid

Over the past two decades, the effects of repeated exposure to the flavors of healthy foods, through amniotic fluid and breast milk, on the future food choices of infants have been studied. By using analytical chemical techniques and sensory tests, it has been ascertained that the volatile compounds contained in food and beverages of the maternal diet are transferred to and modify the flavor of the amniotic fluid [29].

A randomized controlled study in women (n=10) evaluated changes in amniotic fluid odor in women who ingested a garlic capsule or placebo ~45 min prior to routine amniocentesis during the second trimester of pregnancy. Blinded trained study staff performed a sensory analysis: amniotic fluid samples from 4 of the 5 women who consumed a garlic capsule smelled of garlic, unlike the amniotic fluid samples from the women who consumed the placebo [29].

Other studies looked at children's responses to a flavor that was ingested by their mothers during pregnancy; their responses were compared with those of a control group of babies whose mothers did not ingest (or ingested less of) that flavor.

In a randomized clinical trial, a group of pregnant women was assigned to drink carrot juice during the last trimester of pregnancy while the control group had to avoid carrots and carrot juice. When the mothers weaned their babies at 6 months, the ones that had been exposed to carrot flavor in amniotic fluid ate more carrot-flavored cereal and made fewer disgusted faces than the unexposed babies [30].

Other studies have found that maternal intake of garlic, anise or alcohol during pregnancy resulted in significantly greater acceptance by infants when re-exposed to their respective

odors 3 to 14 days after birth compared with infants whose mothers did not ingest or who ingested less of the respective food or substance in pregnancy. The previously exposed infants showed greater orientation of their heads towards the smell, more effective sucking, greater positive facial responses, and greater arousal with increased body movements [31-34].

Four longitudinal cohort studies examined, with the aid of food frequency questionnaires, the relationship between maternal dietary patterns followed during pregnancy, and those of children up to 4 years old. The cohorts ranged in size from 52 to 9,649 mother-infant dyads. Two of the studies were conducted in Australia, one in Japan and one in France and England. These studies showed that maternal diet during pregnancy is significantly related to the subsequent quality of the children's diet [35-38].

Breastfeeding: the flavor of breast milk

The transfer of flavors into breast milk is well established. Using analytical chemical techniques (e.g., gas chromatography-mass spectrometry) and sensory tests, studies have detected the time between the mother's intake of certain foods and the changes in the smell and taste of breast milk. These changes were shown to be evident 30 min-1h after alcohol ingestion [39], and 2-3 hours after ingesting raw garlic or encapsulated garlic extract [40], carrot juice [30], mint and anise [41], and they dissipated over the following 3-8 hours. Infants repeatedly exposed to a carrot flavor (4 days a week for 3 consecutive weeks) through breast milk during the first 2 months of breastfeeding showed greater acceptance of carrot-flavored cereal versus plain cereal over the following 4 months, compared with infants who had no prior exposure to carrot flavor [30].

In general, breastfeeding, unlike formula feeding, provides the baby with a rich source of sensory variety. The types and intensity of the flavors experienced can be unique to each infant and characteristic of the family's culinary traditions. The food their mothers eat will be the same food they eat as they grow up. Longitudinal studies have shown that the strongest predictors of what food babies eat are: (1) how long they were breastfed, (2) whether their mothers ate these foods while pregnant, (3) if they have eaten these foods from an early age [42-44].

The different sensory experiences of flavors through breast milk in babies whose mothers eat a varied diet may also explain why babies who have been breastfed are less demanding and more willing to try new foods in infancy [42,45,46].

Another important aspect to evaluate is whether there are more sensitive periods in flavor learning and in the early development of hedonic responses to flavors. To this end, randomized clinical trials have been conducted, with variations in the age at which exposure began and in the duration of exposure to flavors. It has been shown that acceptance of extensive protein hydrosylate formulas is a function of the absolute amount of exposure, and the moment at which exposure begins is also significant. Even a relatively short taste experience of only one month, before the baby was 3.5 months old, was found to be enough to cause a hedonic tone shift from rejection to acceptance [47].

Conclusion

The myth that "in pregnancy and when breastfeeding you must eat for two" is valid only from a qualitative point of view: by repeatedly exposing the fetus/infant to the flavors of healthy food, first through the amniotic fluid and then through the breast milk, the mother may promote correct education of the baby's ability to appreciate flavors. Furthermore, adequate nutrition prevents excessive maternal weight gain, promotes good blood sugar control and a correct distribution of caloric intake between carbohydrates, proteins and fats, ensuring a correct pattern of fetal DNA methylation.

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