TITLE PAGE

Prenatal Diet and Children's Trajectories of Hyperactivity-inattention and Conduct problems from 3 to 8 years: The EDEN Mother-Child Cohort

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Abbreviations: ADHD (Attention Deficit Hyperactivity Disorder), DP (Dietary Pattern), SDQ (Strengths and Difficulties Questionnaire)

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ABSTRACT

Background

Evidence shows that diet contributes substantially to lifelong physical and mental health. Whereas dietary exposure during gestation and early postnatal life is critical, human epidemiological data are limited regarding its link with children's subsequent externalizing issues. The aim of this study was to investigate the role of maternal diet during pregnancy in offspring's symptoms of Hyperactivity-inattention and Conduct problems from ages 3 to 8 years.

Methods

We used data of 1242 mother-child pairs from a French cohort followed up from pregnancy until the children were 8 years of age. Dietary patterns (DP) of the mother during pregnancy were assessed with food frequency questionnaires. Children's externalizing behavior was assessed with the Strength and Difficulties Questionnaire at ages 3, 5 and 8 years, from which trajectories of Hyperactivity-inattention symptoms and Conduct problems were derived. We conducted multivariable logistic models to study associations adjusted for a range of potential confounders.

Results

Results showed significant relationships between maternal "low Healthy diet" (adjusted Odds Ratio (aOR) = 1.61; IC95%: 1.09-2.37) and "high Western diet" (aOR = 1.67; IC95%: 1.13-2.47) during pregnancy and children's trajectories of high symptoms of Hyperactivity-inattention. The associations took into account relevant confounders such as DP of the children at age 2 years, maternal stress and depression, gestational diabetes and socio-economic variables.

Conclusions

Maternal diet during pregnancy was independently associated with children's Hyperactivity-inattention symptoms but not with Conduct problems. Early prevention addressing lifestyle should specifically target diet in pregnant women.

Key words

Diet, pregnancy, mental health, externalizing, children, epidemiology, ADHD, Conduct problems

KEY POINTS

What's Known

Maternal diet during pregnancy has been associated with offspring’s subsequent externalizing problems. However previous research did not make it possible to specify whether ADHD and Conduct problems are distinctively influenced by prenatal diet.

What's new

Children's Hyperactivity-inattention trajectories from 3 to 8 years, but not Conduct problems trajectories, are related to low Healthy and high Western dietary patterns during pregnancy, independently from post-natal diet and social confounders.

What's clinically relevant

The whole diet of mothers should be considered early on in ADHD prevention.

TEXT

INTRODUCTION

Among lifestyle factors, the contribution of diet to general health and aging is now clearly evidenced. As a consequence, nutritional education and food supplementation have become important cornerstones for health promotion and disease prevention (Ghattas, 2014). Beyond the well-known impact of nutrition on the non-communicable physical diseases (e.g. cancer, cardiovascular diseases, diabetes, obesity), the literature on diet has recently widened its scope to include mental health and neurodevelopmental outcomes (Jacka, Sacks, Berk, and Allender, 2014; Logan et al., 2014; O'Neil et al., 2014). Both healthy (i.e. high in vegetables, fruits, nuts and seafood) and unhealthy Western (i.e. highly processed foods, high in carbohydrates, saturated and trans fats) diets have been linked respectively to reduced and heightened liability for common mental disorders. Most previous studies focused on anxiety/depression and concerned adults and, to a lesser extent, adolescents (Jacka, Sacks, Berk, and Allender, 2014; Martínez-González and Sánchez-Villegas, 2016; O'Neil et al., 2014). The earlier ages from pregnancy to the first years of life have received less attention.

However, as for other exposures and health conditions, it is highly plausible that diet may exert long-term influences on mental health by its action during the developmentally sensitive period of early life, from the time of conception through fetal growth, infancy and toddlerhood. This putative association supposes the direct repercussions of nutrition on the developing brain (e.g. neurotransmission and plasticity) and on fetal programming (i.e. epigenetic modifications). Other processes involving oxidative stress, the microbiote and the immune system might also be involved (Jacka, Sacks, Berk, and Allender, 2014; Logan et al., 2014; O'Neil et al., 2014).

Interestingly, apart from extreme situations such as prenatal exposure to famine, historically shown to increase the risk of schizophrenia and affective disorders in offspring (McGrath, Brown, and St Clair, 2011), recent birth cohort studies in supposedly well-fed populations have found that prenatal diet is related to the most prevalent behavioral issue of childhood, namely externalizing problems. Indeed, offspring externalizing problems studied as a global aggregate (i.e. comprising Attention Deficit Hyperactivity Disorder (ADHD) symptoms and Conduct problems) have been negatively related to prenatal diet quality (Jacka et al., 2013; Steenweg-de Graaff et al., 2014). In addition, studies examining a more specific phenotype such as early-onset persistent Conduct problems (Mesirow, Cecil, Maughan, and Barker, 2016; Rijlaarsdam et al., 2017) found a similar association. Several aspects of these studies are noteworthy: first, most relied on dietary pattern (DP) analysis, which better encompasses the whole diet along with interactions between foods and nutrients than studies focusing on specific foods or nutrients; second, they took important confounders such as post-natal nutrition, maternal depression and social variables into account. However, these investigations were limited in several ways. First, by considering externalizing problems as a global index or by examining ADHD symptoms within the context of early-onset persistent Conduct problems, they do not make it possible to specify whether ADHD and Conduct problems are distinctively influenced by prenatal diet. Nevertheless, although these syndromes are related, ADHD and Conduct problems partly depend on different etiological mechanisms. Conduct problems are indeed more likely to be affected by social variables (e.g. socio-economic and educative disadvantage, hostile parenting) than ADHD, which is conceptualized as a neuro-developmental disorder (Scott, 2015). In addition, whereas animal studies (e.g. those conducted in rodents) suggest that prenatal intake of fat and sucrose as well as micronutrient deficiencies are associated with enhanced ADHD-like behaviors in offspring (Choi et al, 2015; Sullivan, Riper, Lockard, and Valleau, 2015), such an association is less consistent regarding aggressive behaviors. Second, some important confounders including maternal anxiety during pregnancy, gestational diabetes and maternal alcohol consumption (Ornoy, Reece, Pavlinkova, Kappen, and Miller, 2015) have not been addressed by previous research. Third, the generalizability of findings to different settings with distinct dietary habits is uncertain since the studies to date were conducted in Northern European countries (i.e. Netherlands, United Kingdom and Norway), whose populations display comparable DP.

Owing to the concomitant and long-term burden associated with externalizing issues, better knowledge about a potentially modifiable contributor like diet is highly relevant for understanding the mechanisms involved and for prevention. The current study therefore aimed to examine whether dietary intake by women during pregnancy is associated with

Hyperactivity-inattention and Conduct problem trajectories in their offspring from 3 to 8 years.

METHODS

Study design and setting

The EDEN (Etude des Déterminants pré- et postnatals précoces du développement et de la santé de l'ENfant) mother-child cohort study aims to evaluate pre- and postnatal determinants of child development and health, including nutrition. Recruitment of pregnant women (before 24 weeks of amenorrhea) was conducted in two French university hospitals (Nancy and Poitiers, 2003-2005) during the prenatal visit to the Departments of Obstetrics and Gynecology. Exclusion criteria were as follows: multiple pregnancy (i.e. more than one fetus), pre-pregnancy diabetes, illiteracy, and plan to move outside the region within 3 years. Multiple waves of data collection were conducted (pregnancy, at the child's birth, at 4, 8, 12, 24 months, 3, 5 and 8 years). Data were collected from medical records (pregnancy, birth) by trained interviewers (pregnancy, birth, 3, 5 and 8 years) and by mothers' and fathers' self-reports at all study waves. Details on the study design and data can be found in the EDEN cohort profile paper (Heude et al., 2016). Informed written consent from the parents was obtained at enrollment and consent for the child was obtained from both parents after the child's birth. The EDEN cohort received approval from the Bicêtre Hospital ethics committee and the Commission Nationale Informatique et Libertés, which oversees ethical aspects of data collection in France.

Participants

Complete details on participation and attrition are available in the EDEN cohort profile paper (Heude et al., 2016). In brief, among the 2002 women included in the cohort, there were 1899 mother-child pairs at birth. The numbers of participating mother-child pairs at ages 1, 2, 3, 5 and 8 years of the child were respectively 1717, 1611, 1527, 1255 and 883. There was complete data for 1242 mother-child pairs for both SDQ trajectories and maternal diet during pregnancy. Compared to a nationally representative sample of pregnant women in France in 2003, EDEN study participants were similar in terms of parental socio-demographic characteristics (except for educational attainment, which was higher in the EDEN study), offspring birth weight and prematurity rates (Heude et al., 2016). Over the follow-up period, attrition rates were highest in families in which the mother was young, had a low educational level and low income, did not live with the child's father, smoked during pregnancy, had psychological difficulties in pregnancy, and whose child did not have low birth weight (Heude et al., 2016).

Outcome variable: children's externalizing trajectories from 3 to 8 years

Children's externalizing symptoms were ascertained using the Strengths and Difficulties Questionnaire (SDQ) completed by the mothers when children were 3, 5 and 8 years of age (Goodman, 1997; Marzocchi et al., 2004). This validated instrument includes two scales for children's externalizing behavior: Hyperactivity-inattention and Conduct problems. The Hyperactivity-inattention scale comprises the following 5 items: "restless, overactive, cannot stay still for long", "constantly fidgeting or squirming", "easily distracted, concentration wanders", "can stop and think things out before acting (wave 3 years of age) or thinks things out before acting (waves 5 and 8 years of age)", "good attention span, sees work through to the end". The Conduct problems scale comprises the following 5 items: "often loses temper", "generally well behaved, usually does what adult requests", "often fights with other children or bullies them", "often argumentative with adults (wave 3 years of age) or often lies or cheats (waves 5 and 8 years of age)", "can be spiteful to others (wave 3 years of age) or steals from home, school or elsewhere (waves 5 and 8 years of age)". All items refer to the past 6 months or the current school year and are scored 0 (never), 1 (sometimes true) or 2 (certainly true). Items composing each scale were summed to generate a score ranging from 0 to 10, which made it possible to build quantitative scores and then identify empirically individual developmental trajectories of Hyperactivity-inattention symptoms and Conduct problems between 3 and 8 years of age. This identification was conducted through group-based trajectory modeling using semi-parametric mixture models with censored-normal distributions (Nagin, 2005; Nagin and Odgers, 2010). This procedure enables the identification of clusters of individuals following a similar developmental trajectory of the variable of interest (e.g. Hyperactivity-inattention or Conduct problems). The best models in terms of number of groups and polynomial order of the trajectories were determined by using the Bayesian Information Criterion **(BIC)** and maximizing the posterior probability of group membership ($\geq$0.7) (Nagin, 2005; Nagin and Odgers, 2010). To account for missing data and provide the most precise estimates, subjects with at least one data point were included. The SDQ data were available as follows: N=1308 at 3 years, N=1184 at 5 years, N=874 at 8 years. We identified three groups of symptoms for Hyperactivity-inattention (low: 28.6%, moderate: 56.4%, high: 15.0%) and three groups of symptoms of Conduct problems (low: 22.8%, moderate: 61.3%, high: 15.9%). Regarding trajectories of Hyperactivity-inattention, mean probabilities of being in each respective trajectory group were 0.84 (Standard Deviation (SD)=0.16) for the low trajectory, 0.82 (SD=0.14) for the moderate trajectory and 0.85 (SD=0.16) for the high trajectory. **Entropy was equal to 0.65.** Mean SDQ scores in the low, moderate and high trajectory groups were respectively: 1.37 (SD=1.25), 3.71 (SD=1.58) and 6.42 (SD=1.71) at 3 years; 0.75 (SD=0.85), 3.26 (SD=1.44) and 6.77 (SD=1.59) at 5 years; 0.87 (SD=1.03), 3.52 (SD=1.60) and 7.09 (SD=1.80) at 8 years. Regarding trajectories of Conduct problems, mean probabilities of being in each respective trajectory group were 0.83 (SD=0.16) for the low trajectory, 0.84 (SD=0.14) for the moderate trajectory and 0.86 (SD=0.14) for the high trajectory. **Entropy was equal to 0.66.** Mean SDQ scores in the low, moderate and high trajectory groups were respectively: 1.31 (SD=1.16), 3.12 (SD=1.43) and 6.14 (SD=1.40) at 3 years; 0.16 (SD=0.37), 2.41 (SD=1.29) and 5.53 (SD=1.42) at 5 years; 0.34 (SD=0.58), 1.69 (SD=1.18) and 3.77 (SD=1.60) at 8 years. For further analyses, Hyperactivity-inattention and Conduct problems were dichotomized (high symptoms group vs others).

Main exposure: maternal diet during pregnancy

Maternal diet in the last trimester of pregnancy was assessed retrospectively using a validated food frequency questionnaire (Deschamps et al., 2009) that was completed during maternity stay after delivery. Data on maternal diet was available for 1599 mother-child pairs. It included 137 items with seven categories of frequencies, ranging from never to more than once per day. These items were grouped into 44 food groups, and maternal DP during pregnancy were identified by principal component analysis (PCA) in a previous study (Yuan et al., 2017). Two DP were identified: 1) “Healthy” (i.e. characterized by a high intake in fruit, vegetables, fish and whole grain cereals) (lowest quartile vs others) and 2) “Western” (i.e. characterized by a high intake in processed and snacking foods) (highest quartile vs others), corresponding to the first and second component of the principal component analysis, which explained 10.8% and 6.8%, respectively, of the total variance. The score for each DP was calculated at the individual level by summing the observed standardized frequencies of consumption per food group, weighted according to the PCA loadings. Although the percentage of variance explained by both DP in the current study is not very high, it is similar to those estimated in the broader literature focusing on dietary patterns (Bertin et al., 2016; Newby and Tucker, 2004; Northstone and Emmet, 2010). Descriptive statistics of the DP are provided in Tables S1 (contingency table) and S2 (mean scores within quartiles) (supplemental online material). By construction, patterns derived from PCA analyses are considered as independent. Consequently, Healthy and Western DP were weakly correlated (Phi coefficient=-0.1038, $p<0.05$). **Figures S1 and S2** show the distribution of the maternal DP scores in quartiles according to levels of Hyperactivity-inattention and Conduct problems respectively (supplemental online material).

Covariates

Parental characteristics at baseline included maternal education (mean of school years), maternal age at inclusion (years) and maternal pre-pregnancy body mass index (BMI) (kg/m^2). *Pregnancy characteristics* included maternal alcohol intake (>2 glasses / week vs. no or ≤2 glasses / week), maternal daily smoking throughout pregnancy (0 / 1-5 / 5-10 / 10+ cigarettes/day), maternal depression (mean score of depressive symptoms measured with the Center for Epidemiologic Studies Depression Scale Revised, CES-D) (Radloff, 1977), maternal anxiety (mean score of anxiety symptoms measured with the STAI (Spielberger, Gorsuch, Lushene, Vagg, and Jacobs, 1983), diagnosed gestational diabetes (yes / no), and multiparity (yes / no). *Child characteristics at birth* included sex (male / female), birth weight (kg), and gestational age (weeks of amenorrhea). *Postnatal characteristics* included breastfeeding duration (≥6 months / <6 months/no), family income from pregnancy to age 1 (mean of the eight class numbers -1: <450€/month, 2: 450-800€/month, 3: 800-1500€/month, 4: 1500-2300€/month, 5: 2300-3000€/month, 6: 3000-3800€/month, 7: 3800-4500€/month, 8: >4500€/month), postnatal maternal depression at age 1 (mean score on the Edinburgh Postnatal Depression Scale, EPDS) (Cox, Holden, and Sagovsky, 1987), and parental separation before birth assessment (biological father not living with the mother and child, yes / no). *Child dietary patterns at age 2 years* comprised three patterns derived from a food frequency questionnaire by principal component analysis (Lioret et al., 2015): 1) “Processed and fast foods” (i.e. high intake of French fries, processed meat, carbonated soft drinks, chocolate, chips, cookies, pizza, fruit juice, meat, dairy desserts, and ice cream) (highest quartile vs others); 2) “Guidelines” (i.e. high intake of cooked vegetables, rice, fresh fruit, raw vegetables, low-fat fish, potatoes, ham, stewed fruit, and meat) (lowest quintile vs others); 3)

“Baby foods” (high intake of baby foods, breakfast cereals, and stewed fruit and low intake of raw vegetables and fresh fruit) (highest quintile vs others). An additional variable was *recruitment center* (Poitiers / Nancy).

Statistical analysis

First, we described the sample's characteristics. Second, we tested the associations between maternal DP during pregnancy and Hyperactivity-inattention and Conduct problem trajectories (High trajectory versus others), adjusting for covariates (multivariable logistic analyses). As the two maternal DP were independent by construction, they were simultaneously included in the adjusted models. Covariates were maintained in the final models if they were significantly associated with the study outcome ($p<.05$), with nutrition exposure or were theoretically important. Third, interaction between Healthy and Western DP was tested. Fourth, we conducted sensitivity analyses to test the robustness of our findings by 1) using tertiles as cutoffs for the DP variables, 2) restricting the analysis to the non-smoking sub-sample (N=956), 3) restricting the analysis to the non-heavily drinking sub-sample (N=1141), 4) without adjusting for gestational age and birth weight, 5) without adjusting for gestational diabetes, 6) adjusting for Conduct problems when considering Hyperactivity-inattention and reciprocally. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc, Cary, North Carolina). Covariates with missing data were imputed (multiple imputation on 10 data sets) based on exposure (maternal DP during pregnancy), outcome and all other covariates before conducting multivariable analyses. The multiple imputation method was implemented using PROC MI and PROC MIANALYSE.

RESULTS

Table 1 displays the characteristics of the total sample, and according to the levels of maternal DP scores during pregnancy. As compared to mothers with healthier diets, those whose diets were scored in the first quartile of the Healthy DP during pregnancy had a lower education and family income, a higher pre-pregnancy BMI, were younger and more likely to smoke tobacco during pregnancy, to have gestational diabetes and to be multiparous. They were also more likely to have their child in the first and fourth quartiles of the Guidelines and Baby foods DP at age 2 years and less likely to have breastfed for more than 6 months (all $p<0.05$). As compared to mothers with healthier diets, those whose diets were scored in the fourth quartile of the Western DP during pregnancy were also more likely to have a lower education, to be younger, to have more depressive symptoms during pregnancy, to consume more tobacco during pregnancy, to have gestational diabetes, to be multiparous, to have lower family income, to have their child in the fourth and first quartiles of Processed and fast foods and Guidelines DP scores, respectively, at age 2 years (all $p<0.05$). Compared to children of mothers in the other quartiles, children of mothers in the lowest quartile of the Healthy DP were more likely to show a high level of Hyperactivity-inattention (21.4% vs 12.9%; $p=0.0003$) and Conduct problems (19.4% vs 14.7%; $p=0.0484$) from 3 to 8 years. Compared to children of mothers in the other quartiles, children of mothers in the highest quartile of the Western DP were more likely to show a high level of Hyperactivity-inattention (21.6 % vs 12.8%; $p=0.0002$) between 3 to 8 years ($p<0.05$).

Table 2 displays associations between maternal and offspring DP at age 2 years and children's externalizing problems between 3 and 8 years of age, before and after adjusting for covariates. Multivariate logistic regression models showed that the maternal “Low Healthy” and the “High Western” DP were positively related to offspring’s Hyperactivity-inattention symptoms at ages 3 to 8 years, in both the unadjusted and adjusted models. Regarding Conduct problems, the maternal “Low Healthy” and the children's “High Processed and fast foods” DP were significant predictors in the unadjusted models. However, once additional adjustment was made, no maternal DP remained significantly associated with subsequent Conduct problems. The interaction term between Healthy and Western patterns was not significant ($p=.61$). The associations observed between maternal diet during pregnancy and offspring Hyperactivity-inattention symptoms hardly changed in sensitivity analyses (see supplementary online material, Table S3).

DISCUSSION

Main findings

Maternal diet during pregnancy was associated with offspring’s subsequent Hyperactivity-inattention through both pathways of low Healthy and high Western DP. These relationships remained statistically significant after adjusting for numerous potential confounders (including children's postnatal diet, family socio-economic variables, maternal depression and substance exposure during pregnancy) but also for important risk factors not considered in previous studies including gestational diabetes and maternal prenatal anxiety. Importantly, results were inconclusive regarding the association between maternal diet during pregnancy and offspring's subsequent Conduct problems once adjustment variables were taken into account. By disentangling externalizing problems, these results extend prior epidemiological evidence based on DP analysis (Jacka et al., 2013; Steenweg-de Graaff et al., 2014) and show that maternal diet during pregnancy is more likely related to ADHD symptoms rather than Conduct problems. This finding extends human and animal research data by suggesting that variations in the exposure to certain nutrients could increase the likelihood that offspring will display externalizing problems such as ADHD (Hoi et al, 2015; Liu and Raine, 2011; Sullivan, Riper, Lockard, and Valleau, 2015).

Strength and weaknesses of the study

The strengths of our study are the large community-based sample, the longitudinal evaluation of diet and covariates, the developmental trajectory modeling approach, the consideration of the total diet through DP analysis, the adjustment for a wide range of confounders, and the robustness of the results in sensitivity analyses. Its limitations are the selective nonresponse among more socially disadvantaged women and the self-reported nature of dietary intake, which possibly introduced selection and measurement biases. Nevertheless, these limitations may have attenuated the strength of the observed relationship with offspring's externalizing behaviors, resulting in more conservative associations. Furthermore, dietary intake during pregnancy was assessed on the basis of third-trimester data, which makes exposure assessment non-prospective with regard to birth outcomes (e.g. birth weight, gestational age). However, exposure assessment was prospective with regard to offspring's externalizing problems. In addition, it must be acknowledged that the SDQ scales Hyperactivity-inattention and Conduct problems are aggregates themselves. However they represent more subtile phenotypes than a global externalizing index and they are widely used in the literature as proxies of symptoms of ADHD and Conduct problems. **It should be noted that the moderate level of entropy may affect class separation when modeling trajectories possibly conducing to more conservative results. However it is noteworthy that the model selection of children's trajectories of hyperactivity-inattention and conduct problems was based on the BIC and on high levels of posterior probabilities of group memberships (all probabilities > 0.8).** Residual confounding (particularly unmeasured familial confounding including genetic or environmental factors) may also be present in the current study. Further methodological approaches comprising sibling analyses and Mendelian randomization may help in offsetting this possible bias. Another shortcoming is the lack of availability of biological assessments such as genetic, epigenetic, and immunological variables. Such measures in future studies would help in clarifying the precise mechanisms at play.

Interpretation of the findings

Several competing and/or complementary mechanisms can be put forward to interpret our results. First, inadequate nutrition during pregnancy could be causally linked to Hyperactivity-inattention symptoms in children. Indeed, both macronutrient over/under intake (i.e. carbohydrates, fats and total calories) and micronutrient deficiencies (e.g. omega 3, vitamin D, folate, iodine, minerals) have been demonstrated to alter neurodevelopment in offspring (Black et al., 2013; Emmett, Jones, and Golding, 2015). As advocated by the Developmental Origins of Health and Disease hypothesis, fetal programming through epigenetic modifications could underlie the early diet/later mental health relationship (Kim, Bale, and Epperson, 2015). Additional putative mechanisms include prenatal nutritional influences on the microbiote, immune system, oxidative stress or directly on the developing brain (Chmurzynska, 2010; O'Neil et al., 2014). Of note, a recent analysis in the ALSPAC cohort showed that in youths with early-onset and persistent Conduct problems, unhealthy prenatal diet was related to higher ADHD symptoms via higher insulin-like growth factor 2 gene (IGF2) methylation (Rijlaarsdam et al., 2017). Interestingly, IGF2 influences placental, fetal, and brain development (Roberts, Owens and Sferruzzi-Perri, 2008; Pidesley et al., 2012). Although it was based on a small sample and did not disentangle Conduct from ADHD problems, that study is particularly relevant for future research aiming at understanding mechanisms and identifying targets for prevention. Second, the association between prenatal diet and Hyperactivity-inattention could be correlational, merely reflecting a non-causal link. In humans, the effects of prenatal exposures on neurodevelopment and subsequent behaviors are rarely straightforward. Most often they depend on the sequence and time frame of the exposures. They generally imply complex mechanisms, which comprise multiple interactions between exposures, individual vulnerabilities (e.g. genetic/epigenetic variations in both fetus and mother), and environmental pre- and postnatal experiences. In this sense, prenatal maternal diet appears to be intertwined with a host of health behaviors (e.g. smoking, poor physical activity), social (e.g. poverty and poor family education) and biological risk factors.

Consequently it is plausible that prenatal diet acts uniquely in combination with other factors or even solely represents a proxy of a distinct set of truly causal risk factors. An additional alternative hypothesis to causality is Gene-Environment correlation. Maternal ADHD could indeed influence both the prenatal diet behavior (through inadequate dietary habits) and the ADHD phenotype of the child (through the genetic/environmental transmission of ADHD vulnerability by the mother). This hypothesis could not be tested in our data.

Implications

Our results potentially have public health and research entailments. If diet is causally related to subsequent behavioral development, early prevention could reduce the contribution of mental health to health inequalities. Since diet and other psychosocial risk exposures (particularly low maternal education, low income and high risky behaviors) are intricately linked, interventions relying on health literacy based on dietary guidelines may not be sufficient. Beyond folate/iron supplementation and advice to pregnant women regarding diet/health behaviors, intensive universal prevention strategies should be implemented and evaluated. Ideally, they should include a combination of actions at different levels. First, policies making healthy foods cheaper and more accessible, and aiming to reduce or prohibit the promotion of unhealthy foods (especially towards youths) should be implemented. Second, the promotion of a healthy diet should extend to community, school and occupational settings. Third, such interventions should be part of a comprehensive framework that addresses parents'/children's lifestyles with a particular focus on the pre-pregnancy and pregnancy periods, including health behaviors, physical activity, substance use and pro-social behaviors. Regarding research aspects, cross-disciplinary efforts incorporating animal, clinical, population-based, and basic sciences are needed to understand the complex interplay between the micro- and macro-levels, in order to develop efficient preventive interventions (Susser and Keyes, 2017). Finally, to overcome the issues of the multi- and equi-finality of risk factors and outcomes, future investigations should encompass a large set of individual variables (e.g. biological and social) as well as numerous psychiatric and neurodevelopmental outcomes.

Conclusions

The worldwide exposure of the most disadvantaged populations to unhealthy foods has dramatically increased through the globalization of low-cost highly processed foods (FAO, 2013; Ghattas, 2014; Logan et al., 2014). Since diet may improve or jeopardize subsequent developmental outcomes from pregnancy, it is henceforth of the utmost importance to provide a wide access to healthy foods and nutrition education, especially during the sensitive period of gestation.

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