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ORIGINAL ARTICLE

Maternal adiposity prior to pregnancy is associated with ADHD symptoms in offspring: evidence from three prospective pregnancy cohorts

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Objectives: We examine whether pregnancy weight (pre-pregnancy body mass index (BMI) and/or weight gain) is related to core symptoms of attention deficit hyperactivity disorder (ADHD) in school-age offspring.
Design: Follow-up of prospective pregnancy cohorts from Sweden, Denmark and Finland within the Nordic Network on ADHD.
Methods: Maternal pregnancy and delivery data were collected prospectively. Teachers rated inattention and hyperactivity symptoms in offspring. High scores were defined as at least one core symptom rated as 'severe' and two as 'present' (approximately 10% of children scored in this range). Logistic regression and latent class analyses were used to examine maternal pregnancy weight in relation to children's ADHD core symptoms.
Results: Teacher rated 12 556 school-aged children. Gestational weight gain outside of the Institute of Medicine guidelines was not related to ADHD symptoms (below recommendations: odds ratio (OR): 0.96; 95% confidence interval (CI): 0.81, 1.14; above recommendations: OR: 0.98; 95% CI: 0.82, 1.16). To examine various patterns of pre-pregnancy BMI and weight gain, we used latent class analysis and found significant associations between classes that included pre-pregnancy overweight or obesity and a high ADHD symptom score in offspring, ORs ranged between 1.37 (95% CI: 1.07, 1.75) and 1.89 (95% CI: 1.13, 3.15) adjusted for gestational age, birth weight, weight gain, pregnancy smoking, maternal age, maternal education, child gender, family structure and cohort country of origin. Children of women who were both overweight and gained a large amount of weight during gestation had a 2-fold risk of ADHD symptoms (OR: 2.10, 95% CI: 1.19, 3.72) compared to normal-weight women.
Conclusions: We show for the first time that pre-pregnancy BMI is associated with ADHD symptoms in children. Our results are of public health significance if the associations are causal and will then add ADHD symptoms in offspring to the list of deleterious outcomes related to overweight and obesity in the prenatal period.
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Keywords: attention deficit hyperactivity disorder; child; body mass index; pregnancy; fetal origins; cohort studies

Introduction

The prevalence of women entering pregnancy overweight or obese is rapidly increasing across the United States, Europe and Asia.[1] Rising pre-pregnancy body mass index (BMI) is associated with gestational diabetes, pre-eclampsia, labor complications and adverse birth outcomes.[2,3]

Poor birth outcomes have been linked to cognitive deficits and psychiatric disturbances in children[4] including attention deficit/hyperactivity disorder, ADHD[5] and hyperkinetic disorder.[6] Many of these neurodevelopmental disorders have multifactorial etiologies and factors affecting fetal brain development are thought to play an important role. Optimal fetal brain development is highly dependent on energy and

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nutrition supplied by the mother.[7,8] Famine studies suggest a link between maternal starvation (before or during pregnancy) and schizophrenia in adult offspring.[9] To date, there are no studies examining maternal pre-pregnancy weight and ADHD symptoms in childhood.

Extreme pre-pregnancy weight at both sides of the spectrum correlate with altered metabolic, hormonal or ovarian functioning, for example,[10] which could play a role in fetal neurodevelopment. However, evidence is lacking on maternal overweight prior to pregnancy in relation to neurodevelopmental disorders in the offspring.

Fetal brain development is also dependent on maternal energy supply during pregnancy.[11] Thus, it is possible that maternal weight gain could moderate the possible negative impact of extreme pre-pregnancy BMI. If a woman is very lean, then it is possible that greater weight gain could compensate for her low fat stores. Recent evidence showed inadequate weight gain during pregnancy (both low and excessive) was linked to preterm birth at various BMI starting points.[12,13] Women who do not gain weight within the guidelines set by the Institute of Medicine (IOM)[14] are more likely to have suboptimal outcomes than women who gain the recommended amount of weight for their BMI.[15]

We investigated maternal weight in relation to core symptoms of ADHD in offspring using prospective data gathered within three Nordic pregnancy cohorts considering also the combination of pre-pregnancy BMI and pregnancy weight gain. We used the IOM guidelines[14] and latent class analysis to distinguish between various patterns of BMI and weight gain.

Materials and methods

Data originate from three prospective pregnancy cohorts from Sweden, Denmark and Finland that make up the Nordic Network on ADHD.[16] Pregnant mothers, literate in the local language, were consecutively recruited in early pregnancy via governmental-run antenatal health services, which offer high-quality standardized care used by essentially all women.[17] High recruitment rates (91–99%) were achieved in all cohorts. The Local Research Ethics committees approved the studies. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Pregnancy data

Only singleton pregnancies ($N = 14\,519$, live born) were included because weight gain per infant differs between singleton and multiple pregnancies. Data were collected via medical records and questionnaires. Maternal age was grouped into the following categories: younger than 20, 20–24, 25–30, 31–35 and older than 35. Pre-pregnancy BMI (calculated by weight in kg per height in m^2) was rounded to the nearest whole number from data recorded in the medical chart at the time of booking (approximately at gestational week 10) by the midwife as part of the case history. Maternal weight was recorded at delivery or late in gestation for all women and was subtracted from pre-pregnancy weight to obtain weight gain during pregnancy. Gestational age in completed weeks was calculated by ultrasonography in Sweden (approximately at gestational week 18) and ultrasonography (for about 80%), date of last menstrual period, or both in Denmark and Finland. As total weight gain during pregnancy will differ greatly depending on the length of gestation, we computed the total average weekly weight gain across the pregnancy regardless of its length by dividing weight gain by the number of completed gestational weeks. Birth weight was measured immediately after birth.

Completed self-report questionnaires were received during gestational week 16 (Denmark), 20 (Sweden) and 24 (Finland; administered during week 10 and returned during week 24 if the woman was still pregnant). Women provided data on current pregnancy smoking (coded as nonsmoker, 1–10 cigarettes per day or more than 10), maternal education and family structure (cohabitance with the expectant father vs single parenthood or other living arrangement).

Follow-up

Follow-up occurred during 2001–2002 in Sweden and Denmark and 1993–1994 in Finland. National population-based registries in each country identify all residents by unique personal numbers, which we used to obtain current addresses. Thus, participants could be traced even outside the original geographic area. At follow-up, mothers provided additional background data concerning current family structure, either as intact (both biological parents present) or disrupted (single parent or step-parent present). Current maternal education was categorized as either less than vs 4 or more years of college/university education or university degree. Mothers provided consent to contact the child's teacher at follow-up when children were approximately 7–8 years old in Sweden and Finland and 10–12 years old in Denmark.

Teachers rated ADHD symptoms using official translations of the Strengths and Difficulties Questionnaire (SDQ)[18] in Sweden and Denmark and the Rutter scale (RB2)[19] in Finland. These instruments are highly correlated[18] because the SDQ builds on the Rutter scale[20] and have been clinically validated.[19,21] Three core symptoms are measured by both the SDQ and the Rutter and consist of hyperactivity (SDQ: item nos. 2 and 10; RB2: item nos. 1 and 3) and inattention (SDQ: 15 and RB2: 16) and are scored in the same way: 0 (not true), 1 (somewhat true) or 2 (certainly true). These three core symptoms were strongly associated with impairment related to scholastic underachievement in the present cohorts.[16] Symptom occurrence was, as expected, higher for boys than for girls in all cohorts.

Statistical analyses

We analyzed all data with SAS version 8.2 (SAS, Cary, NC, USA) amended with Mplus version 3.12 software (Los Angeles, CA, USA) for latent class analyses. All statistical tests of hypotheses were two-sided at $P<0.05$. Our primary exposure was maternal pre-pregnancy BMI and the primary outcome, the dichotomized ADHD symptom score. We defined a high ADHD symptom score as a total of 4 points or more (range: 0–6), which indicates that at minimum two symptoms were rated as 'somewhat true' and one symptom as 'certainly true.' About 10% of children scored within this range. This score appears to be clinically relevant.[16] The unadjusted and adjusted associations between maternal pre-pregnancy BMI and high ADHD symptom score in the offspring were analyzed using multivariate logistic regression (odds ratio (OR), 95% confidence intervals (CI) reported). All analyses adjusted for cohort membership. Adjustments for possible confounding variables were based on previous literature and our own analyses, which showed an association with ADHD by maternal smoking during pregnancy, weight gain, gestational age, birth weight, infant sex, maternal age, maternal education and family structure (at follow-up); most of them known to associate also with BMI.

To investigate whether weight gain moderated the possible association between pre-pregnancy BMI and high ADHD symptom score, we analyzed average weekly weight gain stratified by pre-pregnancy BMI. Further, we checked whether gaining weight outside of the IOM recommendations per pre-pregnancy BMI increased the risk for high ADHD symptom score in offspring. To examine simultaneously both pre-pregnancy BMI and weight gain, we used Mplus to generate latent class assignment from continuous variables, which takes into account non-normality and non-independence of observations.[22] We evaluated the appropriateness of solutions including three to eight latent classes using entropy, which indicates the percentage of correctly classified cases and Akaike's Information Criterion (AIC), which indicates the model's parsimony in comparison to other models. We included all possible data when generating latent classifications, that is, from original participants in the cohorts for whom anthropomorphic data were available and who had singleton live-born infants, regardless of whether they participated in the follow-up. Logistic regression was performed to test the association between latent classes representing various combinations of maternal pre-pregnancy BMI and weekly weight gain and high ADHD symptom score adjusted for cohort country of origin and including the possibly confounding variables listed above.

Results

Retention of participants at follow-up was based on traceable live births in each cohort and was 290 (74%) in Sweden, 5039 in Denmark (61%) and 9297 in Finland (90%). Maternal consent to contact teachers in Sweden was obtained for 79% and of these 96% of teachers participated. In Denmark, 65% of parents provided permission to contact teachers and 85% of eligible teachers participated. In Finland, we mailed the RB2 forms to the parents who forwarded them directly to teachers, and 92% responded. A total of 12 556 teacher reports were obtained. Attrition analyses for Sweden showed that participants were similar to national norms on socioeconomic status and birth outcomes and that permission to contact the teacher was unrelated to maternal ratings of child behavior, child gender, maternal education or family structure.[23] Table 1 shows characteristics of mothers and children on main study variables by cohort and combined sample.

Pre-pregnancy BMI

Table 2 shows the mean pre-pregnancy BMI and weekly weight gain by cohort country and maternal lifestyle factors. There were slight, statistically significant differences in pre-pregnancy BMI by cohort country. All BMI means fell within the normal range, although Danish women were the leanest. Women from Sweden were heaviest and gained more weight in comparison to the other cohorts. Maternal lifestyle factors were not systematically related to pre-pregnancy BMI, for example, those reflecting disadvantage. Younger women were leaner than older, less educated were heavier, women in intact homes (at follow-up) had been heavier and there were no differences among smoking and nonsmoking women. Weekly weight gain was generally similar across the maternal lifestyle factors.

Logistic regression analysis showed that for every unit increase in pre-pregnancy BMI, there was a 3% increase in odds of having a child with a high ADHD symptom score adjusted only for cohort country (BMI OR = 1.03, 95% CI: 1.01, 1.05). This association remained after full adjustment for the confounders (OR = 1.04; 95% CI: 1.02, 1.07). Because the association may not be strictly linear, we tested BMI categories, <18 (underweight), 19–26 (reference), >26 (overweight) and found that in comparison to normal-weight women, overweight women had increased odds of having children with a high ADHD score, OR = 1.43 (95% CI: 1.12, 1.82), after full adjustment for possible confounders. Leanness was not associated with high ADHD score in offspring, OR = 0.81 (95% CI: 0.61, 1.09).

We examined the cohorts separately to check if the associations held in each cohort or if they were driven by a particular sample. After control for confounders, the pattern between pre-pregnancy BMI and increased risk of ADHD symptoms in offspring held firmly in Finland (Wald $\chi^2 = 7.9$, $P<0.02$) and roughly in Denmark (Wald $\chi^2 = 4.9$, $P<0.09$). In both countries, the associations were in the same direction and of similar magnitude: maternal overweight/obesity was related to high ADHD symptom score in Finnish cohort with OR = 1.47 (95% CI: 1.10, 1.96), and in the Danish with OR = 1.55 (95% CI: 0.98, 2.43). It was not possible to conduct the analyses for the Swedish cohort alone due to the small sample size.

Table 1 Characteristics of mothers and children on study variables according to cohort

	First child in the family	*ABC*	*NFBC*	*All cohorts combined*
Maternal characteristics				
Cohort country	Sweden	Denmark	Finland	
Year of recruitment	1992–1994	1990–1992	1985–1986	
Gestational week at recruitment	10	14	12	
Nulliparity (%)	100	52	34	44
Maternal age during pregnancy (%)				
<20	3	2	8	5
20–24	23	16	23	20
25–30	53	41	41	41
31–35	16	28	15	21
>35	5	13	13	13
Pre-pregnancy body mass index (M, s.d.)	23.52 (3.58)	21.89 (3.38)	22.34 (3.50)	22.18 (3.36)
Weight gain (kg) during pregnancy (M, s.d.)	15.34 (5.10)	14.62 (5.28)	13.63 (4.80)	14.08 (5.04)
Mean weekly weight gain (g)				
Adjusted for gestational age (s.d.)	394 (132)	371 (123)	346 (120)	357 (122)
Smoking during pregnancy (%)				
Nonsmokers	86	68	79	74
1–10 cigarettes per day	11	25	10	17
>10 cigarettes per day	3	7	11	9
Family structure during pregnancy (% single-parenthood)	9	5	5	
Family structure at follow-up (% disrupted)	22	21	5	12
Maternal education at follow-up (% ⩾4 years college education or degree)	10	15	8	11
Infant characteristics				
Gestational age (M, s.d.)	39.2 (1.8)	39.8 (1.8)	39.4 (1.5)	39.6 (1.6)
Birthweight (M, s.d.)	3546 (523)	3524 (536)	3587 (518)	3566 (525)
Sex (% male)	50	49	51	50
Child characteristics				
Age at follow-up	7–8	10–12	7–8	
N at follow-up (% retention)	290 (74%)	5039 (61%)	9297 (90%)	
Total ADHD symptom score (M, s.d.)[a]	1.29 (1.78)	1.05 (1.63)	0.91 (1.50)	0.96 (1.55)
% scoring 0	53	58	65	62
High ADHD symptom score (%)[b]	12.50	10.48	7.39	8.52

Abbreviations: ADHD, attention-deficit hyperactivity disorder; ABC, Aarhus Birth Cohort; M, mean; NFBC, Northern Finland Birth Cohort; s.d., standard deviation.
[a]Sum of ratings on presence of hyperactivity and inattention symptoms (each scored 0 = not true, 1 = somewhat true, 2 = certainly true). [b]Sum score of ⩾4 points.

Weight gain

Weekly weight gain was re-coded in increments of 100 g (starting at zero). We analyzed average weekly weight gain stratified by pre-pregnancy BMI. Stratified analyses showed that for women starting out pregnancy at normal weight or underweight, pregnancy weight gain did not significantly increase their odds of having a child with a high ADHD symptom score (OR: 1.02; 95% CI: 0.95, 1.10; OR: 0.89; 95% CI: 0.69, 1.14, respectively,) after adjustment for confounders. However, for women with high pre-pregnancy BMI, weight gain further increased their odds of having a child with a high ADHD symptom score (OR: 1.24; 95% CI: 1.07, 1.44). Lean women who experienced weight loss had increased risk for a high ADHD symptom score in their offspring (OR: 1.52; 95% CI: 1.07, 2.15), but that was not the case for overweight women, after adjustment for confounders.

Only 36% of women gained the recommended amount of weight during pregnancy, in relation to their pre-pregnancy BMI, 34% gained below, and 30% gained above the recommendations. Non-adherence to the IOM recommendations was not significantly associated with an ADHD symptom high score in offspring, after adjustment for confounders (below recommendations: OR: 0.96; 95% CI: 0.81, 1.14; above recommendations: OR: 0.98; 95% CI: 0.82, 1.16).

Latent class analysis

We used latent class modeling to obtain distinct patterns of maternal weight and obtained a five-factor solution seen in

Table 2 Means for maternal pre-pregnancy BMI and weekly weight gain during pregnancy by background factor categories

	Pre-pregnancy BMI	*95% CI*	*Weekly weight gain (g)*	*95% CI*
Cohort membership				
Sweden	23.5	23.1–23.9	394	380–408
Denmark	21.9	21.8–22.0	371	368–374
Finland	22.3	22.2–22.4	346	343–349
Maternal age				
<20	21.2	21.0–21.5	365	354–376
20–24	21.8	21.6–21.9	361	357–366
25–30	22.1	22.0–22.2	361	356–364
31–35	22.3	22.2–22.4	356	352–360
>35	23.3	23.2–23.5	338	332–344
Maternal education				
No higher education	22.3	22.2–22.4	356	354–359
At least some higher education	21.5	21.4–21.7	353	354–365
Pregnancy smoking				
Nonsmoker	22.3	22.2–22.3	356	354–359
<10 cigarettes	21.8	21.7–22.0	365	359–370
⩾10 cigarettes per day	22.2	22.0–22.4	352	344–359
Family structure				
Intact	22.2	22.2–22.3	354	352–356
Disrupted	21.8	21.6–22.0	368	361–375

Abbreviations: BMI, body mass index; CI, confidence interval.

Table 3 Mean and standard deviations for pre-pregnancy BMI and weekly weight gain for each latent class

	Latent class				
	1	*2*	*3*	*4*	*5*
	Obese	*Overweight*	*Overweight+large weight gain*	*Lean+large weight gain*	*Normal weight (reference group)*
Pre-pregnancy BMI	36.2 (3.2)	28.2 (1.9)	27.8 (3.5)	20.7 (3.05)	21.2 (2.2)
Weekly weight gain (g)	216.2 (164.7)	279.5 (118.6)	633.7 (89.9)	1021.3 (168.2)	362.1 (108.0)
Total weight gain[a] (kg)	8.4 (6.3)	11.0 (4.7)	25.0 (3.5)	39.9 (7.5)	14.3 (4.3)
% of sample	1.8	9.9	1.6	0.2	86.4
n	223	1330	180	33	12753

Abbreviation: BMI, body mass index. [a]Total weight gain was not used to calculate the latent classes and is listed only for illustrative purposes.

Table 3. This solution showed excellent fit with entropy of 0.92, which indicates that 92% of the participants were correctly classified. The overwhelming majority of women fell within the normal range for BMI and weight gain (latent class no. 5), termed as the reference group in the logistic regression analyses.

We conducted multivariable logistic regression analyses for the risk of a high ADHD symptom score in offspring using the latent classes of maternal weight representing the combined pattern of pre-pregnancy BMI and weight gain. We found significant differences between the reference, latent class 5 and the other classes representing excessive pre-pregnancy BMI as shown in Table 4. After full adjustment for possible confounders, the results showed marked differences according to maternal weight. Latent classification clearly showed that excessive pre-pregnancy BMI seems to be more important than weight gain during gestation for risk of a high ADHD symptom score in the offspring. The confidence intervals of the latent classes containing overweight or obesity overlapped, although the odds ratios increased from overweight (OR: 1.37) to obesity (OR: 1.89), to overweight plus excessive weight gain (OR: 2.10).

Discussion

In three affluent societies, maternal overweight or obesity was associated with a higher risk of having a child with a high ADHD symptom score compared to children of women entering pregnancy at normal weight. Pre-pregnancy overweight/obesity consistently emerged as a significant factor for a high ADHD symptom score in offspring, which remained after adjustment for a variety of possibly confounding factors (smoking during pregnancy, weight gain,

Table 4 Multiple logistic regression analyses testing the association between latent classes (LC) representing maternal weight in pregnancy and high ADHD symptom score in offspring

LC[a]	*Maternal weight in pregnancy*	*High ADHD symptom score*	
		OR	*95% CI*
Adjusted for cohort country			
5	Normal (reference group)	1.00	
1	Obese	1.98	1.26, 3.10
2	Overweight	1.24	0.99, 1.55
3	Overweight+large weight gain	2.18	1.29, 3.69
4	Lean+large weight gain	1.50	0.45, 5.03
Fully adjusted model[b]			
5	Normal (reference group)	1.00	
1	Obese	1.89	1.13, 3.15
2	Overweight	1.37	1.07, 1.75
3	Overweight+large weight gain	2.10	1.19, 3.72
4	Lean+large weight gain	1.52	0.43, 5.32

Abbreviations: ADHD, attention-deficit hyperactivity disorder; BMI, body mass index; CI, confidence interval; LC, latent classes; OR, odds ratio. ADHD symptom high score was defined as a score of 4 out of a possible 6 points. [a]Latent classes representing combinations of pre-pregnancy BMI and weight gain; see Table 3 for details. [b]Maternal smoking during pregnancy, maternal education, maternal age, gestational age, birth weight, infant sex, family structure at follow-up and cohort country.

gestational age, birth weight, infant sex, maternal age, maternal education and family structure at follow-up). Participants came from Sweden, Denmark and Finland that offer standardized, high-quality prenatal care and have the lowest maternal and infant mortality rates worldwide. Because all women receive care via tax-paid governmental-run prenatal clinics, the results were most likely not confounded by socio-economic issues related to access to care.

Strengths and limitations

We did not rely on retrospective data; instead, data were concurrently recorded in the medical charts as reported by mothers or measured at the clinics. Pre-pregnancy weight according to women's self-report to the attending midwife at the time of booking is considered the official pre-pregnancy weight and recorded in the medical chart and in the national birth registers in each country. This measure is superior to traditional paper-and-pencil self-report, because the midwife has the opportunity to correct for obvious inaccuracy (for example, by weighing women at the first prenatal visit and asking follow-up questions such as change in dress size). Thus, it is likely that the attending midwife recorded a pre-pregnancy weight that was within reason for each woman. This is important as women do not as a routine have a preconceptual consultation. People in the Nordic countries are followed carefully by school and educational health care systems which increase their awareness about their body measures.

The large number of obtained symptom reports, well over 12 000, provided a large enough sample size to examine various combinations of maternal weight and weight gain and to control for a number of potentially confounding variables. The pooled analysis was sufficiently powered to detect significant relations and the analyses by cohort showed the same patterns of associations. Ages differed between cohorts suggesting that the results are not just specific to a particular age, but pertain to school-age children.

Poor dietary habits related to overweight in pregnancy (and possibly to social disadvantage) may continue postnatally and the latter may be associated with ADHD symptoms. This explanation seems unlikely in this study because we found that BMI was only very weakly related to indices of social adversity. Moreover, it is uncertain as to what extent diet in childhood is related to ADHD symptoms.[24] It is also possible that differential postnatal upbringing by obese women could be related to increased risk of ADHD. However, we find this unlikely and have no data to indicate that obese women are less likely to care their children. Given that teachers reported child symptoms rather than mothers, any possible confounding related to maternal weight and child perception is by-passed.

Our high-core ADHD symptom score does not equate ADHD diagnosis. We were not able to assess all of the symptoms necessary for diagnosis, but the core symptoms that were available are relevant; we have previously found that scholastic impairment was associated to the core symptoms in all cohorts and roughly to the same degree.[16] Impairment at school is one of the criteria for ADHD diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).[25] We were limited to teacher ratings, which are nonetheless valuable because teachers have broad experience with children and their behavioral ratings reflect age-appropriate evaluations.[26] The school setting is particularly well-suited for observing inattention and hyperactivity symptoms.[27] We have found that the hyperactive symptoms assessed here are equally prevalent across the cohorts, although inattention was lower among Finnish children. All symptoms were much more prevalent among boys than girls, which is in keeping with the known gender disparity for ADHD.[25]

Possible mechanisms

The mechanism underlying the association between excessive maternal pre-pregnancy weight and ADHD symptoms in the offspring is unknown; however, we consider several possibilities that merit further investigation. Overweight and obesity predispose to complications, which may be the contributing factors rather than maternal weight *per se*. Successfully managed pre-eclampsia, however, has not been associated with child behavior problems.[28] We found increased risk among children of lean women who lost weight, which suggests that complications may have had an impact. Our measure of weight gain captured average weight gain across gestation. Thus, we were not able to assess difference in the rate of weight gain. Differences in the rate of weight gain may be related to complications. Whether complications lie on the causal pathway or are the causal

factors needs closer attention. Neither gestational age nor birthweight in the fully adjusted models attenuated the associations meaning that the association between maternal BMI and ADHD symptoms was not mediated by for example, preterm birth or poor intrauterine growth.

There may be common genetic pathways underlying both overweight/obesity and predisposition to poor mental health. Overweight and obesity seem to be more prevalent among persons with mental disorder[29] and children with ADHD symptoms.[30,31] ADHD has been mainly linked to dysfunction in dopaminergic and serotonergic systems in genetic studies[32] and recently some evidence points to dysfunctions in the same systems among overweight and obese women.[33,34] Thus, genetic predisposition could account for both overweight and ADHD symptoms.

Perceived stress is related to caloric intake and ingestion of 'comfort food,' that is, with high fat and carbohydrate content. Indeed, weight gain and obesity are related to chronic stress.[35] It is hypothesized that cortisol secretion in response to maternal-perceived stress affects fetal brain development. Evidence shows that perceived psychological stress by women during pregnancy is linked to ADHD symptoms in their children.[23,36] In this view, stress would be the predisposing factor and BMI would be on the causal pathway leading to ADHD symptoms in the offspring.

Persistent organic pollutants concentrate in the food chain and are stored in the adipose tissue of animals and humans and can disrupt mammalian oocyte maturation and follicle physiology.[37] Excessive pre-pregnancy BMI was associated with lower general intelligence in children of low-income women[38] and also recently in the Finnish cohort.[39] It may be that the adipose tissue of overweight and obese women contains larger amounts of neurotoxins or lacks specific micronutrients that negatively affect fetal brain development. Recently, children who had high serum concentrations of persistent organic pollutants were also found to be more likely to have attention-deficit disorder.[40]

Adipose tissue is not inert,[41] but synthesizes leptin according to fat stores and signals metabolic status to the brain. Both in non-pregnant and pregnant states, increasing BMI is related to increasing levels of leptin[42] and is related to pathology with increased levels seen in pre-eclamptic and diabetic women.[43] Data also point to the involvement of leptin in mood disturbances including stress.[44] It is likely that one of the mechanisms linking maternal overweight and obesity in pregnancy to ADHD symptoms in the offspring involves leptin, due to its involvement in multiple functions. However, much work is needed to decipher the cascading actions of various factors.

Conclusion

Our data add to the research that has hitherto been mainly limited to maternal starvation in relation to poor fetal development leading to later cognitive or neurodevelopmental deficits in the offspring.

We provide evidence for the first time linking maternal adiposity prior to pregnancy and ADHD symptoms in offspring. This study is unique in that we included a large number of participants across three countries, which provided the opportunity to control for number of possible confounders. The increased risk for children associated with excessive maternal pre-pregnancy BMI was substantial, and thus clinically relevant, if causal. Our results indicate that high ADHD symptom score in offspring is not related just to obesity, but rather more general overweight. Thus, the public health impact is potentially great. Evidence is still needed to determine the possible underlying mechanisms or metabolic pathways associated with pre-pregnancy overweight. ADHD symptoms have a major impact on the individual, family and society and because problems can persist into adulthood, identification of modifiable risk factors is of public health concern. Taken together, our results could be explained by either genetics, pregnancy or delivery complications, stress, environmental pollutants stored in maternal adipose tissue, micronutrients or leptin levels. These possible mechanisms need not be viewed as mutually exclusive, but they most likely work at different levels.

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Competing interests

None declared.

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