Hyperemesis gravidarum

Definition, treatment, prognosis and offspring outcome

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7 Hyperemesis gravidarum and long-term consequences for psycho-behavioural development of the offspring - The Northern Finland Birth Cohort 1986 study

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Submitted

Abstract

Hyperemesis gravidarum (HG) leads to dehydration, poor nutritional intake, and weight loss. Currently, very little is known about possible long-term consequences of HG for offspring health. The objective of this study was to assess whether HG is associated with psycho behavioural development of the offspring. This study is part of the Northern Finland Birth Cohort 1986, which comprised pregnant women in the two northernmost provinces of Finland. HG was defined as hospitalisation for HG based on the International Classification of Diseases (ICD) code. Psycho-behavioural development was assessed in offspring at 8 years with Rutter Children's Behavioral questionnaire for teachers (RB2) (HG n = 52, reference n = 8009), and at 16 years with the Strengths and Weakness of ADHD symptoms and Normal behaviour (SWAN) questionnaire for parents (HG n = 39, reference n = 6549) and with the Youth Self-report (YSR) questionnaire (HG n = 45, reference n = 6874). We found no differences in offspring RB2, SWAN and YSR questionnaire scores between offspring born to mothers with and without HG. Adjustments for sex, maternal age, education and relationship status did not alter these results (adjusted odds ratio total RB2 score ≥9: 1.44 95%CI 0.7 to 1.7; adjusted difference total SWAN score: -0.10 95%CI -0.25 to 0.05; adjusted difference total YSR score: -1.16 95%CI -5.35 to 3.03). In conclusion, we found no evidence that HG has major negative consequences for the psycho-behavioural development of the offspring. However, further research with larger number of women with HG will be required to investigate potentially more subtle effects of severe HG on offspring's psycho-behavioural development.

Introduction

Nausea and vomiting in pregnancy is common and often self-limiting.[1] When nausea and vomiting is severe or protracted it can lead to dehydration, electrolyte disturbances and significant weight loss necessitating hospital admission.[2, 3] This condition is often referred to as hyperemesis gravidarum (HG) and affects 0.2-3.6% of pregnancies.[4-7] HG has a detrimental effect on maternal well-being and quality of life and poses a severe psychosocial burden.[8-11]

There is increasing evidence from epidemiological studies suggesting that a suboptimal intrauterine environment negatively affects foetal development with lasting consequences for later growth, neurodevelopment and health.[12-15] Organs and tissues are most sensitive to environmental insults during critical periods of rapid development. Since HG occurs in early pregnancy[1], a critical period for foetal brain development[16], it might affect foetal neurodevelopment with lasting consequences for development and behavior. There are two pathways by which this may occur. First, maternal undernutrition due to HG might affect fetal brain development.[17,18] Second, increased maternal stress or increased maternal depression associated with HG may lead to excessive glucocorticoid release[19] causing dysfunction of the fetal hypothalamic-pituitary-adrenocortical (HPA) axis, which can also disrupt the normal development of the brain.[20] Both maternal undernutrition and stress/depression during pregnancy have been shown to be associated with increased risk of mental health problems in (adult) offspring.[21-24]

Studies investigating the consequences of HG on the psycho-behavioural development of the offspring are limited.[25, 26] There are indications that prenatal exposure to HG is associated with neurodevelopmental delay and an increased risk of psychological and behavioural disorders in the offspring.[25,26] Also, nausea and vomiting in pregnancy beyond the first trimester was associated with lower task persistence and more attention and learning problems in the offspring.[27] However, none of the studies on HG used validated screening instruments to assess offspring mental health.[25,26] Furthermore, the design of the studies made them prone to selection bias, as participants were recruited online. So far, large studies with prospective data collection and objectively measured outcomes on multiple time points to study whether HG is associated with the psycho-behavioural development of the offspring have not been performed. Hence, it remains unclear whether HG influences offspring psycho-behavioural development.

The limited findings so far prompted us to further investigate the consequences of HG on the psycho-behavioural development of the offspring. The Northern Finland Birth Cohort 1986 (NFBC1986) is a large, prospective population-based cohort with information about HG

during pregnancy and long-term follow-up of offspring. This provided a unique opportunity to evaluate whether HG affects the psycho-behavioural development in 7-8 and 16 year old offspring.

Methods

Study population

The NFBC1986 recruited women in the provinces of Oulu and Lapland. Women with an expected date of delivery between July 1, 1985 and June 30, 1986 where eligible.[28] In total, 9362 mothers were included and 9479 babies were born. Pregnant women were recruited at maternity health centres at their first antenatal visit, on average 12th gestational week, and the data was gathered prospectively onwards. Women provided information via structured self-report questionnaires, while data on antenatal visits, hospital admissions and birth outcomes were obtained from maternity health centres and hospital medical records.29 The cohort was followed-up in 1992-1994 at offspring age 7-8 and in 2002 at offspring age 16. Follow-up focused on offspring health and wellbeing. All participating adolescents and their parents gave informed consent to use their data for scientific research. We included singleton pregnancies only.

Definition of HG

HG was defined as hospitalisation during pregnancy for HG according to the 1968-1986 International Classification of Diseases-8 (ICD-8) (code: 638),[30] which was extracted from the mothers' hospital medical records. Vikanes *et al*.[31] demonstrated that ICD codes in the birth register of Norway, can be considered valid for the diagnoses of mild HG in registry-based research. The reference group consisted of all women who were not hospitalised for HG during pregnancy.

Outcome measures and covariates

Maternal and offspring characteristics

Information on parity, relationship status, highest maternal education attainment and self-reported maternal pre-pregnancy height (cm) and weight (kg) was obtained through questionnaires. Information on maternal age (years) and offspring sex was obtained from medical records.

During the follow-up in 1992-1994 at offspring age 7-8 the Rutter Children's Behavioral Questionnaire (RB2) score was filled out by teachers. During the follow-up in 2002, at offspring age 16, parents filled out the Strengths and Weakness of ADHD symptoms and Normal behaviour questionnaire (SWAN) questionnaire and offspring filled out the Youth Self-Report questionnaire (YSR).

Offspring Follow-up

RB2 questionnaire

The RB2 score is a widely used questionnaire for teachers to assess emotional and behavioural wellbeing of 8-year-old children. The questionnaire was developed to discriminate between potentially healthy and potentially disturbed children and is validated amongst Finnish school children.[32,33] The questionnaire consists of 26 brief items concerning the child's behaviour, problems and habits within the past 12 months (for example: 'bullies' and 'poor concentration'). Each item can be scored as 0 (does not apply), 1 (applies somewhat) and 2 (certainly applies), yielding a score between 0 and 52. A total cutoff score of ≥9 has been shown to indicate probable psychiatric disturbance in general.[32,33] The RB2 generates three subscales: emotional, anti-social and inattention-hyperactivity.[34]

SWAN questionnaire

The SWAN questionnaire was developed to evaluate symptoms and signs of ADHD and consists of 18 items based on the ADHD symptoms described in the DSM-IV.[3536] The symptoms are translated into statement on how well the child behaves compared to other children (for example: 'how well does this child listen when spoken to directly'). Each item is rated on a 7 point rating scale with the average behaviour scored as 0 (far below average = 3, below average = 2, somewhat below average = 1, somewhat above average = -1, above average = -2 and far above average = -3). The questionnaire is expected to produce a normal distribution of behavioural scores.[35] There are 9 items in the attention subscale and 9 items in the hyperactivity subscale, all items together indicate ADHD combined subtypes.[36]

YSR questionnaire

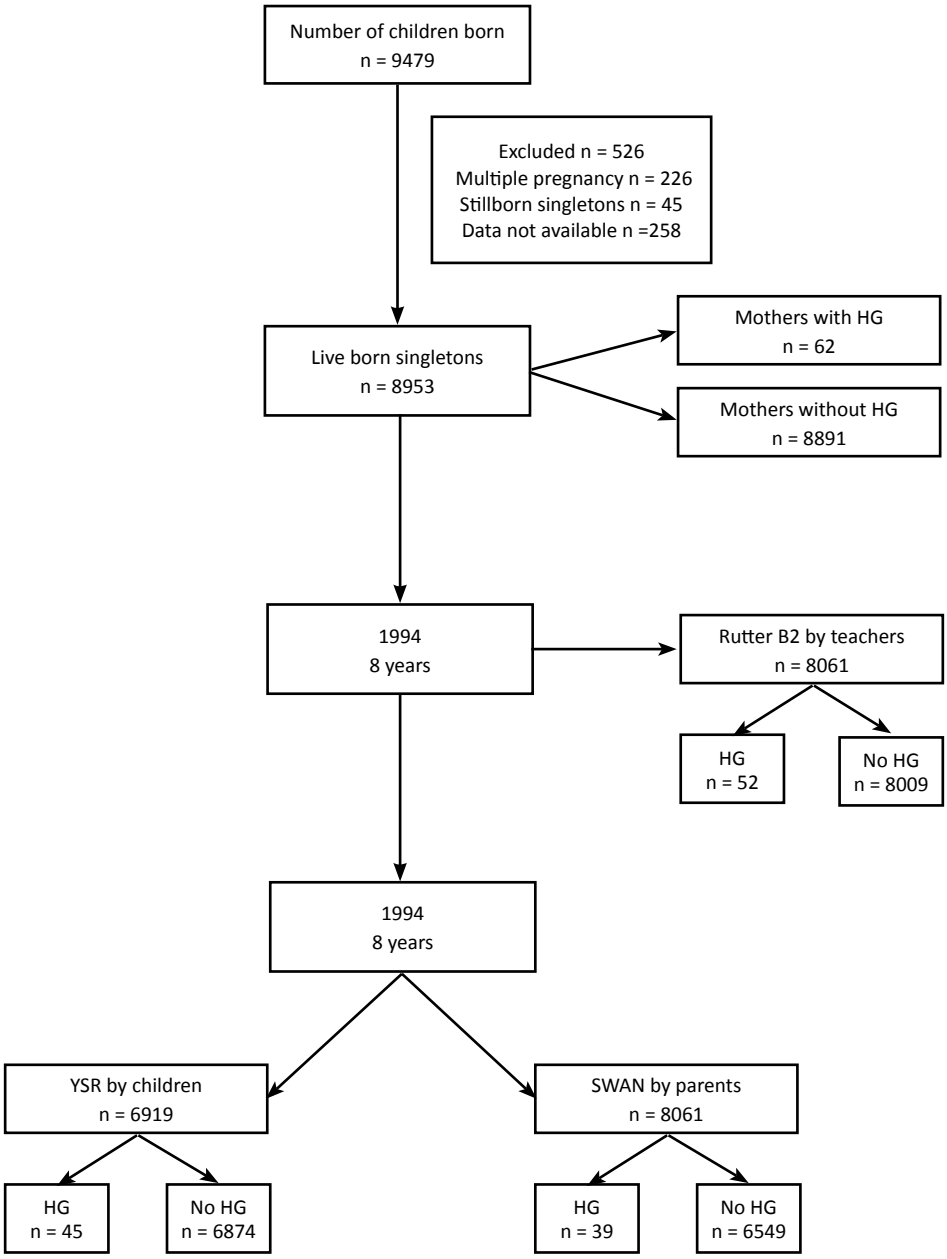
The YSR is a widely used and validated questionnaire derived from the Child Behaviour Check List (CBCL) and was designed to evaluate competencies and problems of 11- to 18-year-olds.[37,38] The questionnaire includes 112 items. Adolescents self-report the applicability of every item on a 3-point scale: 0 (not true), 1 (somewhat true), 2 (very often true) (for example: 'I get in many fights' and 'I worry a lot'). The YSR is not a diagnostic tool, but it is often used to evaluate psychopathology of adolescent in epidemiological research.[39] Eight DSM-IV orientated syndrome subscale can be calculated: withdrawn, somatic complains, anxiety/depression, thought problems, social problems, delinquent behavior and aggressive behaviour.[38] Furthermore, domains for internalising and externalising problems can be calculated. The internalizing problem subscale comprises the withdrawn, somatic complains and anxiety/depression subscales whereas the externalizing domains comprises the delinquent behavior and aggressive behaviour subscales.[38]

Data analysis

We present normally distributed continuous variables as means with SDs and skewed distributions as medians with interquartile ranges (IQRs). We tested data with a normal distribution with the student's *t* test for means and data with a non-normal distribution with the Mann-Whitney *U* test for medians. We present dichotomous and categorical variables as number with percentages. These variables were analysed using the χ2-test or Fisher's exact test for proportions, where appropriate. The SWAN and YSR questionnaires were analysed using multivariate linear regression, reported in differences (*β*) and 95% confidence intervals (CI). The RB2 questionnaire had a non-normal distribution, even after logarithmic transformation, and, also the residuals followed a non-normal distribution. Therefore, the RB2 was analysed using logistic regression, reported in odds ratios (OR) and 95%CI, with a cut-off score ≥9 (indication for probable psychiatric disturbance). We adjusted for sex (model 1), followed by adjustments for low maternal age (<20 years), low maternal education (≤11years) and single relationship status of the mother and in model 2. The first model was chosen to approximate an unadjusted model. The second model was chosen to adjust for possible confounders. We considered low maternal age <20 years, low maternal education (<11 years) and single relationship status as potential confounders because they have been associated with offspring inattention and hyperactivity symptoms within the NFBC cohort.[40] Moreover, it is known that women with HG are younger and have lower education compared to women without HG.[41,42] In order to assess whether there was selective loss to follow-up we compared maternal characteristics of responders and non-responders of the SWAN questionnaire . Lastly, we assessed whether the standard expected differences in the RB2, SWAN and YSR scores between boys and girls were present in this study using student's *t* test, Mann-Whitney *U* test or Chi-square test.

Missing values of baseline characteristics and possible confounders were estimated by multiple imputation. In total, 2.2% of the variables of interest were missing; 13.4% for maternal education and less than 4% for remaining variables. Missing values were imputed using the fully conditional specification (FCS) method to create 5 imputed datasets. Little's MCAR test was significant (p<0.001) indicating that values were not missing completely at random (MCAR) and the imputation was carried out under the missing at random (MAR) assumption that missing data is related to other observed variables.[43] Outcome measures were not imputed. There were no significant differences in distributions of variables and outcomes between original data and pooled imputed data (Supplemental table S1). All analyses were performed using IBM SPSS (ver. 22.0) for Windows.

Figure 1 Flow diagram NFBC 1986 study



Results

Maternal and offspring characteristics

8953 mothers and offspring were included in the study. Of these, 62 women had been admitted to hospital for HG (0.7%). Baseline characteristics are described in Table 1. Mothers who had been admitted for HG were slightly younger and more often nulliparous (50% versus 33%), and gained significantly less weight during early pregnancy than those who had not been admitted to hospital for HG. The percentage of maternal age <20, low maternal education (<11 years) and single relationship status did not differ between the two groups. There were no differences in birth outcomes and neonatal characteristics associated with hospital admission for HG.

Table 1 Maternal characteristics and pregnancy outcomes of women hospitalised for HG and the control group (imputed data)

	Control	**HG**	***P*-value**
n	8891	62	
Maternal characteristics			
Age (years) (mean, SD)	27.8 ± 5.5	26.5 ± 5.7	0.06
Low maternal education (<11 years) (%)	26.3	24.2	0.80
Age <20 years (%)	7.7	8.1	0.51
Single status (%)	4.2	3.2	0.51
Nulliparous (%)	34.0	50.0	0.01
Prepregnancy BMI (kg/m^2) [median (IQR)]	21.6 (20.1-23.8)	21.0 (19.3-23.4)	0.14
Gestational age at inclusion (years) (mean, SD)	10.3 ± 3.7	10.9 ± 3.2	0.28
Weight gain early pregnancy (kg) (mean, SD)	2.1 ± 2.3	0.2 ± 2.9	<0.001
Pregnancy outcomes and neonatal characteristics			
Female (%)	48.4	53.2	0.44
Preterm birth <37weeks (%)	4.9	1.6	0.23
Birth weight (gram, mean ± SD)	3552 ± 558	3552 ± 507	0.99
Apgar score <7 at 5minutes (%)	1.3	1.6	0.86

Abbreviations; BMI: body mass index

Does HG affect psycho-behavioural development in offspring?

The RB2 questionnaire was available for 8061 offspring of whom 52 born to mothers with hospital admission for HG. The SWAN and the YSR questionnaires were available for 6588 and 6919 offspring of whom respectively 39 and 45 offspring born to mothers with hospital admission for HG (Figure 1). Table 2 shows that for all outcome measures, including the subscales of the questionnaires, unadjusted analyses showed similar results for offspring born to mothers with and without HG. Adjustments for sex (model 1) and maternal age <20 years, low maternal education and maternal single relationship status (model 2) did not alter the results (Table 3).

Table 2 Neurobehavioural characteristics according to HG in pregnancy using the RB2 scale at age 8 and the SWAN and YSR at age 16 (imputed data)

	No HG	**HG**	***P*-value**
8-y-olds RB2 score (teacher report)			
n	8009	52	
Total RB2 score [median (IQR)]	2 (0-5)	2 (0-7)	0.99
Probable psychiatric disturbance (RB2 ≥ 9) n (%)	1123 (14)	8 (15)	0.78
- Emotional subscale [median (IQR)]	0 (0-1)	0 (0-2)	0.30
- Anti-social subscale [median (IQR)]	0 (0-1)	0 (0-1)	0.79
-Inattention-hyperactivity score [median (IQR)]	3 (3-5)	3 (3-5)	0.69
16-y-olds SWAN score (parent report)			
n	6549	39	
Total SWAN score (mean, sd)	-1.1 ± 0.9	-1.2 ± 1.0	0.63
- Inattention subscale (mean, sd)	-0.8 ± 1.0	-0.9 ± 1.0	0.95
- Hyperactivity subscale (mean, sd)	-1.3 ± 1.0	-1.4 ± 1.0	0.43
16-y-olds YSR score (self-report)			
n	6874	45	
Total YSR score	27.3 ± 16.2	25.7 ± 16.8	0.51
YSR internalizing subscale	9.6 ± 7.7	9.2 ± 7.6	0.72
YSR externalizing subscale	10.2 ± 6.5	9.2 ± 7.2	0.34
- Withdrawn subscale (mean, sd)	2.50 ± 2.1	2.51 ± 2.0	0.98
- Somatic complains subscale [median (IQR)]	3 (1-5)	2 (1-4)	0.51
- Anxiety/depression subscale [median (IQR)]	3 (1-6)	2 (1-7)	0.67
- Thought problems subscale [median (IQR)]	1 (0-2)	1 (0-2)	0.42
- Social problems subscale [median (IQR)]	1 (0-3)	1 (1-2)	0.73
- Delinquent behavior subscale (mean, sd)	3.20 ± 2.5	3.09 ± 2.8	0.76
- Aggressive behaviour subscale (mean, sd)	6.96 ± 4.6	6.16 ± 4.9	0.25
- Attention problems subscale (mean, sd)	4.36 ± 2.6	4.20 ± 2.8	0.68

RB2, Rutter Children's Behavioral Questionnaire for teachers; SWAN, Strengths and Weakness of ADHD symptoms and Normal behavior questionnaire; YSR, Youth Self-Report.

Table 3 Logistic and linear regression for HG, RB2 at age 8 and SWAN and YSR at age 16 (imputed data)

	Model 1		Model 2	
	B/OR	95%CI	B/OR	95%CI
8-y-olds RB2 score				
Total RB2 score ≥ 9	1.44	0.9, 3.55	1.13	0.53, 3.2
16-y-olds SWAN score				
Inattention score	-0.03	-0.22, 0.16	-0.04	-0.20, 0.11
Hyperactivity score	-0.15	-0.31, 0.02	-0.15	-0.32, 0.01
Combined ADHD score	-0.09	-0.38, 0.20	-0.10	-0.25, 0.05
16-y-olds YSR score				
Withdrawn	0.05	-0.55, 0.65	0.05	-0.57, 0.67
Somatic complains	-0.07	-0.18, 0.63	-0.07	-0.77, 0.63
Anxiety/depression	-0.12	-1.31, 1.10	-0.12	-1.31, 1.10
Thought problems	0.16	-0.11, 0.43	0.16	-0.37, 0.69
Social problems	-0.21	-0.72, 0.30	-0.22	-0.72, 0.29
Delinquent behavior	-0.09	-0.81, 0.63	-0.11	-0.82, 0.61
Aggressive behaviour	-0.73	-2.10, 0.60	-0.75	-2.08, 0.59
Attention problems	-0.10	-0.84, 0.65	-0.11	-0.85, 0.64

Abbreviations: RB2: Rutter Children's Behavioral Questionnaire for teachers; SWAN: Strengths and Weakness of ADHD symptoms and Normal behavior questionnaire; YSR: Youth Self-Report. Model 1, adjusted for sex; model 2, adjused for sex, low maternal education, single status mother and maternal age <20.

Maternal characteristics of responder of SWAN questionnaire

There was attrition at follow-up, with the SWAN questionnaire containing the largest percentage of missing data. Therefore, we compared maternal characteristic of responders and non-responders of the SWAN questionnaire. According to parental questionnaire, mothers who did not fill out the SWAN questionnaire where significantly younger and had significantly more often a single relationship status at inclusion than mothers who filled out the SWAN questionnaire (age: 26.9 ± 5.5 versus 28.0 ± 5.5; p<0.001 and single relationship status: 6.3% versus 3.5%; p<0.0001) (Supplemental Table S2).

Difference between boys and girls

For the RB2 and the SWAN questionnaires boys had a significant overall higher score than girls (total RB2 3 (1-7) versus 1 (0-4); p<0.001) (total SWAN -1.0 ± 0.9 versus -1.2 ± 0.9; p<0.001) and for the YSR girls had a significant overall higher score than boys (total YSR 22.2 ± 1.4 versus 32.0 ± 16.9; p<0.001).

Discussion

Main findings

In this large prospective birth cohort study, we were unable to detect any effects of prenatal exposure to HG on offspring psycho-behavioural development. Our findings suggest that major effects of HG on offspring's psycho-behavioural development are unlikely. However, subtle effects, which have also been found in other studies, cannot be excluded.[25,26]

Strength and limitations

This study was part of a large population based cohort with prospective data collection. At the time of participant selection, all pregnant women in Finland received free antenatal care, making sampling bias unlikely. Psycho-behavioural development was assessed twice over a period of 16 years, using validated screening instruments. The significant differences between boys and girls in all three questionnaires are in line with existing literature,[44-46] suggesting that the data collection is valid. A limitation in our study is the lack of validated information about maternal psychological stress during pregnancy and detailed information on parental mental health at follow-up (offspring age 8 and 16 years). It is well known that offspring of parents with psychological health problems have a higher risk of developing psychological health disorders themselves including depression,[47] autism[48] and behaviour disorders.[49] Another limitation is the statistical power. Due to the small number of HG patients and limited follow-up our study had limited statistical power to detect more subtle effects on psycho-behaviour development. A last important limitation is the difference in percentage of missing data between the HG and the reference group. At offspring age 8, the RB2 questionnaire was missing in 16% (10/62) of the HG group and 10% (880/8889) of the reference group. At offspring age 16, the SWAN questionnaire and the YSR questionnaire were missing in 37% (23/62) and 27% (17/62) of the HG group and in 26% (2340/8889) and 23% (201/8889) of the reference group, respectively. We found that SWAN questionnaire was more frequently missing when the mother was younger or single. This conforms the presence of selective lost to follow-up, which may lead to selection bias. Based on previous literature, showing an association between low maternal age and single relationship status and offspring inattention and hyperactivity symptoms[40], this would possibly cause and underestimation of the studied effects. However, adjustments have been made for these confounders.

Interpretation

Our findings differ from those of Fejzo *et al*.[25] and Mullin *et al*.[26] who found an increased risk of psychological and behavioural disorders in offspring of women with HG. Both studies included a larger number of participants than the current study (Fejzo *et al*. n = 312 and

Mullin *et al*. n = 87). However, these studies used retrospective designs, recruited women online and did not use validated screening instruments hence these studies are prone to recall and selection bias.

Multiple studies have suggested an association between severe forms of HG and negative offspring outcomes.[2,50-54] Severe HG is often defined as HG with substantial weight loss, electrolyte disturbances or persistence of symptoms in the second trimester. Since, in our study, the diagnosis of HG was solely based on hospital admission and the ICD code, no further information on disease severity such as metabolic disturbances, duration of symptoms and impact on maternal wellbeing was available. The only factor possibly related to disease severity available was maternal weight gain in early pregnancy. Although we found that women admitted to the hospital for HG gained significantly less weight in early pregnancy, overall the difference in weight gain between women with and without HG was only 2 kg. This suggests that maternal undernutrition may have been mild and therefore, it is likely that we studied a group of women who on average had relatively mild HG. We therefore could not assess effects of severe HG on psycho-behavioural development in offspring.

Conclusion

Based on our findings it is unlikely that mild HG causes major psycho-behavioural developmental problems for the offspring in childhood or adolescence. However, further research including a larger number of women with HG and more information on disease severity, maternal wellbeing during pregnancy and parental psychological health will be required to investigate potentially more subtle effects of (severe) HG on offspring's psycho-behavioural development.

Acknowledgement

We thank professor Anna-Liisa Hartikainen (launch of NFBC1986), the participants in the study and the NFBC project centre.

Table S1 Baseline characteristics of mothers and offspring in original and imputed data

	Missing (%)	Original data	Imputed data
Maternal and child characteristics			
HG	0.0	62	62
Age (years, mean)	0.0	27.8 ± 5.5	27.8±5.5
prepregnancy BMI (kg/m^2) [median (IQR)]	1.0	21.6 (20.0-23.8)	21.6 (20.0-23.8)
Nulliparous (%)	2.2	34.1	34.1
Weight gain early pregnancy (median (IQR))	2.7	2.0 (1.0-3.0)	2.0 (1.0-3.0)
Weight loss >5% during early pregnancy (%)	3.4	0.70	0.74
Low maternal education (<11 years) (%)	13.4	26.3	26.3
Single relationship status mother (%)	0.0	4.2	4.2
8-y-olds Rutter B2 score (teacher report)			
n			
Total Rutter score [median (IQR)]	0.0	0 (0-5)	0 (0-5)
- Neurotic subscale [median (IQR)]	0.0	0 (0-1)	0 (0-1)
- Anti-social subscale [median (IQR)]	0.0	0 (0-1)	0 (0-1)
-Inattention-hyperactivity score [median (IQR)]	0.0	3 (3-5)	3 (3-5)
16-y-olds SWAN (parent report)			
n			
Total SWAN score (mean, sd)	0.0	-1.1 ± 0.9	-1.1 ± 0.9
- Inattention subscale (mean, sd)	0.0	-0.9 ± 1.0	-0.9 ± 1.0
- Hyperactivity subscale (mean, sd)	0.0	-1.4 ± 1.0	-1.4 ± 1.0
16-y-olds YSR (self-report)			
n			
Total YSR score	0.0	27.2 ± 16.2	27.2 ± 16.2
- Withdrawn subscale (mean, sd)	0.0	2.5 ± 2.2	2.5 ± 2.2
- Somatic complains subscale [median (IQR)]	0.0	3 (1-5)	3 (1-5)
- Anxiety/depression subscale [median (IQR)]	0.0	3 (1-6)	3 (1-6)
- Thought problems subscale [median (IQR)]	0.0	1 (0-2)	1 (0-2)
- Social problems subscale [median (IQR)]	0.0	1 (0-3)	1 (0-3)
- Delinquent behavior subscale (mean, sd)	0.0	3.2 ± 4.2	3.2 ± 4.2
- Aggressive behaviour subscale (mean, sd)	0.0	7.0 ± 4.6	7.0 ± 4.6
- Attention problems subscale (mean, sd)	0.0	4.4 ± 2.6	4.4 ± 2.6

Abbreviations: RB2: Rutter Children's Behavioral Questionnaire for teachers; SWAN: Strengths and Weakness of ADHD symptoms and Normal behavior questionnaire; YSR: Youth Self-Report.

Table S2 Maternal characteristics of women/parents who filled out the SWAN questionnaire and who did not fill out the SWAN questionnaire

	SWAN performed	**No SWAN performed**	***P*-value**
n	6588	2365	
Maternal characteristics			
Age (years) (mean, SD)	28.0 ± 5.5	26.9 ± 5.5	<0.001
Low maternal education (<11 years) (%)	25.7	26.5	0.11
Age <20 years (%)	6.7	10.5	<0.001
Single status (%)	3.5	6.3	<0.001
Nulliparous (%)	35.5	33.6	0.09
Prepregnancy BMI (kg/m^2) [median (IQR)]	21.6 (20.1 - 23.8)	21.7 (20.0 - 24.0)	0.35
Gestational age at inclusion (years) (mean, SD)	10.8 ± 3.5	11.0 ± 3.7	0.32
Weight gain early pregnancy (kg) (mean, SD)	2.2 ± 2.5	2.0 ± 2.2	0.06

Abbreviations: BMI: body mass index, SWAN: Strengths and Weakness of ADHD symptoms and Normal behaviour

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