
Supplementary Material

Severe nausea and vomiting in pregnancy: psychiatric and cognitive problems, and brain structure in children

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Table S1. The difference in cognitive and psychiatric measurements between the exposure to SNVP during pregnancy and control groups.

NIH Toolbox Cognition Battery											
Cognitive measurement*	Controls	SNVP	t value	Cohen's d	p value	Cognitive measurement	Controls	SNVP	t value	Cohen's d	p value
nihtbx_picvocab	85.0±8.07	82.1±7.91	-4.37	-0.085	1.3×10 ⁻⁵	nihtbx_picture	103.3±12.1	101.3±12.0	-1.74	-0.034	0.081
nihtbx_flanker	94.3±8.86	92.9±9.80	-1.44	-0.028	0.151	nihtbx_reading	91.3±6.80	89.1±6.93	-4.59	-0.090	4.4×10 ⁻⁶
nihtbx_list	97.4±11.8	94.1±12.6	-3.30	-0.064	9.5×10 ⁻⁴	nihtbx_fluidcomp	92.2±10.4	89.5±10.9	-2.54	-0.050	0.011
nihtbx_cardsort	92.9±9.36	91.2±9.63	-1.81	-0.035	0.071	nihtbx_cryst	86.9±6.98	84.1±6.88	-5.39	-0.105	7.2×10 ⁻⁸
nihtbx_pattern	88.4±14.5	87.1±15.0	-0.75	-0.015	0.455	nihtbx_totalcomp	86.9±8.94	83.7±9.12	-4.34	-0.085	1.4×10 ⁻⁵
Parent Child Behavior Checklist Raw Scores Aseba											
Psychiatric measurement**	Controls	SNVP	t value	Cohen's d	p value	Psychiatric measurement	Controls	SNVP	t value	Cohen's d	p value
cbcl_scr_syn_anxdep	2.42±3.00	3.07±3.31	7.30	0.141	3.0×10 ⁻¹³	cbcl_scr_dsm5_depress	1.18±1.91	1.65±2.41	6.96	0.135	3.6×10 ⁻¹²
cbcl_scr_syn_withdep	0.96±1.62	1.37±2.06	6.26	0.121	3.9×10 ⁻¹⁰	cbcl_scr_dsm5_anxdisord	1.95±2.36	2.63±2.69	9.09	0.176	1.1×10 ⁻¹⁹
cbcl_scr_syn_somatic	1.43±1.88	1.88±2.24	7.06	0.137	1.8×10 ⁻¹²	cbcl_scr_dsm5_somaticpr	1.05±1.47	1.34±1.68	5.87	0.114	4.4×10 ⁻⁹
cbcl_scr_syn_social	1.47±2.15	2.24±2.63	8.74	0.169	2.8×10 ⁻¹⁸	cbcl_scr_dsm5_adhd	2.45±2.86	3.10±3.21	6.20	0.120	6.0×10 ⁻¹⁰
cbcl_scr_syn_thought	1.53±2.10	1.98±2.50	6.69	0.129	2.3×10 ⁻¹¹	cbcl_scr_dsm5_opposit	1.67±1.97	2.12±2.20	6.44	0.125	1.2×10 ⁻¹⁰
cbcl_scr_syn_attention	2.77±3.34	3.55±3.85	6.54	0.127	6.4×10 ⁻¹⁴	cbcl_scr_dsm5_conduct	1.15±2.17	1.69±2.79	5.10	0.099	3.5×10 ⁻⁷
cbcl_scr_syn_rulebreak	1.08±1.72	1.53±2.18	5.34	0.103	9.5×10 ⁻⁸	cbcl_scr_07_sct	0.48±0.94	0.68±1.22	5.85	0.113	5.0×10 ⁻⁹
cbcl_scr_syn_aggressive	3.03±4.10	4.12±4.96	6.87	0.133	6.8×10 ⁻¹²	cbcl_scr_07_ocd	1.29±1.77	1.61±2.03	6.37	0.123	1.9×10 ⁻¹⁵
cbcl_scr_syn_internal	4.81±5.33	6.32±6.32	8.37	0.162	6.2×10 ⁻¹⁷	cbcl_scr_07_stress	2.71±3.19	3.71±3.83	8.70	0.168	3.9×10 ⁻¹⁸
cbcl_scr_syn_external	4.11±5.48	5.65±6.75	6.78	0.131	1.2×10 ⁻¹¹	cbcl_scr_syn_totalprob	17.02±16.9	22.74±20.8	8.89	0.172	6.9×10 ⁻¹⁹

Note: *A high cognitive score means better performance, and a high psychiatric score means a worse mental state. All cognitive measures were lower in the group with the exposure to SNVP.

**All psychiatric measures were higher in the group with the exposure to SNVP, indicating that the children with exposure to SNVP tend to have psychiatric problems.

nihtbx_picvocab: NIH Toolbox Picture Vocabulary Test Age 3+ v2.0 Uncorrected Standard Score; **nihtbx_flanker:** NIH Toolbox Flanker Inhibitory Control and Attention Test Ages 8-11 v2.0 Uncorrected Standard Score; **nihtbx_list:** NIH Toolbox List Sorting Working Memory Test Age 7+ v2.0 Uncorrected Standard Score; **nihtbx_cardsort:** NIH Toolbox Dimensional Change Card Sort Test Ages 8-11 v2.0 Uncorrected Standard Score; **nihtbx_pattern:** NIH Toolbox Pattern Comparison Processing Speed Test Age 7+ v2.0 Uncorrected Standard Score; **nihtbx_picture:** NIH Toolbox Picture Sequence Memory Test Age 8+ Form A v2.0 Uncorrected Standard Score; **nihtbx_reading:** NIH Toolbox Oral Reading Recognition Test Age 3+ v2.0 Uncorrected Standard Score; **nihtbx_fluidcomp:** Cognition Fluid Composite Uncorrected Standard Score; **nihtbx_cryst:** Crystallized Composite Uncorrected Standard Score; **nihtbx_totalcomp:** Cognition Total Composite Score Uncorrected Standard Score; **cbcl_scr_syn_anxdep:** Anxious/Depressed CBCL Syndrome Scale; **cbcl_scr_syn_withdep:** Withdrawn/Depressed CBCL Syndrome Scale; **cbcl_scr_syn_somatic:** Somatic Complaints CBCL Syndrome Scale; **cbcl_scr_syn_social:** Social Problems CBCL Syndrome Scale; **cbcl_scr_syn_attention:** Attention Problems CBCL Syndrome Scale; **cbcl_scr_syn_rulebreak:** Rule-Breaking Behavior CBCL Syndrome Scale; **cbcl_scr_syn_aggressive:** Aggressive Behavior CBCL Syndrome Scale; **cbcl_scr_syn_internal:** Internalizing Problems CBCL Syndrome Scale; **cbcl_scr_syn_external:** Externalizing Problems CBCL Syndrome Scale; **cbcl_scr_dsm5_depress:** Depressive Problems CBCL DSM5 Scale; **cbcl_scr_dsm5_anxdisord:** Anxiety Problems CBCL DSM5 Scale; **cbcl_scr_dsm5_somaticpr:** Somatic Problems CBCL DSM5 Scale; **cbcl_scr_dsm5_adhd:** ADHD CBCL DSM5 Scale; **cbcl_scr_dsm5_opposit:** Oppositional Defiant Problems CBCL DSM5 Scale; **cbcl_scr_dsm5_conduct:** Conduct Problems CBCL DSM5 Scale; **cbcl_scr_07_sct:** Sluggish Cognitive Tempo (SCT) CBCL Scale2007 Scale; **cbcl_scr_07_ocd:** Obsessive-Compulsive Problems (OCD) CBCL Scale2007 Scale; **cbcl_scr_07_stress:** Stress Problems CBCL Scale2007 Scale.

Table S2 Detailed description of participants and measurements in the ABCD study

Participants	
	<p>The dataset used for this investigation was from the Annual Curated Data Release 2.0 from the ABCD consortium (https://abcdstudy.org/). A sample of 10,713 participants aged 9 to 11 years was included from the ABCD study, which is a large national-based longitudinal study that recruited children across 21 research sites across the US. At each ABCD data collection site, participants were predominantly recruited through local elementary and charter schools. ABCD employed a probability sampling strategy to identify schools within the 21 catchment areas as the primary method for contacting and recruiting eligible children and their parents. The ABCD investigators obtained written and oral informed consent from parents and children, respectively. The participants in the ABCD study closely match the US population of 9 to 11 years old children on several key demographic variables, including gender, race/ethnicity, household income, and parental education and marital status. More details of the subjects, and the collection and preprocessing parameters of the data are provided at the ABCD website (https://abcdstudy.org/scientists/protocols/) and also are described elsewhere.</p>
Cognition measures	
	<p>Cognitive abilities were assessed by the ABCD <i>Youth NIH TB Summary Scores</i> (abcd_tbss01) which consists of 10 validated and reliable psychometric test scores: Picture Vocabulary Test Score (nihtbx_picvocab); Flanker Inhibitory Control and Attention Test Score (nihtbx_flanker); List Sorting Working Memory Score (nihtbx_list); Dimensional Change Card Sort Test Score (nihtbx_cardsort); Pattern Comparison Processing Speed Test Score (nihtbx_pattern); Picture Sequence Memory Test Score (nihtbx_picture); Oral Reading Recognition Test Score (nihtbx_reading); Cognition Fluid Composite Score (nihtbx_fluidcomp); Crystallized Composite Score (nihtbx_cryst); Cognition Total Composite Score (nihtbx_totalcomp). A high score means better cognitive ability.</p>
Emotional and psychiatric problems	
	<p>The Parent Child Behavior Checklist Scores (abcd_cbcls01) were used to assess the dimensional psychopathology and adaptive functioning in children. CBCL has high test-retest stability and good internal consistency, and comprises of 113 items that measure broad scopes of child behavior across the past six months. Each item was rated using a three-point rating scale (not true, somewhat or sometimes true, very often or always true). It contains eight empirically-based syndrome scales related to psychiatric problems: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, aggressive behavior. Internalizing and externalizing scores were derived from the following syndrome scores: anxious/depressed, withdrawn/depressed, somatic complaints, rule-breaking behavior and aggressive behavior. The total score of psychiatric problems is calculated by sum these sub-scores. The DSM-oriented scales have been introduced in the revision of CBCL after 2001. The DSM-oriented scales, including depressive</p>

	<p>problems (Depressive Problems CBCL DSM5 Scale), anxiety problems (Anxiety Problems CBCL DSM5 Scale), somatic problems (Somatic Problems CBCL DSM5 Scale), ADHD problems (ADHD CBCL DSM5 Scale), oppositional defiant problems (Oppositional Defiant Problems CBCL DSM5 Scale) and conduct problems (Conduct Problems CBCL DSM5 Scale), are based on the original CBCL item pool by expert ratings of similarity to DSM-IV criteria and have also been demonstrated to show good psychometric properties. In 2007, the CBCL officially identified 3 separate constructs including sluggish cognitive tempo (SCT), obsessive-compulsive problems (OCD) and stress, which has been used in previous studies. Therefore, there are 20 scores in the Parent Child Behavior Checklist Scores.</p>
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Table S3. Detailed description of registers used in the study

Data source	Information
National Patient Register	Provides information for all citizens on diagnoses and operations performed at a hospital since 1977. Each hospital discharge is recorded and classified according to the ICD-8 codes (1977-1993) and ICD-10 (1994 onwards)
National Prescription Register	Holds unique information on all redeemed prescriptions purchased by patients (medical treatment given only in hospital is not included) since 1995
Danish Civil Registration System	Provides the unique individual personal identification number, information on sex, place of birth, marital status, and vital statistics since 1968
The Danish Medical Birth Registry	The Medical Birth Registry includes birth characteristics, such as gestational age, birth weight, date of birth, sex, singleton or not since 1968
The Danish Register of Cause of Death	Danish law mandates registration of the date of the cause of death for all Danish citizens who die in Denmark since 1970
Integrated database for labour market research	Provides information on persons' establishments and their relation since 1981
Psychiatric central research register	Provides information of patients treated at psychiatric departments since 1969

Table S4. The diagnostic classification of psychiatric disorders according to ICD-8 and ICD-10 system

Diagnosis	ICD-8	ICD-10
Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	306.x9, 308.0x	F90-F98
Attention-deficit/hyperactivity disorders	308.01	F90, F98.8
Conduct disorders/oppositional defiant disorder	308.03, 308.04, 308.05, 308.06	F91
Emotional disorders	308.02	F93
Pervasive developmental disorders	299.00, 299.01, 299.02, 299.03	F84
Autism spectrum disorders	299.00	F84.0
Developmental disorders	306.0x, 306.1x, 306.3x	F80-83

Table S5. Brain regions with their cortical volume or area significantly altered in the children whose mothers had SNVP during pregnancy (FDR corrected, $p < 0.05$).

Brain region	t value	Cohen's d	p value	FDR p
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI total	-4.01	-0.078	0.00006	0.011
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI total	-3.98	-0.077	0.00007	0.011
Cortical volume in mm ³ for cortical Destrieux ROI total	-4.02	-0.078	0.00006	0.011
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI middle frontal gyrus	-3.70	-0.072	0.00022	0.020
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI postcentral gyrus	-3.69	-0.071	0.00022	0.020
Cortical area in mm ² for left hemisphere cortical Destrieux ROI anterior part of the cingulate gyrus and sulcus	-3.30	-0.064	0.00096	0.027
Cortical area in mm ² for left hemisphere cortical Destrieux ROI lateral occipito-temporal gyrus	-3.39	-0.066	0.00070	0.027
Cortical area in mm ² for left hemisphere cortical Destrieux ROI central sulcus	-3.32	-0.064	0.00090	0.027
Cortical area in mm ² for right hemisphere cortical Destrieux ROI anterior part of the cingulate gyrus and sulcus	-3.42	-0.066	0.00064	0.027
Cortical area in mm ² for right hemisphere cortical Destrieux ROI precuneus	-3.34	-0.065	0.00084	0.027
Cortical area in mm ² for left hemisphere cortical Destrieux ROI total	-3.55	-0.069	0.00039	0.027
Cortical area in mm ² for right hemisphere cortical Destrieux ROI total	-3.43	-0.066	0.00060	0.027
Cortical area in mm ² for cortical Destrieux ROI total	-3.51	-0.068	0.00044	0.027
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI superior frontal gyrus	-3.37	-0.065	0.00076	0.027
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI temporal pole	-3.35	-0.065	0.00081	0.027
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI superior parietal lobule	-3.43	-0.066	0.00060	0.027
Cortical area in mm ² for left hemisphere cortical Destrieux ROI superior segment of the circular sulcus of the insula	-3.20	-0.062	0.00137	0.033
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI lateral occipito-temporal gyrus	-3.22	-0.062	0.00130	0.033
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI precuneus	-3.23	-0.062	0.00126	0.033
Cortical area in mm ² for left hemisphere cortical Destrieux ROI transverse frontopolar gyri and sulci	-3.13	-0.061	0.00174	0.038
Cortical area in mm ² for left hemisphere cortical Destrieux ROI middle frontal gyrus	-3.12	-0.060	0.00180	0.038
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI transverse frontopolar gyri and sulci	-3.11	-0.060	0.00187	0.038
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI superior segment of the circular sulcus of the insula	-3.09	-0.060	0.00204	0.040
Cortical area in mm ² for left hemisphere cortical Destrieux ROI postcentral gyrus	-3.05	-0.059	0.00229	0.041
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI anterior part of the cingulate gyrus and sulcus	-3.07	-0.059	0.00217	0.041
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI calcarine sulcus	-3.04	-0.059	0.00234	0.041
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI superior frontal gyrus	-3.03	-0.059	0.00243	0.041
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI intraparietal sulcus and transverse parietal sulci	-3.02	-0.058	0.00258	0.042
Cortical area in mm ² for left hemisphere cortical Destrieux ROI superior frontal gyrus	-2.93	-0.057	0.00341	0.046
Cortical area in mm ² for left hemisphere cortical Destrieux ROI precuneus	-2.89	-0.056	0.00387	0.046
Cortical area in mm ² for left hemisphere cortical Destrieux ROI inferior temporal gyrus	-2.85	-0.055	0.00440	0.046
Cortical area in mm ² for left hemisphere cortical Destrieux ROI postcentral sulcus	-2.90	-0.056	0.00369	0.046
Cortical area in mm ² for right hemisphere cortical Destrieux ROI superior parietal lobule	-2.90	-0.056	0.00372	0.046
Cortical area in mm ² for right hemisphere cortical Destrieux ROI superior segment of the circular sulcus of the insula	-2.85	-0.055	0.00435	0.046
Cortical area in mm ² for right hemisphere cortical Destrieux ROI pericallosal sulcus	-2.90	-0.056	0.00377	0.046
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI precentral gyrus	-2.87	-0.055	0.00412	0.046
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI central sulcus	-2.95	-0.057	0.00314	0.046
Cortical volume in mm ³ for left hemisphere cortical Destrieux ROI postcentral sulcus	-2.85	-0.055	0.00438	0.046
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI anterior part of the cingulate gyrus and sulcus	-2.94	-0.057	0.00327	0.046
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI posterior-dorsal part of the cingulate gyrus	-2.92	-0.056	0.00354	0.046
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI triangular part of the inferior frontal gyrus	-2.86	-0.055	0.00427	0.046
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI postcentral gyrus	-2.89	-0.056	0.00382	0.046
Cortical volume in mm ³ for right hemisphere cortical Destrieux ROI superior segment of the circular sulcus of the insula	-2.89	-0.056	0.00389	0.046

Table S6. The mediations on psychiatric problems implemented in the children by the volume and area of different cortical regions in the effects of exposure to severe and prolonged nausea and vomiting in pregnancy (SNVP) (FDR corrected, $p < 0.05$).

Cortical volume										
Brain region	path A		path B		path C'		path C		path AB	
	beta	p value	beta	p value	beta	p value	beta	p value	beta	p value
left hemisphere anterior part of the cingulate gyrus and sulcus'	-0.092	4.94E-04	-0.792	6.55E-06	4.75	<1.0E-10	4.82	<1.0E-10	0.073	6.62E-03
left hemisphere middle frontal gyrus	-0.096	2.48E-04	-0.846	1.80E-06	4.74	<1.0E-10	4.82	<1.0E-10	0.081	4.13E-03
left hemisphere superior frontal gyrus	-0.088	5.62E-04	-0.925	3.18E-07	4.74	<1.0E-10	4.82	<1.0E-10	0.082	4.76E-03
left hemisphere lateral occipito-temporal gyrus	-0.089	9.44E-04	-0.658	1.38E-04	4.77	<1.0E-10	4.82	<1.0E-10	0.058	1.43E-02
left hemisphere postcentral gyrus	-0.105	7.87E-05	-0.938	8.13E-08	4.73	<1.0E-10	4.82	<1.0E-10	0.098	1.66E-03
left hemisphere precentral gyrus	-0.071	4.70E-03	-0.823	7.21E-06	4.77	<1.0E-10	4.82	<1.0E-10	0.059	1.87E-02
left hemisphere temporal pole	-0.087	9.48E-04	-0.928	1.53E-07	4.74	<1.0E-10	4.82	<1.0E-10	0.080	5.74E-03
left hemisphere central sulcus	-0.074	4.93E-03	-0.881	5.64E-07	4.76	<1.0E-10	4.82	<1.0E-10	0.065	1.57E-02
left hemisphere superior segment of the circular sulcus of the insula	-0.077	2.77E-03	-1.029	9.63E-09	4.74	<1.0E-10	4.82	<1.0E-10	0.079	8.72E-03
left hemisphere postcentral sulcus	-0.071	7.43E-03	-0.634	2.79E-04	4.78	<1.0E-10	4.82	<1.0E-10	0.045	3.53E-02
right hemisphere anterior part of the cingulate gyrus and sulcus	-0.088	7.46E-04	-0.656	2.12E-04	4.77	<1.0E-10	4.82	<1.0E-10	0.058	1.45E-02
right hemisphere superior frontal gyrus	-0.078	2.55E-03	-1.099	1.01E-09	4.74	<1.0E-10	4.82	<1.0E-10	0.085	7.44E-03
right hemisphere superior parietal lobule	-0.089	8.48E-04	-0.685	8.53E-05	4.76	<1.0E-10	4.82	<1.0E-10	0.061	1.25E-02
right hemisphere postcentral gyrus	-0.081	2.69E-03	-0.784	4.79E-06	4.76	<1.0E-10	4.82	<1.0E-10	0.064	1.36E-02
right hemisphere precuneus	-0.080	2.08E-03	-0.815	4.43E-06	4.76	<1.0E-10	4.82	<1.0E-10	0.065	1.19E-02
right hemisphere superior segment of the circular sulcus of the insula	-0.073	5.46E-03	-0.650	2.17E-04	4.78	<1.0E-10	4.82	<1.0E-10	0.048	2.99E-02
right hemisphere intraparietal sulcus and transverse parietal sulci	-0.076	4.52E-03	-0.569	1.01E-03	4.78	<1.0E-10	4.82	<1.0E-10	0.043	3.62E-02
Cortical area										
left hemisphere anterior part of the cingulate gyrus and sulcus	-0.097	2.16E-04	-0.854	1.34E-06	4.74	<1.0E-10	4.82	<1.0E-10	0.083	3.74E-03
left hemisphere middle frontal gyrus	-0.081	1.66E-03	-0.991	3.79E-08	4.74	<1.0E-10	4.82	<1.0E-10	0.080	6.98E-03
left hemisphere superior frontal gyrus	-0.076	2.40E-03	-1.137	9.32E-10	4.74	<1.0E-10	4.82	<1.0E-10	0.086	7.11E-03
left hemisphere lateral occipito-temporal gyrus	-0.097	3.83E-04	-0.683	5.82E-05	4.76	<1.0E-10	4.82	<1.0E-10	0.066	8.87E-03
left hemisphere postcentral gyrus	-0.080	2.02E-03	-1.030	8.38E-09	4.74	<1.0E-10	4.82	<1.0E-10	0.082	7.14E-03
left hemisphere precuneus	-0.077	3.62E-03	-0.711	4.79E-05	4.77	<1.0E-10	4.82	<1.0E-10	0.055	2.03E-02
left hemisphere inferior temporal gyrus	-0.073	4.94E-03	-0.650	2.59E-04	4.78	<1.0E-10	4.82	<1.0E-10	0.048	2.94E-02
left hemisphere central sulcus	-0.082	1.18E-03	-1.000	5.46E-08	4.74	<1.0E-10	4.82	<1.0E-10	0.082	5.92E-03
left hemisphere superior segment of the circular sulcus of the insula	-0.082	1.38E-03	-1.121	4.65E-10	4.73	<1.0E-10	4.82	<1.0E-10	0.092	4.84E-03
left hemisphere postcentral sulcus	-0.070	6.95E-03	-0.575	1.21E-03	4.78	<1.0E-10	4.82	<1.0E-10	0.040	4.37E-02
right hemisphere anterior part of the cingulate gyrus and sulcus	-0.097	1.74E-04	-0.842	2.42E-06	4.74	<1.0E-10	4.82	<1.0E-10	0.082	3.76E-03
right hemisphere superior parietal lobule	-0.074	5.18E-03	-0.579	1.01E-03	4.78	<1.0E-10	4.82	<1.0E-10	0.043	3.80E-02
right hemisphere precuneus	-0.086	1.08E-03	-0.675	1.28E-04	4.77	<1.0E-10	4.82	<1.0E-10	0.058	1.47E-02
right hemisphere superior segment of the circular sulcus of the insula	-0.072	5.79E-03	-0.746	2.50E-05	4.77	<1.0E-10	4.82	<1.0E-10	0.054	2.35E-02
right hemisphere pericallosal sulcus	-0.078	3.45E-03	-0.596	5.80E-04	4.78	<1.0E-10	4.82	<1.0E-10	0.047	2.96E-02

Table S7. The mediations implemented in the children by the volume and area of different cortical regions in the effects of exposure to SNVP on cognition (FDR corrected, $p < 0.05$).

Cortical volume										
Brain region	path A		path B		path C'		path C		path AB	
	beta	p value	beta	p value	beta	p value	beta	p value	beta	p value
left hemisphere transverse frontopolar gyri and sulci	-0.086	1.42E-03	0.243	1.63E-03	-0.89	2.87E-05	-0.92	1.86E-05	-0.021	2.87E-02
left hemisphere anterior part of the cingulate gyrus and sulcus	-0.096	2.98E-04	0.676	<1.0E-10	-0.85	6.63E-05	-0.92	1.86E-05	-0.065	9.08E-04
left hemisphere middle frontal gyrus	-0.105	6.90E-05	0.496	3.71E-10	-0.86	5.28E-05	-0.92	1.86E-05	-0.052	8.68E-04
left hemisphere superior frontal gyrus	-0.091	4.03E-04	0.506	3.95E-10	-0.87	4.69E-05	-0.92	1.86E-05	-0.046	2.28E-03
left hemisphere lateral occipito-temporal gyrus	-0.094	5.42E-04	0.425	3.40E-08	-0.88	4.15E-05	-0.92	1.86E-05	-0.040	3.76E-03
left hemisphere postcentral gyrus	-0.107	6.18E-05	0.407	1.92E-07	-0.87	4.50E-05	-0.92	1.86E-05	-0.044	1.69E-03
left hemisphere precentral gyrus	-0.077	2.58E-03	0.647	2.89E-15	-0.87	4.91E-05	-0.92	1.86E-05	-0.050	5.17E-03
left hemisphere temporal pole	-0.090	6.50E-04	0.616	5.77E-15	-0.86	5.55E-05	-0.92	1.86E-05	-0.056	1.91E-03
left hemisphere central sulcus	-0.078	3.12E-03	0.551	2.77E-12	-0.87	4.36E-05	-0.92	1.86E-05	-0.043	6.94E-03
left hemisphere superior segment of the circular sulcus of the insula	-0.082	1.56E-03	0.665	<1.0E-10	-0.86	5.42E-05	-0.92	1.86E-05	-0.055	3.29E-03
left hemisphere postcentral sulcus	-0.070	9.03E-03	0.391	5.08E-07	-0.89	3.22E-05	-0.92	1.86E-05	-0.027	2.25E-02
right hemisphere anterior part of the cingulate gyrus and sulcus	-0.092	4.76E-04	0.661	<1.0E-10	-0.85	6.14E-05	-0.92	1.86E-05	-0.061	1.35E-03
right hemisphere posterior-dorsal part of the cingulate gyrus	-0.084	2.10E-03	0.508	2.85E-11	-0.87	4.34E-05	-0.92	1.86E-05	-0.043	5.66E-03
right hemisphere superior frontal gyrus	-0.085	1.04E-03	0.571	1.32E-12	-0.87	4.86E-05	-0.92	1.86E-05	-0.049	3.14E-03
right hemisphere superior parietal lobule	-0.089	9.11E-04	0.348	8.00E-06	-0.88	3.49E-05	-0.92	1.86E-05	-0.031	8.77E-03
right hemisphere postcentral gyrus	-0.083	2.39E-03	0.306	6.51E-05	-0.89	3.12E-05	-0.92	1.86E-05	-0.025	1.77E-02
right hemisphere precuneus	-0.083	1.69E-03	0.389	9.69E-07	-0.88	3.56E-05	-0.92	1.86E-05	-0.032	9.17E-03
right hemisphere calcarine sulcus	-0.081	2.62E-03	0.405	1.66E-07	-0.88	3.61E-05	-0.92	1.86E-05	-0.033	1.00E-02
right hemisphere superior segment of the circular sulcus of the insula	-0.080	2.63E-03	0.453	8.40E-09	-0.88	3.84E-05	-0.92	1.86E-05	-0.036	8.40E-03
right hemisphere intraparietal sulcus and transverse parietal sulci	-0.075	5.56E-03	0.471	1.07E-09	-0.88	3.75E-05	-0.92	1.86E-05	-0.035	1.25E-02
Cortical area										
left hemisphere transverse frontopolar gyri and sulci	-0.090	1.06E-03	0.421	2.74E-08	-0.88	3.99E-05	-0.92	1.86E-05	-0.038	5.30E-03
left hemisphere anterior part of the cingulate gyrus and sulcus	-0.103	9.33E-05	0.856	<1.0E-10	-0.83	1.02E-04	-0.92	1.86E-05	-0.088	2.48E-04
left hemisphere middle frontal gyrus	-0.090	5.09E-04	0.700	<1.0E-10	-0.85	6.36E-05	-0.92	1.86E-05	-0.063	1.33E-03
left hemisphere superior frontal gyrus	-0.081	1.30E-03	0.713	<1.0E-10	-0.86	5.72E-05	-0.92	1.86E-05	-0.058	2.74E-03
left hemisphere lateral occipito-temporal gyrus	-0.105	1.26E-04	0.482	2.12E-10	-0.86	5.15E-05	-0.92	1.86E-05	-0.051	1.14E-03
left hemisphere postcentral gyrus	-0.083	1.50E-03	0.493	7.12E-10	-0.87	4.20E-05	-0.92	1.86E-05	-0.041	5.21E-03
left hemisphere precuneus	-0.085	1.43E-03	0.404	2.39E-07	-0.88	3.73E-05	-0.92	1.86E-05	-0.034	7.40E-03
left hemisphere inferior temporal gyrus	-0.078	2.94E-03	0.598	5.26E-14	-0.87	4.65E-05	-0.92	1.86E-05	-0.047	6.05E-03
left hemisphere central sulcus	-0.087	5.84E-04	0.669	4.44E-16	-0.86	5.84E-05	-0.92	1.86E-05	-0.058	1.64E-03
left hemisphere superior segment of the circular sulcus of the insula	-0.090	5.30E-04	0.787	<1.0E-10	-0.84	7.29E-05	-0.92	1.86E-05	-0.071	1.14E-03
left hemisphere postcentral sulcus	-0.070	8.04E-03	0.465	4.69E-09	-0.88	3.55E-05	-0.92	1.86E-05	-0.032	1.70E-02
right hemisphere anterior part of the cingulate gyrus and sulcus	-0.104	7.05E-05	0.834	<1.0E-10	-0.83	9.88E-05	-0.92	1.86E-05	-0.087	2.14E-04
right hemisphere superior parietal lobule	-0.075	4.99E-03	0.436	2.89E-08	-0.88	3.57E-05	-0.92	1.86E-05	-0.032	1.34E-02
right hemisphere precuneus	-0.090	7.20E-04	0.421	9.15E-08	-0.88	3.98E-05	-0.92	1.86E-05	-0.038	4.76E-03
right hemisphere superior segment of the circular sulcus of the insula	-0.080	2.30E-03	0.553	2.59E-12	-0.87	4.48E-05	-0.92	1.86E-05	-0.044	5.57E-03
right hemisphere pericallosal sulcus	-0.084	1.86E-03	0.483	4.37E-10	-0.88	4.17E-05	-0.92	1.86E-05	-0.041	5.83E-03

Table S8 Incidence rate and hazard ratio of specific psychiatric disorders in offspring born during 1995-2012 in Denmark according to maternal hyperemesis gravidarum

	No of Cases N	Incidence rate Rate per 1000 person-years	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Behavioral and emotional disorders*				
No HG	41 869	3.07	REF	REF
Maternal HG	595	3.67	1.27 (1.17-1.38)	1.20 (1.10-1.30)
Attention-deficit/hyperactivity disorders				
No HG	32 177	2.57	REF	REF
Maternal HG	437	2.85	1.23 (1.12-1.35)	1.16 (1.06-1.28)
Conduct disorders/oppositional defiant disorders				
No HG	2024	0.15	REF	REF
Maternal HG	29	0.18	1.31 (0.91-1.89)	1.06 (1.71-1.57)
Emotional disorders				
No HG	2884	0.21	REF	REF
Maternal HG	44	0.27	1.34 (1.00-1.81)	1.33 (0.98-1.89)
Pervasive developmental disorders				
No HG	17 478	1.31		
Maternal HG	232	1.46	1.23 (1.08-1.40)	1.19 (1.05-1.36)
Childhood autism				
No HG	6877	0.50	REF	REF
Maternal HG	100	0.61	1.32 (1.08-1.61)	1.19 (0.97-1.45)
Developmental disorders#				
No HG	3362	0.24	REF	REF
Maternal HG	55	0.33	1.43 (1.10-1.86)	1.33 (1.02-1.75)

HG: hyperemesis gravidarum; HR: Hazard ratio; Model 1= children's age at time scale; Model 2= children's age at time scale, sex, birth of year, parity, parental age at birth, maternal education level, maternal country of origin, maternal cohabitation and parental psychiatry disorders; *indicates behavioral and emotional disorders with onset usually occurring in childhood and adolescence; #indicates developmental disorders including language, learning and motor skills disorders

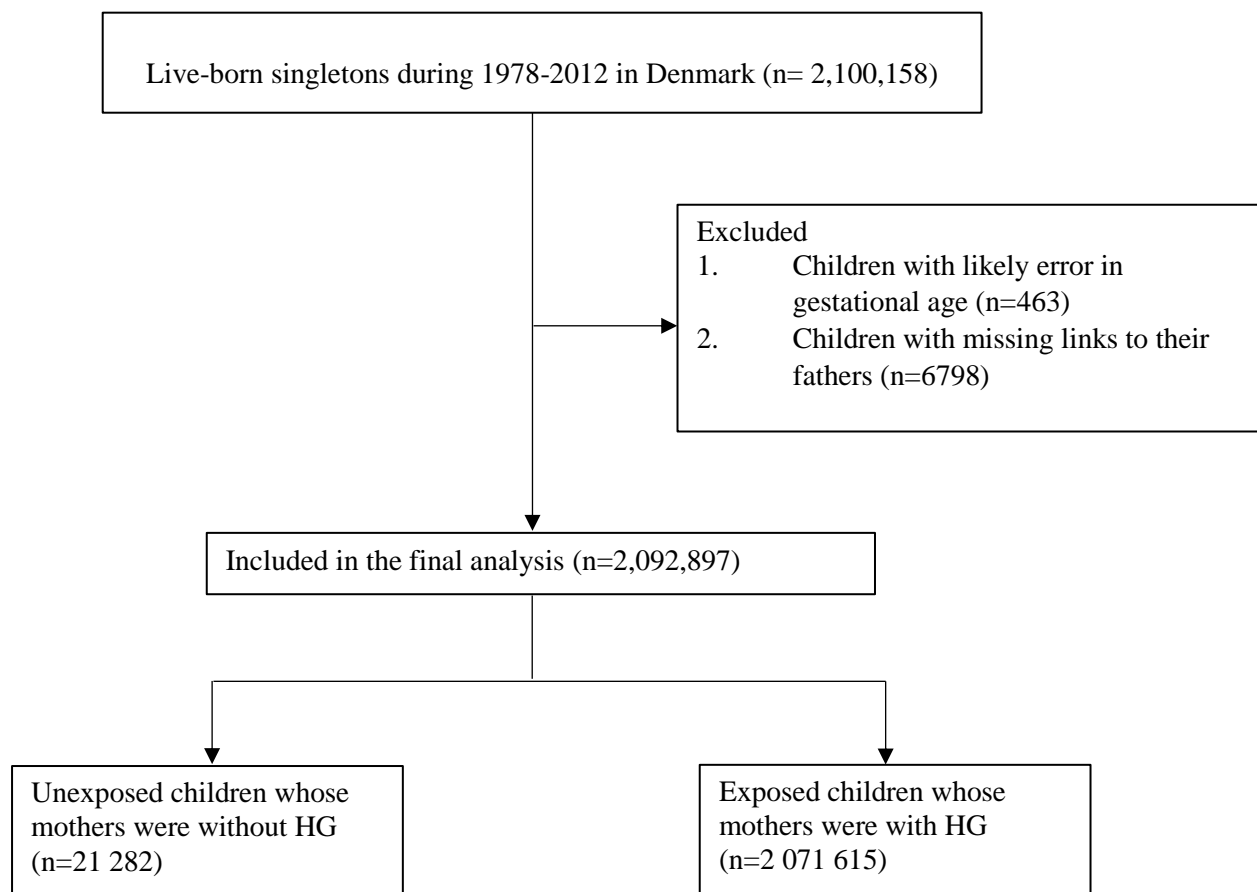


Figure S1 Flowchart showing the identification of the eligible participants and analysis sample

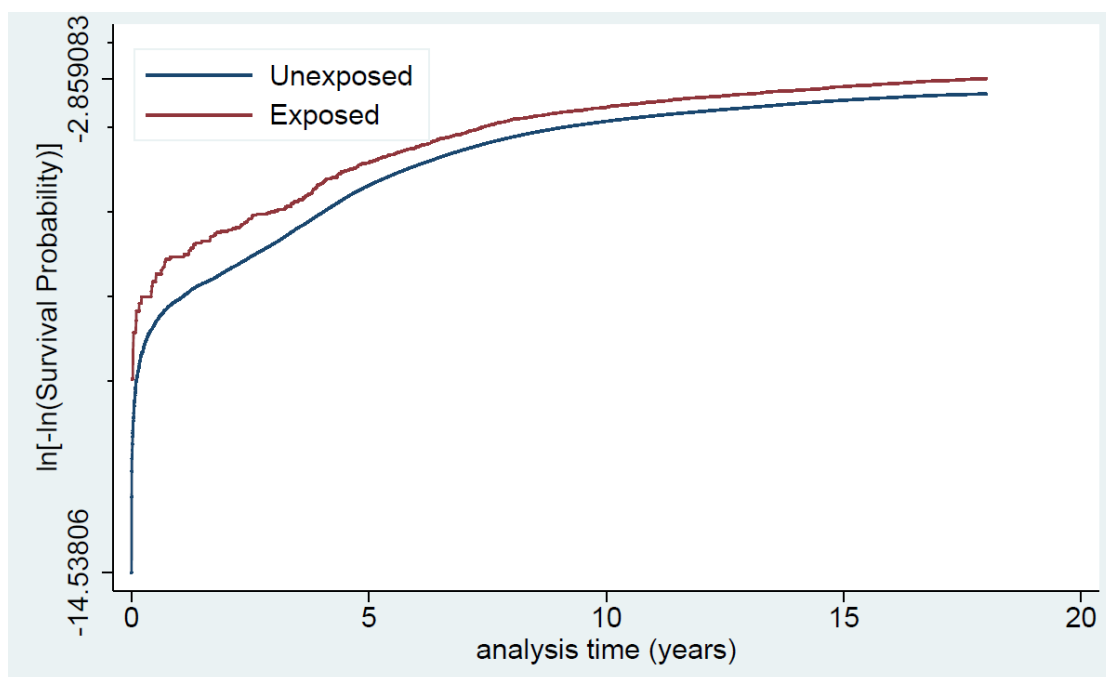
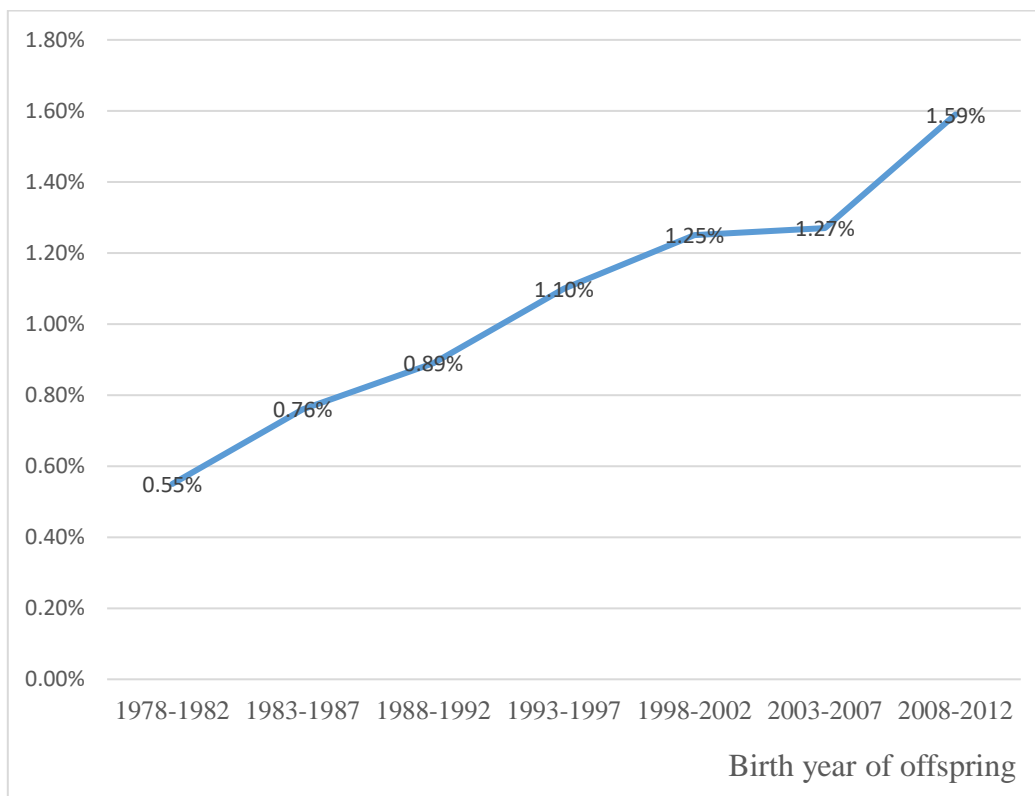


Figure S2 The log-minus-log survival curve



Supplementary Figure 3 The proportion of offspring born to mothers with hyperemesis gravidarum by birth year