



Eat2beNICE

Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing Behaviours

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D 1.2: Effects of dietary intake during pregnancy on offspring impulsivity and compulsivity

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Introduction

Neurodevelopmental disorders most often debut in childhood and are an important cause of long-term disability in children. Before reaching puberty, no less than 5% of Norwegian children will have been diagnosed with one or more of neurodevelopmental disorders, such as Attention deficit hyperactivity disorder (ADHD), cerebral palsy, epilepsy or autism spectrum disorder.¹ Worldwide, ADHD affects about 5% of children and is seen in about 2.5% of adults.² In Norway, the prevalence among children and adolescents is approximately 3-4%.^{1,3}

ADHD is defined according to a set of characteristic symptoms, which include core symptoms related to hyperactivity, inattention and impulsivity. These are dimensional traits, observed at various levels in all humans. To qualify for an ADHD diagnosis, these traits, or symptoms, are extreme in such a way that they interfere with and impair a person's daily life; at school, at work or in social settings.

ADHD is a complex multifactorial disorder with a high heritability estimated to be over 70% from family, twin and adoption studies.⁴ However, heritability of less than 100% from twin studies indicate that both genes and environment contribute to the development of symptoms related to ADHD.⁴



The causes behind ADHD are, however, complex and remains elusive. A recent genome wide association study of ADHD identified 12 significant loci. When taking all common variants into account, approximately 22% of the heritability can be explained.⁷ The causes behind ADHD are, however, complex and remains elusive. Findings point at the dopaminergic system being associated with ADHD.⁸ Reduced striatal and hippocampus volumes have been found among patients with ADHD, with most pronounced findings in childhood, indicating brain maturation delay as a component in ADHD.^{9,10}

While several perinatal risk factors have shown associations with later ADHD⁵, none of them are confirmed as causal.⁶ The identification of modifiable early-life risk factors, such as nutritional factors, is of importance because they have the potential to prevent neurodevelopmental disorders like ADHD.

1. Deliverable report

Note: publishers' policies prevent sharing of detailed results prior to publication in a peer-reviewed journal. Detailed results, tables and uncompromised figures will be made available upon acceptance and/or as soon as the publisher's embargo has been lifted.

Intake of sweetened carbonated beverages during pregnancy and risk of ADHD-like symptoms in the offspring at 8 years of age.

Maternal beverage intake during pregnancy have been linked to adverse outcomes in the offspring. In humans, sugar-sweetened beverages have been associated with preterm delivery¹¹ and congenital heart defects.¹² In pregnant mouse, prenatal sucrose diluted water has been associated with changes in dopaminergic system and increased impulsivity and decreased attention.¹³ We are not aware of any studies exploring the association between maternal intake of sweetened carbonated beverage and neurodevelopmental outcomes in offspring 8 years later. In this study we aimed to explore whether intake of sweetened carbonated beverages during pregnancy is associated with increased risk of ADHD symptoms of offspring at 8 years of age, using data from the Norwegian Mother, Father and Child Cohort Study (MoBa).

This study was based on data from The Norwegian Mother and Child Cohort Study (MoBa) and The Medical Birth Registry of Norway (MBRN). MoBa is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health. Participants were recruited from across Norway from 1999-2008.¹⁴ The women consented to participation in 40.6% of the invited pregnancies. The cohort now includes 114 500 children and 95 200 mothers. Maternal diets were assessed in MoBa through a food frequency questionnaire (FFQ) covering habitual diet during the first half of pregnancy from 2002. The MBRN is a national health registry containing information about all births in Norway from 1967.¹⁵ MoBa is routinely linked with the MBRN for the included MoBa pregnancy.

The establishment of MoBa and initial data collection was based on a license from the Norwegian Data protection agency and approval from The Regional Committee for Medical Research Ethics. The MoBa cohort is currently regulated by the Norwegian Health Registry Act. The current study was approved by The Regional Committee for Medical Research Ethics (2015/2055) and is based on version 12 of the quality-assured data files released for research in 2019.

Our study population included mother-child pairs in singleton births, who had available information from the FFQ filled out midpregnancy and who had completed Questionnaire 8 when the offspring was 8 years of age. We further excluded mothers with ADHD resulting in a final study populations of 39 987 mother-child pairs (see more details in flowchart in Figure 1).

Maternal intake of carbonated sweet beverages was registered in pregnancy around week 22 in the FFQ. Respondents were instructed to report their average intake since they became pregnant. There were 39 questions about beverages, of which nine were relevant for the current study. These included five questions about intake of carbonated sweet beverages (i.e. sugar sugar-sweetened cola-drinks, other sodas, energy drinks and artificially sweetened cola drinks and other sodas,), two questions about non-carbonated sweet drinks (i.e. sugar sweetened and artificially sweetened cordial), and two questions about juice and nectar. The alternative answers options were given as servings per day (between 1 and 8), servings per week between 1–2 and 5–6), or servings per month (between 0 and 2–3). A serving was defined as 250 mL for all these beverages. We combined the intake of carbonated sweet beverages (sugar- and artificially sweetened) and categorized into levels of daily intake: No intake, 1 glass daily, 2-3 glasses daily and 4 glasses daily or more. Soda (soft drinks or fizzy drinks) are in this paper defined as non-alcoholic carbonated beverages either sugar-sweetened or artificially sweetened.



Questionnaire 8 (Q8) was mailed to the mothers when the child was 8 years of age and included questions on the child's behaviour. The Parent/Teacher Rating Scale for Disruptive Behaviour Disorders (RS-DBD) contains 41 DSM-IV questions with 18 of these questions linked to ADHD. In Q8 this rating scale has been modified slightly and contains 18 questions linked to ADHD. The questions are rated by the mother on a four-point Likert scale (1 = never/rarely, 2 = sometimes, 3 = often, 4 = very often). We defined the outcome of ADHD in offspring in two ways: We calculated the average of 18 questions for each person and scaled the responses to a T score with a mean of 50 and standard deviation of 10. Offspring ADHD symptom scores were also dichotomized using six or more symptoms of inattentiveness and/or hyperactivity occurring often or very often as cut-off, in accordance with the DSM criteria (six of more of nine symptoms/traits), excluding those with 1-5 symptoms in this analyses.

Maternal education level, maternal age, maternal pre-pregnancy BMI, birth year, season and parity were considered possible confounders a priori for the association between maternal intake of carbonated sodas and offspring ADHD symptoms. Other components of the maternal diet were added as adjustment variables; calculated total maternal fiber intake and maternal intake of other non-carbonated sweet drinks (categorized into number of glasses daily in a similar manner as for carbonated beverages (categorized into none, 1 glass, 2-3 glasses and 4 or more glasses for each category: orange juice, other juices and fruit syrup). The association was evaluated using standardized ADHD scores as the outcome, modelled by linear regression. Main analyses were conducted in STATA version 16.1 (College Station, TX). Associations were also analysed using log-binomial regression for the dichotomized outcome.

Table 1 shows characteristics of the 39 870 women who answered both the FFQ at midpregnancy and when the child was eight years (Q8), and who make up our study population (Table 1). The majority (60%) of mothers were above 30 years when they gave birth, were nulliparous (46%) and had high education (4 years or more of college/university;- 69%). As many as 87% of mothers reported no daily intake of sweetened carbonated beverages, while 4% reported 1 glass daily, 5% reported drinking 2-3 glasses daily and 4% drinking 4 glasses or more daily.

For women with no daily intake of sweetened carbonated beverages, the absolute risk of having an offspring with 6 or more ADHD symptoms was 5%, while for women drinking 1, 2-3 and ≥ 4 glasses daily, the risks were 6%, 8% and 8%, respectively.

For the standardized ADHD score, there was an 0.31 (-0.16-0.78) increase for women who drank 1 sweetened carbonated beverage daily in pregnancy had on average 0.29 (95% confidence intervals - 0.18-0.77) higher scores compared to women with no daily intake. The corresponding numbers were 1.05 (0.60-1.49) for women who drank 2-3 glasses and 1.41 (0.81-2.00) for women who drank 4 or more glasses daily (Table 2). When adjusting for daily intake of other sweet beverages midpregnancy such as juice and fruit syrup, and total fiber intake, for maternal education, age, parity, prepregnancy BMI, for birth year and birth season, the regression coefficients were attenuated: 0.25 (-0.22-0.73), 0.87 (0.41-1.33) and 0.98 (0.38-1.58) for intake of 1, 2-3 and ≥ 4 glasses daily, respectively. When additionally adjusting for total energy intake, and maternal depression and anxiety, regression coefficients were further attenuated: 0.01 (-0.46-0.48), 0.52 (0.06-0.98), 0.34 (-0.28-0.96) for intake of 1, 2-3 and ≥ 4 glasses daily, respectively.



In this large pregnancy cohort with offspring followed up until 8 years of age, we found a small association between maternal intake of 2-3 glasses daily of carbonated sweetened beverages and offspring ADHD symptoms at 8 years of age. The crude results were attenuated when adjusting for maternal intake of other sweet beverages, total fiber intake, total energy intake, maternal education, age, parity and prepregnancy BMI, as well as offspring birth year and birth season. When stratifying on offspring sex there was a tendency towards stronger associations for male offspring. While residual confounding in observational studies cannot be excluded, our results support the existence of a weak positive relationship between high intake of carbonated sweetened beverages and offspring ADHD symptoms. Although the underlying mechanisms or clinical implications of these findings are not clear, it emphasizes the need to systematically explore risk factors for neurodevelopmental symptoms and disorders.

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2. Tables and other supporting documents where applicable and necessary

Figure 1. Flowchart of the study population.

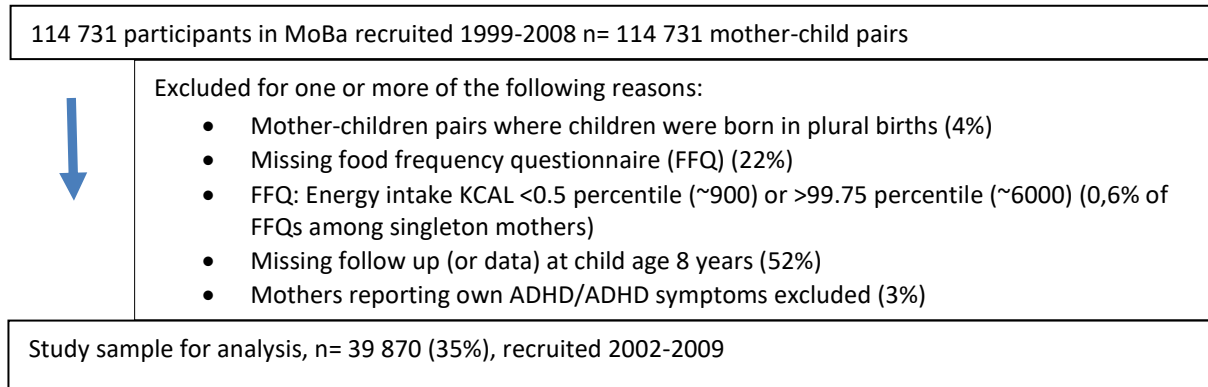


Table 1. Demographic characteristics of the MoBa study population.

Background characteristics	Study population (%)
Mothers- child units	39 870 (100)
Maternal age at delivery (years)	
<20	176 (0.4)
20-24	2 925 (7.3)
25-29	12 801 (32.1)
30-34	16 344 (41.0)
35 years and older	7 624 (19.1)
Maternal parity	
0	18 273 (45.8)
1	14 064 (35.3)
2	5 986 (15.0)
3	1 209 (3.0)
4+	338 (0.9)
Maternal education	
Less than high school	599 (1.5)

High school	10 903 (27.4)
4 years or more of college/university	27 522 (69.0)
Missing education	840 (2.1)

Table 2. Unadjusted and different adjustments for the association between carbonated beverages and offspring ADHD symptoms using linear regression. Total n=39 760 §

Carbonated beverages during pregnancy from Q2 (daily intake)	Unadjusted regression coefficient (95% CI)*	Adjusted coefficient (95% CI)**	Adjusted coefficient (95% CI) ***
None	0 (ref)	0 (ref)	0 (ref)
1 glass	0.29 (-0.18-0.77)	0.25 (-0.22-0.73)	0.01 (-0.46-0.48)
2-3 glasses	1.05 (0.60-1.49)	0.87 (0.41-1.33)	0.52 (0.06-0.98)
4 glasses or more	1.41 (0.81-2.00)	0.98 (0.38-1.58)	0.34 (-0.28-0.96)

§ For mother-offspring units to join the analyses on a standardized mean score of offspring ADHD symptoms 9 or more out of 18 questions were required to be answer. For n=110, the offspring had answered 8 or less questions and were excluded from the analyses.

* Unadjusted regression coefficient from a model with the ADHD scores standardized to a mean of 50 and a standard deviation of 10.

** Adjusted for daily intake of other sweet beverages midpregnancy such as juice and fruit syrup, and total fiber intake, for maternal education, age, parity, prepregnancy BMI, for birth year and birth season.

***as above but additional adjusting for total energy intake (KCAL) and maternal depression and anxiety.

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