

THE EFFECT OF LOW TO MODERATE PRENATAL ALCOHOL EXPOSURE AND BINGE DRINKING EPISODES ON DRAW-A-PERSON AT AGE 5 YEARS

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'Running head': prenatal alcohol exposure and draw-a-person skills

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Abstract

This study examined the effects of maternal alcohol consumption and binge drinking during pregnancy on children's Draw-A-Person (DAP) scores. Participants were 1,533 5-year-olds from the Danish National Birth Cohort. Regression analyses revealed an adverse effect of nine or more drinks per week. A drop in mean DAP score of 6.26 (95 % CI: -12.24; -0.39) was observed in the fully adjusted model. A significant interaction between average weekly consumption and binge episodes also was observed. Findings suggest that prenatal exposure to moderate weekly doses of alcohol and binge drinking episodes are associated with lowered scores on the DAP

1. Introduction

Research and clinical science has consistently demonstrated that prenatal exposure to alcohol is a

significant teratogen for the human brain (Greene, et al., 1991; Mattson et al., 2010). Depending on the frequency, amount, and timing of *in utero* exposure, as well as other extant factors (e.g., genetics, nutrition, environment, etc.), alcohol has been shown to have adverse effects on all neurodevelopmental domains including intelligence, motor skills, executive functioning, learning, memory, and attention. One area of particular vulnerability is grapho-motor skills (Kopera-Frye & Zielinski, 1995; Uecker & Nadel, 1996). Grapho-motor/visual-spatial coordination is an area of functioning that appears to cascade into difficulty with higher order cognitive functions such as math concepts and skills later in development (Kable & Coles, 2003; Kable & Coles, 2007).

Negative effects of heavy alcohol exposure on short and long-term outcomes in children are well- documented. But whether these effects are observed at low to moderate maternal consumption during pregnancy has not been demonstrated (Clarren, 1986). To date, most studies have failed to observe adverse neurodevelopmental effects at lower levels of prenatal alcohol exposure. Areas investigated include intelligence, motor skills, attention, and executive functioning (Alati et al., 2008; Fried, O'Connell, & Watkinson, 1992; Kelly et al., 2009; Kelly et al., 2012; Kelly et al., 2013; Kesmodel et al., 2012a;

O'Leary, Taylor, Zubrick, Kurinczuk, & Bower, 2013), although grapho-motor skills have not been studied specifically.

The intertwined risk of chronic (average) drinking and binge episodes is not completely understood. While most research to date has focused on chronic alcohol consumption, there is growing evidence that the blood alcohol concentration (BAC) of the mother is the major factor that determines the impact on the fetus (Goodlett, Horn, & Zhou, 2005; Maier, Miller, & West, 1999). Brain growth is particularly susceptible to high BACs (Kelly et al., 2012) and some human studies suggest that binge drinking during pregnancy may be associated with poor neurodevelopmental outcomes (Henderson, Kesmodel, & Gray, 2007; Streissguth, Barr, & Sampson, 1990). While few pregnant women drink alcohol on a daily basis, many women report isolated episodes of binge drinking (five or more drinks on a single occasion), particularly before pregnancy is recognized (Kesmodel, Kesmodel, Larsen, & Secher, 2003; Kesmodel, 2001). Thus, potential effects of binge drinking episodes are another important issue which should be further investigated.

Recognizing the need for additional research on the effects of neurodevelopmental outcomes among children whose mothers consumed alcohol during pregnancy, data from the Lifestyle During Pregnancy Study (LDPS) were examined. The LDPS (Kesmodel et al., 2010) is a large Danish prospective follow- up study of mothers (with data about alcohol consumption

during pregnancy) and neurodevelopmental outcomes among their 5-year-old children. Previous analyses from this dataset have been reported elsewhere for intelligence (Falgreen Eriksen et al., 2012; Kesmodel et al., 2012b), attention (Underbjerg et al., 2012), executive functioning (Skogerbø et al., 2012) and behavioral problems (Skogerbø et al., 2013). Findings indicated negative effects for children of women drinking 9 or more drinks per week. Analysis of this sample for the effects of maternal binge drinking on intelligence, attention or executive functioning, did not yield consistent findings, although most analyses showed no observable effect.

The aim of the present study was to examine the effects of low to moderate maternal alcohol consumption and binge drinking during pregnancy on children's grapho-motor skills as measured by the Draw-a-Person Intellectual Ability Test for Children, Adolescents and Adults (DAP). In addition, correlation between performance on the DAP and IQ, as measured by the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R; Wechsler, 1999), was explored. Finally, the relation between average weekly consumption and binge drinking patterns was examined.

2 Methods

2.1 Participants

The study was approved by the DNBC Board of Directors, the DNBC Steering committee, the regional Ethics Committee, the Danish Data Protection Agency, and the Institutional Review Board at the Centers for Disease Control and Prevention. Signed informed consent was obtained for the LDPS.

Participants were sampled from the Danish National Birth Cohort (DNBC) (Kesmodel et al., 2012a; DNBC, 2010), a large prospective study of 101,042 pregnant Danish women and their children. Participants were recruited in 1997-2003 at their first prenatal visit by their general practitioner. Based on information on

alcohol consumption before and during pregnancy, 3,478 women and their children were invited to a 5-year follow-up examination in the Lifestyle During Pregnancy Study (LDPS) (Kesmodel et al., 2012a); of those, 1,782 (51%) participated in a three hour individual test session. Specific criteria for extraction of potential participants for the present study from the DNBC are described in detail elsewhere (see Kesmodel et al., 2010).

The present analysis includes 1,533 children with available drawings and their mothers (95 children failed to complete a drawing, complete the test battery, or had other missing data). An additional 154 children were excluded due to inability to speak Danish, having impaired hearing or vision causing inability to complete the cognitive tests, being a multiple birth, and/or having congenital diseases likely to cause intellectual disability (e.g. Down Syndrome) (see Kesmodel et al., 2012a).

At the age of 60–64 months, the children participated in a comprehensive psychological assessment of global and specific cognitive functions. The full test battery is described elsewhere (Kesmodel et al., 2012a). Testing took place in four major cities of Denmark (Copenhagen, Odense, Aalborg, and Aarhus). Test procedures were standardized in detail and carried out by ten trained psychologists blinded to the children's exposure status. Tester differences were taken into account by the inclusion of indicator variables in the statistical analyses.

2.2 Measures

2.2.1 Exposure assessment

The information on alcohol consumption during the index pregnancy was obtained from a telephone interview conducted with all women included in the DNBC (median, 17 weeks of gestation; range 7–39 weeks of gestation) (DNBC, 2010). The information included data on the average number of drinks per week of beer, wine, and spirits currently consumed at the time of the prenatal interview, as well as a

second question about consumption before pregnancy. The definition of a drink followed the definition from the Danish Health and Medicines Authority, with one standard drink being equal to 12 g of pure alcohol. Average consumption was categorized into strata of weekly exposure: 0, 1–4, 5–8, and ≥ 9 . Additional information was obtained on the number of binge episodes (i.e., an intake of five or more drinks on a single occasion), and the timing (gestational week) of these episodes (Kesmodel et al., 2012a).

2.2.2 Outcome variables

The DAP test was administered as part of the LDPS test battery. Standard administration of the DAP was used (Reynolds & Hickman, 2004). The child was given a blank sheet of paper and a pencil and then asked to draw a boy or girl (consistent with the child's own gender). The child was given 5 minutes to complete the drawing.

The DAP was scored according to standardized criteria outlined in the American DAP manual (Reynolds & Hickman, 2004). In this scoring system, 21 components of the drawing, (head/face, arms/hand, legs/feet, accessories, etc.), are assigned 0 – 4 points depending on presence, degree of details and dimensioning. Total raw score had a possible range from 0 to 49. One modification to the coding system was that "crowns" were not scored as an accessory since it is traditional for girls to receive "princess outfits" for the 5th birthday and approximately 32% of girls included them which could have introduced a gender artifact. Drawings were scored by trained coders who were blind to the child's exposure status and were not part of the data collection team. Inter-rater reliability of scoring was assessed for ten percent of the drawings and ranged from 89 to 100 percent agreement ($Kappa = 0.86$ ($p < 0.01$)).

The American DAP manual provides conversion of raw scores to an IQ scale, but

it was considered problematic to use these norms for Danish children. Consequently, scaled scores were developed by normalizing raw scores to an IQ scale with mean = 100 and SD = 15 in the total Danish sample. Analyses were conducted and are reported for both the raw scores and the normalized IQ scores.

2.2.3 Covariates

A large number of covariates were included and specifics of how they were operationalized are described elsewhere (see Kesmodel et al., 2010). Information on the following variables was obtained from the prenatal telephone interview and included: parity, prenatal maternal smoking, and maternal pre-pregnancy body mass index (BMI). A questionnaire administered at the 5-year follow-up provided information on the following variables: maternal marital status, parental education, an index of the quality of postnatal family/home environment, maternal depression, current maternal as well as paternal alcohol intake, child health status (including medications), postnatal parental smoking, and child's hearing and vision. Maternal age was obtained from the Danish Civil Registration System, as were the age and sex of the child. Birth weight (grams) and gestational age (days) were obtained from the Danish Medical Birth Registry.

Maternal IQ and child IQ were assessed at the follow-up examination. Child IQ was assessed using the Wechsler Primary and Preschool Scales of Intelligence-Revised (WPPSI-R) (Wechsler, 1999), one of the most widely used tests of intelligence for children aged three to seven years. For practical reasons, we used a short version comprising three verbal subtests: Arithmetic, Information, and Vocabulary; and three non-verbal subtests: Object Assembly, Block Design, and Geometric Design. Standard procedures were used to prorated IQs from the shortened form of the tests (Wechsler, 1999). Because no Danish WPPSI-R norms were

available at the time of the study, Swedish norms were used to derive scaled scores and IQs.

Maternal verbal IQ was assessed using two verbal subtests (information and vocabulary) from the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1995) and the Raven's Standard Progressive Matrices provided non-verbal IQ (Raven, 1958). Raw scores of each test were standardized based on the results from the full sample, and were weighted equally in a combined score that was re-standardized to an IQ scale with a mean of 100 and an SD of 15.

3. Statistical analysis

All statistical analyses were conducted with Stata 11 (StataCorp LP, College Station, TX, USA), and

were weighted by sampling probabilities with robust variance estimation. Statistical tests were two-tailed and declared significant at the 5% level. Estimates are accompanied by 95% confidence intervals.

The number of missing values in each of the variables ranged from 0 to 32. Missing values were imputed by modeling variables through analysis of patterns of other variables in the dataset considered to be most predictive (specific equations are available upon request), thus generating 100 completed data sets. All conclusions were maintained when a complete case analysis was conducted with the 1,525 cases that had complete data for all core confounders and 1,484 cases that had complete data for all potential confounders. The results of the imputed analyses are reported. All imputations were performed with the `ice` add-on command and the built-in `mi estimate` command of Stata 11.

Multiple linear regression was used to evaluate the association between alcohol exposure and standardized DAP scores. Maternal average consumption was analyzed as a categorical variable (coded as 0, 1–4, 5–8, or 9 or more

drinks/week) while binge episodes were analyzed as a binary variable (coded yes/no), and categorical as number of binge episodes (coded 0, 1, 2, or 3 or more episodes) and timing of binge episodes (coded week 1-2, week 3-4, week 5-8, or week 9 or later in pregnancy). Because information on timing of binge episodes was missing for 9 mothers, the main analyses of binge drinking comprised 1,524 children.

Parental education, maternal IQ, maternal smoking during pregnancy, the child's age and sex as well as who conducted the test were considered core confounders and adjusted in a separate model. A full model further adjusted for potential confounders, which included maternal age, maternal pre-pregnancy BMI, marital status, parity, postnatal smoking, child postnatal health, hearing, vision and home environment. In the analyses of maternal average alcohol consumption, binge drinking (coded yes/no) was included as a potential confounding factor, whereas the average number of drinks per week consumed by the mother during pregnancy (coded as 0, 1–4, 5–8 or 9 or more drinks/week) was included as a potential confounding factor in the analyses of effects of binge drinking.

Interactions between average consumption and a binary binge drinking variable were analyzed with both unadjusted and adjusted models. Since gestational age and birth weight may mediate effects of maternal alcohol consumption, separate analyses including these variables as additional covariates were conducted. Finally, the correlations of DAP IQ with the WPPSI-R Full Scale, verbal, and performance IQs were analyzed both as bivariate correlations and partial correlations controlling for sex.

4. Results

Women reporting no average weekly alcohol consumption during pregnancy tended to be younger,

non-smoking and primiparous, with less education and lower IQ compared to women having consumed 1-4 or 5-8 drinks per week (Table 1). Smoking and suboptimal home environment were more often observed among women consuming 5 units or more per week (Table 1). Median weekly alcohol intake was 1

drink in exposure category 1 – 4, five drinks in category 5 – 8, and 10 drinks in the 9 or more drinks per week category. Similar characteristics were observed for women who reported no binge episodes in early pregnancy (data not shown)¹.

Table 1: Sample characteristics across levels of average maternal alcohol intake in pregnancy

	Average number of drinks per week				Total
	0	1-4	5-8	9+ ¹	
Number of participants	715	630	169	19	1,533
Sampling fraction	8.0 (1.5/49.6)	5.5 (1.2/22.8)	65.6 (34.3/76.5)	95.0 (57.9/95.0)	9.7 (1.5/49.6)
Timing of interview (<i>Gestational week</i>)	16.0 (13.0/23.0)	17.0 (13.0/24.0)	17.0 (13.0/23.0)	17.0 (12.0/28.0)	17.0 (13.0/23.0)
Family characteristics					
Maternal age, years (<i>Mean ± SD</i>)	29.8 ± 4.3	31.4 ± 4.1	33.1 ± 4.4	35.2 ± 4.3	30.9 ± 4.4
Parity					
0 (%)	55.8	49.8	29.6	15.8	50.0
1 (%)	30.8	31.1	41.4	42.1	32.2
2+ (%)	13.4	19.0	29.0	42.1	17.8
Maternal BMI, kg/m ² (<i>Median, 10/90 pctile</i>)	22.7 (19.4/29.1)	22.6 (19.6/28.4)	22.5 (19.9/27.7)	21.6 (18.0/29.4)	22.6 (19.6/28.7)
Maternal marital status ² <i>Single (%)</i>	13.0	12.1	10.3	5.3	12.2
Parental education, years (<i>Median, 10/90 pctile</i>)	12.5 (11.0/16.0)	13.0 (11.0/16.0)	13.0 (11.0/17.0)	12.5 (11.0/17.0)	13.0 (11.0/16.0)
Family/home index <i>Suboptimal</i> ³ (%)	18.3	15.5	26.1	35.3	17.5

¹ Interview questions for average weekly alcohol consumption and binge drinking were asked separately thus a woman could report no average weekly drinking and also a binge episode, however for analyses participants were grouped according to average intake. A total of 266 women reported no average consumption of alcohol and no binge episodes.

Maternal IQ (<i>Mean ± SD</i>)	98.7 ± 15.1	101.2 ± 14.7	100.7 ± 15.8	102.4 ± 13.8	100.0 ± 15.0
Maternal smoking in pregnancy	29.8	24.3	39.6	52.6	28.9
<i>Smokers (%)</i>					
Postnatal parental smoking	30.8	31.5	39.8	52.2	32.3
<i>Smokers (%)</i>					
Maternal binge drinking in pregnancy ^A (%)	65.6	77.1	58.0	42.1	69.2
Child characteristics					
Sex					
<i>Male (%)</i>	48.4	52.4	56.2	52.6	50.9
Age at testing, years	5.2	5.2	5.2	5.3	5.2
(<i>Median, 10/90 pctile</i>)	(5.1/5.3)	(5.1/5.3)	(5.1/5.3)	(5.2/5.3)	(5.1/5.3)
Birth weight, grams	3600.1	3612.5	3552.7	3426.1	3597.8
±	± 529.3	± 508.2	± 482.1	± 586.4	± 516.6
Gestational age, days	281.0	282.0	282.5	275.0	281.0
(<i>Median, 10/90 pctile</i>)	(267.0/293.0)	(269.0/293.0)	(267.0/292.0)	(256.0/294.0)	(267.0/293.0)
Health status					
<i>Condition/medicine⁵ (%)</i>	3.1	2.9	5.8	5.9	3.5
Hearing abilities					
<i>Normal (%)</i>	96.6	94.0	95.9	84.2	95.2
Vision abilities					
<i>Normal (%)</i>	97.5	97.5	95.3	89.5	97.1

1. Range 9-14 drinks/week.
2. Single if single either in pregnancy or at follow-up (60-64 months postpartum).
3. Defined as a score on at least 2 of the following items: single parent household; changes in care giving; day care >8 hrs/day before age 3; 14 or more days away from home; irregular breakfast meals; maternal depression; high maternal or paternal alcohol use.
4. Defined as intake of 5 drinks or more at one occasion.
5. Medical conditions or regular medications that may influence test performance.

Table 2 shows the results of the main analysis of the association between alcohol exposure categories and scores on the DAP. The unadjusted model showed a small positive, non-significant effect of 1–4 units/per week on DAP raw scores and DAP IQ compared to the reference group. Exposure to 5-8 units/week had a small negative, insignificant effect. Exposure to 9 or more units/week was associated with a significantly lower average DAP IQ compared with the abstaining reference category (mean difference = 8.39, 95% CI = -14.58; -2.21). The number of observations in this group (9 or more units/week) was small, however, resulting in a wide CI and high uncertainty as to the size of the true effect. In the analyses, after adjusting for core and potential confounders, a similar pattern was observed with slightly smaller average differences, still insignificant for 1–4 and 5–8 units categories as compared to the reference. For 9 or more units/week, the effect was still significant after adjustment for core and all potential confounders (mean difference -6.26, 95% CI -12.14; -0.39). Table 2 shows essentially the same pattern of results for the DAP raw scores.

Table 2. Associations between maternal alcohol intake in pregnancy and DAP¹ raw scores and IQ scores.

Average no. drinks/week in pregnancy	Mean score	Crude		Adjusted for core confounders ²		Adjusted for core and potential confounders ³	
		Mean Difference	95% CI	Mean difference	95% CI	Mean difference	95% CI
	Raw score						
0	98.95	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	100.52	1.57	[-0.63; 3.78]	1.61	[-0.33; 3.56]	1.51	[-0.49; 3.51]
5-8	97.12	-1.83	[-5.22; 1.56]	-0.10	[-3.04; 2.84]	-0.14	[-3.23; 2.96]
9+	90.55	-8.39	[-14.58; -2.21]	-7.48	[-12.89; -2.06]	-6.26	[-12.14; -0.39]
<i>p value</i> ⁴		0.007		0.008		0.040	
	IQ score						
0	12.15	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	12.7952	0.64	[-0.33; 1.62]	0.65	[-0.21; 1.51]	0.61	[-0.28; 1.49]
5-8	11.28	-0.87	[-2.35; 0.62]	0.10	[-1.40; 1.19]	-0.13	[-1.49; 1.24]
9+	8.45	-3.70	[-6.25; -1.15]	3.34	[-5.56; -1.12]	-2.80	[-5.24; -0.37]
<i>p value</i>		0.004		0.005		0.032	

1. Draw-a-Person Intellectual Ability Test for Children, Adolescents, and Adults.
2. Parental education, maternal IQ, prenatal maternal smoking, the child's sex and age, and tester.
3. Parental education, maternal IQ, prenatal maternal smoking and binge drinking, maternal age, parity, prenatal and postnatal marital status, postnatal parental smoking, maternal pre-pregnancy BMI, the child's sex, age, health status, hearing and vision on the day of testing, family/home environment, and tester.
4. *P*-value for the hypothesis of no difference in attention scores across levels of average alcohol intake.

As shown in Tables 3a and 3b, the results for binge drinking showed small and insignificant differences in DAP raw score and DAP IQ for all binge categories (yes/no, number, and timing of episodes). Analyses testing DAP raw scores for interactions between average consumption and binge drinking episodes showed significant interactions for both the unadjusted ($p = 0.003$) and adjusted analyses ($p = 0.002$ and 0.01 for analyses of core and all potential confounders). For analyses of the DAP IQ scores, the corresponding p -values were 0.004 , 0.003 , and 0.01 . Because of the significant interactions, results of stratified analyses are presented in Tables 4a and 4b. For both raw and IQ scores, the tables show only significant associations between average consumption level and DAP score for children of mothers with binge drinking episodes. While the effect was only observed for the small group with a consumption level of 9 or more drinks per week, it is noteworthy

that the effect on raw scores was significant for the much larger group of children whose mothers consumed 5-8 drinks per week during pregnancy.

Finally, the significant effect of an average consumption of 9 or more drinks per week remained significant in supplementary analyses including gestational age and birth weight as covariates (results not shown). DAP and WPPSI-R IQ scores showed similar trends across alcohol categories (results not shown).

The correlations between DAP raw scores and WPPSI-R were 0.39 , 0.25 , and 0.41 (results not shown). The correlations between the DAP IQ and WPPSI-R Full Scale, verbal, and performance IQs were 0.36 , 0.21 , and 0.38 respectively, while the corresponding partial correlations controlling for sex were 0.33 , 0.22 , and 0.33 .

Table 3a. Associations between maternal binge drinking in pregnancy and DAP¹ raw scores, Denmark 2003-2008

	Crude			Adjusted for core confounders ²		Adjusted for potential	
	Mean score	Mean difference	95% CI	Mean difference	95% CI	Mean difference	95% CI
Binge drinking in							
N	12.27	Reference	-	Reference	-	Reference	-
Y	12.75	0.48	[-0.30; 1.26]	0.29	[-0.42; 1.00]	0.13	[-0.60; 0.86]
<i>p</i> -		0.230		0.416		0.72	
Number of binge drinking episodes in							
0	12.27	Reference	-	Reference	-	Reference	-
1	12.80	0.53	[-0.33; 1.39]	0.27	[-0.50; 1.04]	0.16	[-0.62; 0.94]
2	12.63	0.36	[-0.76; 1.48]	0.24	[-0.76; 1.24]	-0.12	[-1.17; 0.92]
3	12.71	0.44	[-1.07; 1.94]	0.54	[-0.91; 1.98]	0.45	[-1.03; 1.93]
<i>p</i> -		0.678		0.855		0.87	
Timing of binge drinking episodes in pregnancy (gestational							
No binge drinking	12.27	Reference	-	Reference	-	Reference	-
1	12.97	0.69	[-0.42; 1.81]	0.45	[-0.58; 1.48]	0.32	[-0.75; 1.40]
3	12.49	0.22	[-0.89; 1.33]	-0.05	[-1.03; 0.92]	-0.24	[-1.23; 0.75]
5	13.76	1.48	[0.37; 2.60]	1.07	[0.01; 2.13]	1.02	[-0.03; 2.07]
9	12.67	0.39	[-0.76; 1.55]	0.54	[-0.54; 1.62]	0.33	[-0.79; 1.45]
Multiple episodes	12.44	0.16	[-0.98; 1.31]	0.21	[-0.82; 1.24]	-0.01	[-1.09; 1.07]
<i>p</i> -		0.177		0.404		0.38	

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3. Parental education, maternal IQ, prenatal maternal smoking and average weekly alcohol intake, maternal age, parity, prenatal and postnatal marital status, postnatal parental smoking, maternal pre-pregnancy BMI, the child's sex, age, health status, hearing and vision on the day of testing, family/home environment, and tester.
4. *P*-value for the hypothesis of no difference in DAP scores across levels of average alcohol intake.

Table 3b. Associations between maternal binge drinking in pregnancy and DAP¹ IQ scores, Denmark 2003-2008

	Crude			Adjusted for core confounders ²		Adjusted for potential confounders ³	
	Mean score	Mean difference	95% CI	Mean difference	95% CI	Mean difference	95% CI
Binge drinking in pregnancy							
No	99.32	Reference	-	Reference	-	Reference	-
Yes	100.28	0.96	[-0.81; 2.74]	0.56	[-1.04; 2.16]	0.15	[-1.49; 1.80]
<i>p-value</i> ⁴		0.286		0.495		0.854	
Number of binge drinking episodes in pregnancy							
0	99.32	Reference	-	Reference	-	Reference	-
1	100.32	1.00	[-0.95; 2.95]	0.41	[-1.32; 2.15]	0.15	[-1.62; 1.91]
2	100.18	0.87	[-1.63; 3.38]	0.62	[-1.61; 2.85]	-0.24	[-2.58; 2.10]
3+	100.25	0.94	[-2.50; 4.37]	1.20	[-2.09; 4.49]	0.94	[-2.44; 4.32]
<i>p-value</i>		0.766		0.880		0.930	
Timing of binge drinking episodes in pregnancy [gestational week]							
No binge drinking	99.32	Reference	-	Reference	-	Reference	-
1-2	100.68	1.37	[-1.16; 3.89]	0.83	[-1.50; 3.16]	0.52	[-1.90; 2.95]
3-4	99.70	0.39	[-2.12; 2.89]	-0.22	[-2.42; 1.98]	-0.67	[-2.89; 1.56]
5-8	102.41	3.10	[0.57; 5.62]	2.17	[-0.23; 4.58]	2.04	[-0.35; 4.43]
9+	99.97	0.66	[-1.96; 3.27]	0.97	[-1.49; 3.43]	0.45	[-2.10; 3.01]
Multiple episodes	99.73	0.41	[-2.18; 3.01]	0.53	[-1.80; 2.85]	-0.02	[-2.46; 2.42]
<i>p-value</i>		0.265		0.538		0.497	

1. Draw-a-Person Intellectual Ability Test for Children, Adolescents, and Adults
2. Parental education, maternal IQ, prenatal maternal smoking, the child's sex and age, and tester.
3. Parental education, maternal IQ, prenatal maternal smoking and average weekly alcohol intake, maternal age, parity, prenatal and postnatal marital status, postnatal parental smoking, maternal pre-pregnancy BMI, the child's sex, age, health status, hearing and vision on the day of testing, family/home environment, and tester.
4. *P*-value for the hypothesis of no difference in DAP scores across levels of average alcohol intake.

Table 4a. Associations between maternal alcohol intake in pregnancy and DAP¹ raw scores by prenatal binge drinking status.

Average no. drinks/week in pregnancy	Mean score	Crude		Adjusted for core confounders ²		Adjusted for potential confounders ³	
		Mean Difference	95% CI	Mean difference	95% CI	Mean difference	95% CI
No binge drinking (n = 472)							
0	11.95	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	12.70	0.75	[-0.56; 2.06]	0.74	[-0.42; 1.89]	0.67	[-0.51; 1.85]
5-8	12.83	0.88	[-0.67; 2.43]	1.49	[0.03; 2.95]	1.71	[0.14; 3.28]
9+	11.09	-0.86	[-4.26; 2.54]	-0.87	[-4.02; 2.29]	-0.81	[-4.67; 3.04]
<i>p value</i> ⁴		0.485		0.151		0.133	
Binge drinking (n = 1061)							
0	12.82	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	12.98	0.17	[-0.81; 1.13]	0.04	[-0.79; 0.86]	0.16	[-0.70; 1.01]
5-8	10.11	-2.71	[-4.74; -0.68]	-1.59	[-3.16; -0.02]	-1.32	[-2.82; 0.18]
9+	5.86	-7.00	[-9.73; -4.19]	-6.26	[-8.38; -4.14]	-5.48	[-7.70; -3.26]
<i>p value</i>		<0.001		<0.001		<0.001	

1. Draw-a-Person Intellectual Ability Test for Children, Adolescents, and Adults.
2. Parental education, maternal IQ, prenatal maternal smoking, the child’s sex and age, and tester.
3. Parental education, maternal IQ, prenatal maternal smoking and binge drinking, maternal age, parity, prenatal and postnatal marital status, postnatal parental smoking, maternal pre-pregnancy BMI, the child’s sex, age, health status, hearing and vision on the day of testing, family/home environment, and tester.
4. *P*-value for the hypothesis of no difference in DAP scores across binge categories.

Table 4b. Associations between maternal alcohol intake in pregnancy and DAP¹ IQ scores by prenatal binge drinking status.

Average no. drinks/week in pregnancy	Mean score	Crude		Adjusted for core confounders ²		Adjusted for potential confounders ³	
		Mean Difference	95% CI	Mean difference	95% CI	Mean difference	95% CI
No binge drinking (n = 472)							
0	98.51	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	100.38	1.87	[-1.08; 4.82]	1.87	[-0.75; 4.49]	1.72	[-0.96; 4.39]
5-8	100.73	2.22	[-1.33; 5.72]	3.58	[0.23; 6.93]	4.07	[0.47; 7.67]
9+	96.91	-1.60	[-9.39; 6.18]	-1.56	[-8.80; 5.68]	-1.44	[-10.26; 7.37]
<i>p value</i> ⁴			0.431		0.127		0.113
Binge drinking (n = 1061)							
0	100.43	<i>references</i>	-	<i>references</i>	-	<i>references</i>	-
1-4	100.82	0.38	[-1.82; 2.58]	0.07	[-1.80; 1.94]	0.32	[-1.61; 2.26]
5-8	94.40	-6.03	[-10.67; -1.40]	-3.53	[-7.10; 0.05]	-2.91	[-6.31; 0.50]
9+	84.31	-16.12	[-23.40; -8.84]	-14.44	[-19.88; -8.99]	-12.70	[-18.36; -7.05]
<i>p value</i>			<0.001		<0.001		<0.001

1. Draw a Person Intellectual Ability Test for Children, Adolescents, and Adults
2. Parental education, maternal IQ, prenatal maternal smoking, the child’s sex and age, and tester.
3. Parental education, maternal IQ, prenatal maternal smoking and binge drinking, maternal age, parity, prenatal and postnatal marital status, postnatal parental smoking, maternal pre-pregnancy BMI, the child’s sex and age, health status, hearing and vision on the day of testing, family/home environment, and tester.
4. *P* value for the hypothesis of no difference in DAP scores across binge categories.

5. Discussion

This study examined potential effects of low to moderate prenatal alcohol consumption and binge

drinking on grapho-motor skills, as measured by the DAP, of children at age five years. An adverse effect was found for children whose mothers consumed nine or more drinks per week and reported binge episodes during early pregnancy. Children of mothers who drank at this moderate level and binged scored on average 6 points lower compared to children of mothers who did not consume any alcohol during pregnancy. This estimate was, however, accompanied by a wide confidence interval due to the small number of women in this consumption category, but the findings are consistent with previous studies of the LDPS which examined other areas of neurodevelopment (Kesmodel, et al., 2012a). While the majority of children scored within the normal range on the DAP, the lower performance of children with prenatal alcohol exposure as a group that is six points lower compared to children without prenatal alcohol exposure is functionally relevant since it is approximately half a standard deviation. Over the course of development, it would be expected that this gap would widen and children with exposure would encounter more and more difficulty with grapho-motor skills such as learning to write or complete complex assembly tasks.

Previous studies have found significant bivariate correlations between DAP and the WPPSI-R full scale IQ (Reynolds & Hickman, 2004). This finding was replicated in the present study with a sample of children with prenatal exposure to alcohol. As would be expected, the correlation with performance IQ was higher than with verbal IQ (0.38 vs. 0.21). Similar trends were observed across all alcohol exposure categories.

An important finding of this study was the statistically significant interaction between maternal average consumption level and binge

drinking episodes during pregnancy. While children whose mothers drank

9 or more drinks per week performed worse on the DAP than children whose mothers did not consume alcohol while pregnant, this effect was more pronounced for children of mothers who in addition to high average consumption also had binge drinking episodes. However, this finding must be viewed with caution given the small number of children in this category. Table 1 shows only 19 children in the category and among these only 8 were children of mothers with binge episodes. Although with such a small sample size the results might be sensitive to weighting according to sampling fractions, a supplementary analysis showed similar results for an unweighted analysis.

If the interaction between average consumption and binge drinking episodes observed for the DAP scores is replicable in future studies, it would reinforce the suggestion of adverse effects being associated with high BAC in very important ways. Although such studies for neurodevelopment are yet to be conducted, a study of fetal death has shown such an effect (Strandberg-Larsen et al., 2008). Clearly, maternal characteristics associated with an alcohol consumption pattern of a relatively high average level in combination with binge drinking episodes must be factored into the fuller picture. The present study tried to address this issue by inclusion of a wide range of potential confounding factors included in statistical models. In particular, this study controlled for parental education and maternal intelligence, which have been shown to be critical in the prediction of child intelligence and other neurodevelopmental functions (Eriksen et al., 2013).

Studies of neurodevelopmental outcomes for children with low to moderate prenatal exposure to alcohol remain challenging and have significant limitations. As with all studies about lifestyle behaviors during pregnancy,

exposure information may be subject to recall bias. This is especially true for alcohol because of social stigma associated with drinking during pregnancy, although in some locations such as Denmark, this may be less of an issue. Further, this study used only one measure of graphomotor skills, the Draw-a-Person test. It is possible that this measure failed to detect very subtle effects below the exposure level of nine drinks per week or in the absence of binge episodes. Finally, although many covariates were included, the possibility of residual confounding from unaccounted factors remains.

6. Conclusion

This study showed decreased performance on the DAP for 5-year-old children who were prenatally exposed to nine or more alcoholic drinks per week and whose mothers experienced binge drinking episodes during early gestation. Very importantly, this study showed a significant interaction between average weekly consumption of alcohol during pregnancy and binge episodes. This finding indicates that studies of neurodevelopmental outcomes in relation to prenatal alcohol exposure should account both for average weekly consumption of alcohol and binge drinking episodes. These findings support recommendations that women should not consume alcohol during pregnancy, and be especially aware of the dangers of binge drinking.

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