Is prenatal alcohol exposure related to inattention and hyperactivity symptoms in children? Disentangling the effects of social adversity

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Background: Studies concerning whether exposure to low levels of maternal alcohol consumption during fetal development is related to child inattention and hyperactivity symptoms have shown conflicting results. We examine the contribution of covariates related to social adversity to resolve some inconsistencies in the extant research by conducting parallel analyses of three cohorts with varying alcohol consumption and attitudes towards alcohol use. **Methods:** We compare three population-based pregnancy-offspring cohorts within the Nordic Network on ADHD from Denmark and Finland. Prenatal data were gathered via self-report during pregnancy and birth outcomes were abstracted from medical charts. A total of 21,678 reports concerning inattention and hyperactivity symptoms in children were available from the Strengths and Difficulties Questionnaire or the Rutter Scale completed by parents and/or teachers. **Results:** Drinking patterns differed cross-nationally. Women who had at least some social adversity (young, low education, or being single) were more likely to drink than those better off in the Finnish cohort, but the opposite was true for the Danish cohorts. Prenatal alcohol exposure was not related to risk for a high inattention-hyperactivity symptom score in children across cohorts after adjustment for covariates. In contrast, maternal smoking and social adversity during pregnancy were independently and consistently associated with an increase in risk of child symptoms. **Conclusions:** Low doses of alcohol consumption during pregnancy were not related to child inattention/hyperactivity symptoms once social adversity and smoking were taken into account. **Keywords:** ADHD, alcohol, inattention/hyperactivity symptoms, prenatal, social factors, behavior problems, cross-cultural, longitudinal studies. **Abbreviations:** LAA: liberal attitude to alcohol; SAA: strict attitude to alcohol.

Ample experimental work using animal models shows that prenatal exposure to high levels of alcohol is neurotoxic (Ikonomidou et al., 2000) and some human studies link high levels of alcohol consumption in pregnancy to neurobehavioral deficits in children (Streissguth, Bookstein, Sampson, & Barr, 1989). We focus on the possible association between prenatal alcohol exposure and inattention and hyperactivity. These symptoms are connected with poor scholastic performance in general population samples (Rodriguez et al., 2007), are core symptoms of attention deficit hyperactivity disorder (ADHD; APA, 1994), and are commonly seen in all forms of fetal alcohol spectrum disorders (FASD; e.g., Kodituwakku, 2007).

Despite findings that prenatal alcohol exposure in high doses is a possible causal factor of neurobe-

havioral symptoms, some issues remain. Prenatal alcohol exposure affects males and females differently (Weinberg, Sliwowska, Lan, & Hellemans, 2008) and despite the fact that ADHD symptoms are more common among males, human studies do not typically report results separately by sex. Further, human studies have produced inconsistent findings in regard to inattention and hyperactivity (Coles, 2001) and bring up the issue of whether social factors play a role. The incidence of severe cases of FASD varies by socioeconomic status (SES; Abel, 1995) and many studies of heavy alcohol users have often been conducted on low SES samples, a limitation previously highlighted by Linnet and colleagues (2003). The relation between SES and alcohol use is complex (Ebrahim et al., 1998; Rosell, De Faire, & Hellenius, 2003) and low to moderate use is seen more frequently in higher SES groups (e.g., Sayal, Heron, Golding, & Emond, 2007).

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Moreover, other social factors, e.g., single-parent-hood, are related to both lower SES (Gladstone, Levy, Nulman, & Koren, 1997) and behavioral problems in children (Biederman et al., 1995). Thus, social risks may confound drinking patterns differentially, which makes direct comparisons across studies difficult. These problems may account for inconsistencies if these social forces are related to the endpoint.

A related issue has to do with attitudes towards drinking in general and during pregnancy, which vary between populations and culture (May et al., 2006). Many societies stigmatize drinking among pregnant women while light drinking in others is accepted. This has consequences for the quality of the data on alcohol use we obtain and for the confounder structure in the population we compare.

Drinking is often accompanied by other risk factors related to social adversity (Leonardson, Loudenburg, & Struck, 2007) and other substance use, which raises a third issue: the co-occurrence of alcohol with smoking. These two behaviors often co-occur (Pirie, Lando, Curry, McBride, & Grothaus, 2000; Ethen et al., 2008), although the relation may be complex (Murray, Cribbie, Istvan, & Barnes, 2002). Both smoking and alcohol consumption covary with SES and with indices of social adversity (Mohsin & Bauman, 2005) and with the endpoint. Inattention and hyperactivity symptoms in childhood have been linked to prenatal smoking exposure in prospective studies (Kotimaa et al., 2003; Linnet et al., 2005; Rodriguez & Bohlin, 2005). However, it is still undetermined to what extent these prenatal exposures are independently related to symptoms in childhood in the context of social adversity.

Our aim was to study prenatal alcohol exposure in three large population-based pregnancy cohorts launched during the 1980s or 1990s in Denmark and Finland in relation to inattention and hyperactivity symptoms in children. Smoking cessation was recommended in both countries, but there were no official recommendations concerning alcohol use in pregnancy during the 1980s in Denmark, while abstinence or limited intake was recommended in both Finland and Denmark in the 1990s. Generally, alcohol consumption in Denmark is characterized by frequent light drinking (i.e., liberal attitude to alcohol (LAA)); in comparison, less frequent but somewhat heavier drinking is common in Finland, albeit socially unacceptable (i.e., strict attitude to alcohol (SAA)). Our strategy was to take advantage of these differences. We expected confounding by social factors to differ between the Finnish and Danish cohorts and that social confounding would be more likely in Finland (characterized by SAA). Our previous work showed that prenatal smoking was related to inattention and hyperactivity symptoms (Obel et al., 2008). Here, we extend this work by focusing on alcohol consumption in light of social adversity and examining sex differences.

We took an additive approach to social adversity in that we did not consider one factor to be more adverse than another, but created a composite variable that reflected whether or not some adversity related to socio-demographics was experienced, which is a similar approach to that taken by Rutter and co-workers (Rutter, Tizard, Yule, Graham, & Whitmore, 1976). We conducted parallel analyses to make direct comparisons possible to determine whether alcohol consumption during pregnancy was related to reports of inattention and hyperactivity symptoms in boys and girls. Prenatal ethanol exposure in animal models affects males and females differently (Hofmann, Ellis, Yu, & Weinberg, 2007). Our prediction was that unadjusted associations between alcohol exposure and behavioral problems would be more pronounced in the Finnish data, because a higher portion of drinkers in that population would have social problems or psychological reasons to drink, as drinking is considered socially unacceptable (SAA), than in the Danish population (LAA). Although analyses can never fully adjust for life-long social conditions, this difference was expected to diminish after adjustment for smoking and social determinants of alcohol behavior.

Methods

Cohorts

Data come from three prospective pregnancy cohorts within the Nordic Network on ADHD, two from Denmark (LAA) and one from Finland (SAA). Pregnant mothers, literate in the local language, were consecutively recruited in early pregnancy via governmentally run antenatal health services, which offer high-quality standardized care used by essentially all women (Delvaux & Buekens, 1999). Recruitment periods were relatively short and we did not identify the very small subsample of siblings. Data come from self-administrated questionnaires on current socio-demography and lifestyle habits collected during pregnancy in each cohort.

At follow-up, mothers of live-born children were traced through the national population-based registries in each country that identify residents by unique personal numbers, which we linked to obtain current addresses. We used data for singletons only and excluded twins because negative birth outcomes are more common among twins. Owing to the time constraints of data collection, the possibility of sibling pairs being included in the cohorts was very limited; approximately 50 sibling pairs were present in the Aarhus Birth Cohort (ABC), 347 sibling pairs in Healthy Habits for Two (HHT), and none in the Northern Finland Birth Cohort (NFBC). All cohorts collected data on child behavior symptoms from parents and/or teachers via postal questionnaire (Table 1). Permission to contact teachers was obtained from parents in the cohorts where teachers' ratings were solicited. The local research ethics committees approved the studies.

Table 1 Background characteristics

	Aarhus Birth Cohort (ABC)	Healthy Habits for Two (HHT)	Northern Finland Birth Cohort 1986 (NFBC)
Location	Aarhus Denmark	Aalborg/Odense, Denmark	Oulu and Lapland Provinces, Finland
Gestational week	16	36	24
Year of birth	1990–2	1984–7	1985–6
N ¹	8244	11148	9203
Prenatal Exposures			
Alcohol consumption, N (%)			
Nondrinker	4437 (53.8)	3943 (35.4)	7734 (84.7)
Drinker	3496 (42.4)	7203 (64.6)	1195 (13.1)
Missing	311 (3.8)	2 (.02)	206 (2.3)
1–4 drinks per week	3166 (38.4)	6124 (54.9)	900 (9.9)
≥ 5 drinks per week	330 (4.0)	1004 (9.1)	30 (.3)
Missing	311 (3.8)	77 (.7)	471 (5.2)
Smoking, N (%)			
Nonsmoker	5547 (67.3)	6171 (55.4)	6477 (70.9)
Smoker	2664 (32.3)	4914 (44.1)	2589 (28.3)
Missing	33 (.4)	63 (.6)	69 (.8)
Maternal age			
<20 years	158 (1.9)	338 (3.0)	397 (4.4)
≥ 20 years	8086 (98.1)	10800 (96.9)	8738 (95.6)
Missing	0 (.0)	10 (.1)	0 (.0)
Mother's education, N (%)			
<11 years	2561 (31.1)	7308 (65.6)	2100 (23.0)
≥11 years	3373 (40.9)	3804 (34.1)	5815 (63.7)
Missing	2310 (28.0)	36 (.3)	1220 (13.4)
Family structure, N (%)			
Single	1253 (15.2)	646 (5.8)	465 (5.1)
Married/cohabiting	4683 (56.8)	9904 (88.8)	8641 (94.6)
Missing	2308 (28.0)	598 (5.4)	29 (.3)
Social adversity ² , N (%)			
0	2783 (33.8)	3668 (32.9)	6532 (71.5)
1	2528 (30.7)	6696 (60.1)	2241 (24.5)
≥2	663 (8.1)	777 (10.0)	333 (3.6)
Missing	2270 (27.5)	7 (.1)	29 (.3)
Follow-up characteristics			
Year of follow-up	2001	2002	1993–4
Age at follow up	10, 11 or 12 years	7–15 years	8 years
Retention, % ³	61	70	91
Boys, %	51	51	51
Inattention / hyperactivity symptoms ⁴			
Available Informant	Parents	Teachers	Mothers only
High scores, N (%)			Teachers only
Boys	373 (8.8)	386 (9.1)	545 (9.5)
Girls	80 (2.0)	206 (5.1)	215 (4.0)

¹Total participants during pregnancy $N = 28,595$.

²Total number of adversities present (young maternal age, low educational attainment, and single-parenthood).

³Total participants at follow-up $N = 21,678$ (ABC = 5636 (of which parent data = 5109 and teacher data = 4334); HHT = 7752; NFBC = 8290)

⁴Sum score of core symptoms (fidgety, restless, and inattentive) from the SDQ (Denmark) or Rutter scale (Finland). Scores ranged 0–6; high scores defined as ≥4.

Aarhus Birth Cohort (ABC) 1990–92

All Danish-speaking women receiving prenatal care through Aarhus University Hospital, Denmark, were eligible and 98% were recruited at approximately gestational week 16, $N = 8244$ (Henriksen, Hedegaard, & Secher, 1994).

At follow-up in 2001 when children were 10–12 years old, parents reported on child health, behavior, and social conditions. Permission to contact children's primary teacher was solicited from participants and 65% of parents consented. We received completed child behavior questionnaires from 62% ($n = 4968$) of the

original sample with live births and known address ($n = 8036$) and 85% of eligible teachers ($n = 4208$), i.e., 52% of the whole sample.

Healthy Habits for Two (HHT) 1984–87

More than 80% of all pregnant women who attended their last routine antenatal visit around their 36th gestational week in Odense and Aalborg provinces, Denmark, participated, $N = 11,148$ (Olsen & Frische, 1993).

Follow-up questionnaires on child behavior, development, and general health conditions were mailed to

10,363 mothers in 2002 when adolescents were 15 years old. We received more than 70% ($N = 7844$). Teacher reports were not solicited.

Northern Finland Birth Cohort (NFBC) 1986

Approximately 99% of all pregnant women from the Oulu and Lapland provinces in northern Finland, who were expected to deliver between July 1985 and June 1986 ($N = 9362$), gave birth to 9203 live-born singletons (Järvelin, Hartikainen-Sorri, & Rantakallio, 1993). All participants completed a self-administered questionnaire, distributed at the first prenatal visit and returned by the 24th gestational week.

At follow-up in 1993–94 when children were 7–8 years old, we obtained teacher reports on child behavior. Parents who consented to contact with the teacher forwarded the questionnaire directly to teachers and we received reports for 92% ($N = 8525$) of the target population (children alive and address known). Parents reported on child behaviors other than the core ADHD symptoms we study and thus are not included in this report.

Prenatal measures

Data on alcohol consumption was self-reported on the prenatal questionnaires in all cohorts. The reports referred to the average consumption across pregnancy up until week 36 in ABC and HHT, and up until week 24 for NFBC.

Alcohol consumption per week was reported in ABC using 1, 1–4, or ≥ 5 categories, an exact number in HHT, and as 0, 5–20, or >20 in NFBC.

In order to perform parallel analyses for each cohort we transformed the variables using all possible information and maintaining as much detail as possible, which yielded the following categories: <1 , 1–4, or ≥ 5 or more alcoholic beverages per week. This categorization has been shown to be a reliable way of assessing self-reported alcohol intake during pregnancy (Kesmodel & Olsen, 2001). We used a dichotomized measure indicating whether or not women drank any alcoholic beverages during pregnancy. Women self-reported smoking habits. Response categories varied across the cohorts so we dichotomized smoking into nonsmoker versus smoker.

Socio-demographic data were collected in all cohorts. As an index of environmental adversity, each socio-demographic variable that we had available in all datasets was dichotomized to represent social adversity or not. Young maternal age, which is considered an index of biological immaturity and poorer social conditions (Chen et al., 2007), was coded as 1 for those younger than 20 years, i.e., representing adversity, and other ages as 0. Maternal education, an index of social class and negatively related to birth outcomes (Mortensen et al., 2008), was coded as <11 years (coded as 1) or ≥ 11 years (coded as 0), corresponding to compulsory education (i.e., high school level) or higher education. Family structure was defined as either single (coded as 1), which included other arrangements (e.g., living with relatives) or living with the expectant father (married or cohabitating, coded as 0). Single cohabita-

tion status is a risk factor for poor birth outcomes (Raatikainen, Heiskanen, & Heinonen, 2005). The three variables were summed to create a composite score, intended to reflect the cumulative load of maternal social adversity present during pregnancy, ranging between 0 and 3. Owing to incomplete data, as shown in Table 1 for over 2000 women, we allowed for one missing value. Because only a few participants had experienced all three indicators ($n = 141$) we collapsed this category to ≥ 2 , yielding the following categorizations: 0, 1, or ≥ 2 indicators.

Birth outcomes, recorded immediately after delivery, were abstracted from the medical charts. Gestational age in completed weeks was calculated from ultrasonography (for about 80%), date of last menstrual period, or both in all cohorts.

Behavioral outcomes

Parents and/or teachers rated inattention/hyperactivity symptoms using official translations of the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) or the Rutter scale (RB2; Rutter, 1967). These instruments have been clinically validated (Goodman, 1994; Goodman, Ford, Simmons, Gatward, & Meltzer, 2000) and are highly correlated (Goodman, 1994). The SDQ and the Rutter scale both measure hyperactivity (SDQ: items 2 and 10; RB2: items 1 and 3) and inattention (SDQ: 15 and RB2: 16) in the same way. Items are scored as: 0 (not true), 1 (somewhat true), or 2 (certainly true). We focused on these symptoms which were measured in all cohorts.

Both parents and teachers completed the SDQ in ABC, which referred to behavior during the past six months. In HHT a modified version of SDQ was used in which mothers retrospectively reported child behavior covering the entire school period from ages 7 to 15 years. The NFBC collected teacher reports on the Rutter scale pertaining to the previous 6 months.

We calculated total sum score for the three core inattention/hyperactivity symptoms (range: 0–6). This measure is similar to the hyperactive score as calculated according to the Rutter scale. We defined a high score corresponding to 4 or more points, which indicates that children had at least one 'severe' rating and two other symptoms were present. Children with scores of 4 or more showed scholastic impairment in the ABC and NFBC cohorts (Rodriguez et al., 2007).

Statistical analyses

We produced statistical analyses with SAS version 9.1; all statistical tests of hypotheses were two sided at $p < .05$. Our strategy was to conduct identical analyses in each cohort to determine whether any association with alcohol in addition to smoking and social adversity was replicable across time and national borders, and if so, whether the associations were of a similar magnitude. Our primary exposure was maternal alcohol consumption during pregnancy and the primary outcome was the dichotomized inattention/hyperactivity symptom score. To address the importance of environmental factors we examined patterns of drinking and social adversity, smoking, and attrition across cohorts.

We conducted multiple logistic regression models in each cohort, separately by gender. The first model examined unadjusted associations and the second model adjusted for smoking, social adversity, birth weight and gestational age.

Results

A total of 28,595 women were recruited in pregnancy. Table 1 shows background characteristics. Retention at follow-up was based on traceable live births in each cohort. As expected, women in Denmark (LAA) more often reported alcohol consumption than in Finland (SAA), and women from the Danish HHT during the 1980s reported the highest consumption. Cohorts were somewhat more similar on smoking status. In all cohorts, women with ≥ 2 indicators of social adversity clearly represented the extreme end of the continuum.

Attrition analyses showed that missing data on alcohol was related to maternal characteristics (Supplementary Table A), e.g., with young maternal age in ABC or age not reported in HHT. Attrition was highest in ABC and teacher data were missing especially for children of young mothers, 16%.

The social adversity variables were significantly correlated in each cohort, indicating that variables clustered in the same way, and indicate that usage of a composite variable is justified (Supplementary Table B).

Table 2 presents the characteristics of women by alcohol consumption and smoking. As expected, drinking patterns reflected cultural and time trends. Generally women from the Danish cohorts who consumed alcohol were older and more educated, while their counterparts in the Finnish cohort were more often single in addition to being smokers. The composite of social adversity clearly shows that alcohol consumption and adversity concurred in Finland, whereas the opposite was true in Denmark. Smoking was related to social adversity in all cohorts.

To test whether alcohol consumption was independently related to child inattention/hyperactivity symptoms, we ran multiple logistic regression models by sex and cohort. The unadjusted results for alcohol exposure in boys (Table 3a) show significant associations between alcohol consumption and symptoms; however, the associations are in opposite directions between Danish and Finnish cohorts. Reduced risk is seen in the two Danish cohorts (LAA), while in Finland (SAA) an increase in risk is seen. The adjusted models show attenuated, statistically non-significant, associations with alcohol in all cohorts, with the exception of teacher data in ABC. The parent data in ABC showed that missing data on alcohol was associated with increased risk of symptoms for children, data not shown. For girls (Table 3b), the unadjusted results show reduction in

risk associated with 1–4 drinks per week, but the association only reached significance in ABC (parent and teacher data). Adjusted results revealed non-significant relations concerning alcohol exposure in HHT and NFBC cohorts as before, and associations with alcohol in ABC attenuated to non-significance. In both Danish cohorts, where some selective attrition could be observed with respect to alcohol consumption, we found that missingness on alcohol was associated with increase in risk, which was particularly strong in parent data from ABC and accounted for the overall significance in the unadjusted analyses (data not shown). Exposure to maternal smoking in almost all analyses and social adversity in all analyses were independently associated with increased risk of a high inattention/hyperactivity score in both boys and girls. Control of birth outcomes did not change the associations. We re-ran analyses entering the interaction term for alcohol consumption $\times$ smoking and found no significant interaction effects in any cohort or in either gender. We also corrected for the possibility of biased standard error estimates due to the inclusion of sibling pairs. Results for HHT (included 347 sibling pairs) using GEE (generalized estimating equations) were unchanged (in most cases only at the third decimal place).

Discussion

Taking all cohorts together, we found no consistent association between prenatal alcohol exposure and a high inattention/hyperactivity symptom score in children as reported by parents and/or teachers. As expected, only in the Finnish cohort was prenatal exposure to alcohol associated in unadjusted analyses with increased risk of behavioral deviations, and only in boys. Our data indicate that this may well be caused by different patterns of drinking alcohol while pregnant in the two countries and/or by confounding by social factors. If so, studies generally have to be interpreted with caution when coming from populations with strong social norms for abstinence during pregnancy.

The present results are a good illustration of potential confounding seen in the literature when sufficient attention is not given to covariates or if sufficiently complete data are unavailable. Indeed, unadjusted analyses showed results in opposite directions. The characteristics of women in the two countries differed markedly in relation to their reported alcohol consumption: higher consumption was related to greater adversity among Finnish women (SAA), whereas the reverse was true for women in the Danish cohorts (LAA). After adjustment for social adversities, smoking and birth outcomes, the associations with alcohol exposure attenuated.

Drinking differed markedly as expected between cohorts owing to differences in national attitudes,

Table 2 Weekly alcohol consumption and smoking by maternal characteristics and cohort

	N (%)					
	ABC			HHT		
	Nr. of Drinks/Week		Smoking	Nr. of Drinks / Week		Smoking
	1-4	≥5		1-4	≥5	
Maternal Age						
< 20 years	26 (22.8)	1 (.9)	76 (48.1)	94 (28.0)	6 (1.8)	224 (66.5)
20-24	309 (25.0)	10 (.8)	560 (42.0)	1423 (48.5)	132 (4.5)	1493 (50.7)
25-30	1216 (37.2)	97 (3.0)	1013 (30.2)	3132 (59.5)	486 (9.3)	2203 (41.9)
31-35	1124 (49.6)	122 (5.4)	674 (29.3)	1160 (59.1)	278 (14.2)	785 (39.9)
> 35 years	491 (46.6)	100 (9.5)	341 (31.9)	310 (54.5)	99 (17.4)	204 (35.9)
<i>p-value</i>		<.0001	<.0001		<.0001	<.0001
Education						
< 11 y	899 (36.2)	85 (3.4)	1027 (40.2)	3874 (53.4)	488 (6.7)	3646 (50.2)
> 11 y	1623 (48.4)	175 (5.2)	740 (22.0)	2236 (59.1)	515 (13.6)	1254 (33.1)
<i>p-value</i>		<.0001	<.0001		<.0001	<.0001
Family structure						
single- parenthood	462 (37.3)	76 (6.1)	535 (42.8)	327 (51.0)	67 (10.5)	420 (65.3)
married/ cohabitating	2064 (44.9)	183 (4.0)	1228 (26.3)	5490 (55.8)	896 (9.1)	4187 (42.5)
<i>p-value</i>		<.0001	<.0001		.06	<.0001
Social adversity						
0	1364 (49.4)	128 (4.6)	552 (19.9)	2165 (59.3)	491 (13.5)	1184 (32.4)
1	974 (39.6)	103 (4.2)	878 (34.8)	3634 (54.7)	466 (7.0)	3199 (48.1)
2-3	198 (30.6)	29 (4.5)	351 (53.1)	324 (42.0)	47 (6.1)	530 (68.5)
<i>p-value</i>		<.0001	<.0001		<.0001	<.0001
Smoking						
Nonsmoker	949 (41.5)	152 (3.3)		2617 (56.8)	461 (8.7)	443 (7.3)
Smoker	2207 (36.8)	175 (5.9)		3483 (53.7)	536 (9.5)	457 (18.6)
<i>p-value</i>		<.0001			.005	<.0001
Alcohol consumption						
Nondrinker			1480 (33.5)			1799 (46.0)
1-4 drinks per week			949 (30.1)			2617 (42.9)
≥5 drinks per week			152 (46.5)			461 (46.2)
<i>p-value</i>			<.001			.005
						1913 (24.8)
						443 (49.2)
						24 (80.0)
						<.0001

Table 3 Multiple logistic regression results for high inattention-hyperactivity symptom score by prenatal exposures (a, Boys and b, Girls).

		High scorer	Unadjusted model			Adjusted model		
Cohort	Variable	<i>N</i> (%)	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
(a)								
ABC	Alcohol consumption				.09			.38
Parent	abstainer	210 (16.4)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	149 (13.2)	.78	.62–.97	.03	.85	.67–1.07	.17
	≥ 5 drinks per wk	18 (14.9)	.89	.53–1.50	.66	.92	.54–1.56	.76
	Smoking							.26
	no	255 (13.8)				Ref	–	–
	yes	130 (18.2)				1.15	.90–1.47	.26
	Social adversity							<.0001
	0	140 (11.4)				Ref	–	–
	1	178 (16.2)				1.43	1.12–1.83	.004
	2–3	68 (28.8)				2.84	2.01–4.02	<.0001
	Birth weight ¹					.98	.96–1.01	.20
	Gestational age ²					1.00	.93–1.07	.95
ABC	Alcohol consumption				.003			.03
Teacher	abstainer	215 (20.4)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	139 (14.7)	.67	.53–.85	.001	.74	.58–.94	.01
	≥ 5 drinks per wk	15 (14.6)	.67	.38–1.18	.16	.68	.38–1.21	.19
	Smoking							.01
	no	227 (15.1)				Ref	–	–
	yes	145 (23.4)				1.40	1.09–1.80	.01
	Social adversity							<.0001
	0	119 (11.9)				Ref	–	–
	1	189 (20.4)				1.77	1.38–2.29	<.0001
	2–3	64 (31.7)				2.85	1.97–4.11	<.0001
	Birth weight ¹					.97	.95–.999	.04
	Gestational age ²					1.03	.96–1.11	.37
HHT	Alcohol consumption				.01			.17
Parent ³	abstainer	212 (15.7)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	290 (12.9)	.80	.66–.96	.02	.86	.71–1.04	.13
	≥ 5 drinks per wk	40 (10.6)	.64	.45–.91	.01	.75	.52–1.09	.13
	Smoking							<.0001
	no	266 (11.2)				Ref	–	–
	yes	277 (17.4)				1.48	1.22–1.79	<.0001
	Social adversity							<.0001
	0	126 (8.3)				Ref	–	–
	1	365 (16.3)				2.01	1.62–2.50	<.0001
	2–3	54 (24.3)				2.87	1.98–4.16	<.0001
	Birth weight ¹					1.00	.98–1.02	.88
	Gestational age ²					.98	.92–1.05	.56
NFBC	Alcohol consumption				.04			.36
Teacher ⁴	abstainer	407 (11.3)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	60 (14.8)	1.36	1.01–1.82	.04	1.16	.86–1.57	.34
	≥ 5 drinks per wk	3 (27.3)	2.94	.78–11.11	.11	2.14	.55–8.28	.27
	Smoking							<.0001
	no	291 (9.7)				Ref	–	–
	yes	202 (16.8)				1.64	1.33–2.02	<.0001
	Social adversity							.001
	0	319 (10.5)				Ref	–	–
	1	143 (13.8)				1.28	1.03–1.60	.03
	2–3	33 (22.9)				2.17	1.42–3.32	.0003
	Birth weight ¹					.99	.97–1.01	.21
	Gestational age ²					1.06	.98–1.14	.15
(b)								
ABC	Alcohol consumption				.09			.53
Parent	abstainer	117 (8.7)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	70 (6.6)	.74	.54–1.00	.05	.85	.62–1.17	.33
	≥ 5 drinks per wk	11 (10.7)	1.25	.65–2.40	.51	1.13	.57–2.27	.72
	Smoking							.02
	no	116 (6.5)				Ref	–	–
	yes	87 (11.5)				1.46	1.05–2.02	.02
	Social adversity							<.0001
	0	60 (4.8)				Ref	–	–

Table 3 (Continued).

Cohort	Variable	High scorer	Unadjusted model			Adjusted model		
		N (%)	OR	95% CI	p	OR	95% CI	p
1	91 (8.9)				1.83	1.28–2.61	.001	
2–3	55 (19.6)				4.08	2.66–6.26	<.0001	
ABC Teacher	Birth weight¹					1.00	.97–1.04	.96
	Gestational age²					.97	.88–1.07	.54
	Alcohol consumption				.08			.27
	abstainer	50 (4.4)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	24 (2.6)	.59	.36–.96	.03	.67	.40–1.12	.13
	≥ 5 drinks per wk	5 (5.0)	1.15	.45–2.95	.77	1.15	.44–3.00	.78
	Smoking							.10
	no	41 (2.7)				Ref	–	–
	yes	37 (5.6)				1.52	.92–2.51	.10
	Social adversity							<.0001
	0	16 (1.5)				Ref	–	–
	1	41 (4.6)				2.76	1.51–5.02	.001
	2–3	23 (8.6)				4.54	2.26–9.13	<.0001
	Birth weight¹					1.01	.96–1.07	.68
	Gestational age²					.98	.85–1.13	.74
HHT Parent ³	Alcohol consumption				.91			.90
	abstainer	73 (5.9)	Ref	–	–	Ref	–	–
	1–4 drinks per wk	118 (5.6)	.94	.70–1.27	.68	1.01	.74–1.37	.96
	≥ 5 drinks per wk	22 (5.9)	1.00	.61–1.63	.99	1.12	.68–1.85	.66
	Smoking							<.0001
	no	84 (3.9)				Ref	–	–
	yes	131 (8.2)				1.84	1.37–2.47	<.0001
	Social adversity							.01
	0	47 (3.6)				Ref	–	–
	1	148 (6.6)				1.70	1.20–2.39	.003
	2–3	20 (9.1)				1.97	1.11–3.48	.02
	Birth weight¹					.98	.95–1.02	.27
	Gestational age²					.94	.85–1.04	.21
	Alcohol consumption				.52			.39
	abstainer	103 (3.0)	Ref	–	–	Ref	–	–
NFBC Teacher ⁴	1–4 drinks per wk	8 (2.0)	.66	.32–1.36	.25	.60	.29–1.25	.17
	≥ 5 drinks per wk	0 (.0)	–	–	.99	–	–	.98
	Smoking							.04
	no	70 (2.4)				Ref	–	–
	yes	44 (3.9)				1.57	1.04–2.38	.04
	Social adversity							.02
	0	67 (2.3)				Ref	–	–
	1	39 (3.9)				1.65	1.09–2.50	.02
	2–3	9 (6.0)				2.25	1.03–4.89	.04
	Birth weight¹					1.03	.98–1.07	.22
	Gestational age²					1.02	.88–1.18	.81

¹OR for birth weight represents the change per 100 grams.²OR for gestational age represents the change per weeks.³Parents were the only available informant.⁴Teachers were the only available informant.

but also because of the time period involved. More women consumed alcohol in the mid-1980s than in the early 1990s in Denmark when recommendations changed. In this way, we can observe whether prevalence of alcohol consumption varies with high ADHD scores in children. Our results showed that social adversity, regardless of the prevalence of alcohol consumption, was significantly related to high ADHD scores.

We found no evidence for sexual dimorphic association with alcohol, as results did not substantially differ across gender. Much research shows that the prevalence of ADHD differs by sex and it is important to see if these differences relate to etiological factors.

Animal studies (Weinberg et al., 2008) show sexual dimorphism in relation to alcohol exposure with anxiety measures. Our results suggest that alcohol does not contribute to ADHD symptoms in either sex.

We had small attrition with respect to missing values for alcohol consumption for the pregnancy data, at most nearly 4% in the ABC cohort. However, missingness seems to have been selective, because young women were less likely to report their alcohol consumption in ABC or both maternal age and alcohol were missing in HHT. Moreover, ABC had the highest attrition at follow-up in general and a portion of children were lost to follow-up in relation to

missing values on one of the social adversity variables, leading not only to less power but also to bias. Analyses showed that in the two Danish cohorts, where attrition was greater, missingness on alcohol was related to somewhat higher risk.

Social adversity was consistently associated with substantially increased risk of a high inattention/hyperactivity symptom score in children across all cohorts. Our social adversity variables were selected because they index low SES, and to some extent biological risk during pregnancy, perhaps indexing unmeasured confounding such as diet or psychological stress related to economic and social difficulties. The composite variable represents the cumulative load of indicators of adversity. The presence of just one adversity was enough to increase risk for the child by about 90% (odds averaged across cohorts from Table 3) and the presence of two adversities increased risk by 2.5 times. These results show very powerful associations that have implications for public health. In terms of mechanisms, it may be that social adversity is related to stress and previous work has linked prenatal maternal stress to ADHD symptoms in children (Rodriguez & Bohlin, 2005). Moreover, these social adversity factors may exert a powerful impact during postnatal development, e.g., in terms of poor material resources and parenting. These postnatal influences may have an additive effect and increase risk for children. Women from the Danish cohorts who consumed low amounts also had more resources in pregnancy (e.g., cohabitating) than the corresponding Finnish cohort. ADHD is associated with low educational attainment and more risk-taking behavior (Able, Johnston, Adler, & Swindle, 2007) as well as being largely explained by genetic factors (Schonwald & Lechner, 2006). Thus, our social adversity variable may not represent purely social programming, but may also carry some genetic loading.

Our work cannot answer questions regarding genetic differences between these populations which are known to stem from different genetic pools (Peltonen, Pekkarinen, & Aaltonen, 1995). Subtle genetic differences in the capacity to metabolize alcohol may be present between the populations. Furthermore, such metabolic differences most likely exist at the individual level, which underscores upholding conservative clinical recommendations to pregnant women.

Reporting bias due to stigmatization may be a limitation because we relied on self-reported alcohol consumption. A recent paper (Kelly et al., 2008) collected self-reports of pregnancy alcohol consumption retrospectively (9 months after the birth) and found that limited alcohol intake was not related to increased problems among 3-year-olds. Nonetheless, the reliability of reporting alcohol consumption may differ across populations depending on the stigmatization the behavior has locally and the procedures for obtaining data. However, smoking would also be expected to be affected by this sort of bias as

women were recommended not to smoke in all cohorts, yet we observed consistent associations that indicated an increased risk of symptoms by about 50% for boys and girls with self-reported smoking. Alcohol consumption and smoking were patterned differentially in relation to our social adversity index across cohorts, suggesting that social forces, perhaps even postnatally, may buffer children who were exposed to low levels of alcohol. Most women were generally low consumers of alcohol, thus the sort of adversity accompanying heavy alcohol use was most probably very limited among the alcohol-using families in this study.

Can we resolve the inconsistencies in the literature with regard to low alcohol exposure during prenatal development and neurobehavioral deficits in children with this study? This question, to be fully answered, requires multiple studies; the present work makes a step in the right direction as epidemiological studies need to take more of a hypothesis-testing approach by weighing in alternative explanations. Confounding by social factors will depend on culturally based attitudes regarding alcohol and if this confounding is not fully controlled for, the results will differ across cultural settings. The fact that we were able to detect strong and consistent associations with smoking and social adversity indicates that the endpoint measures were sufficiently sensitive. These results should not be taken to mean that alcohol consumption during pregnancy brings no harm to the child – there are a broad range of adverse effects related to alcohol exposure – but rather that low consumption is not likely to increase children's risk of reported inattention and hyperactivity symptoms. Social adversity played a major role, not only for alcohol consumption during pregnancy but also for increased risk of inattention/hyperactivity symptoms in children.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table A and Table B.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

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Rodriguez designed the analytic strategy and wrote the manuscript. Kotimaa compiled the datasets, performed initial analyses and Kotimaa and Obel contributed to initial manuscript preparation. All authors contributed to study concept and critical revision. Kaakinen performed statistical analyses,

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Key points

- Studies of prenatal exposure to maternal alcohol consumption in relation to inattention-hyperactivity symptoms in children are inconsistent.
- We compare three large prospective pregnancy-offspring cohorts that differ on attitudes concerning alcohol consumption.
- Alcohol consumption during pregnancy socially patterned differently across cohorts. Social adversity was related to consumption in Finland while the opposite was true for Denmark.
- After controlling for social adversity and smoking we found that alcohol did not increase risk for inattention-hyperactivity symptoms in children.
- Social adversity during pregnancy was a powerful and consistent risk factor for inattention-hyperactivity symptoms in children.

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