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Time-specific and Cumulative Effects of Exposure to Parental Externalizing Behavior on Risk for Young Adult Alcohol Use Disorder

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Abstract

Background—Previous studies indicate that parental externalizing behavior (EB) is a robust risk factor for alcohol use disorder (AUD) in their children, and that this is due to both inherited genetic liability and environmental exposure. However, it remains unclear whether the effects of exposure to parental EB vary as a function of timing and/or chronicity.

Methods—We identified biological parents with an alcohol use disorder, drug abuse, or criminal behavior, during different periods of their child's upbringing, using Swedish national registries. Logistic regression was used to determine whether the effect of parental EB exposure during different developmental periods differentially impacted children's risk for young adult AUD (ages 19–24). In addition, we tested how multiply affected parents and/or sustained exposure to affected parents impacted risk.

Results—While parental EB increased risk for young adult AUD, timing of exposure did not differentially impact risk. Having a second affected parent increased the risk of AUD additionally, and sustained exposure to parental EB across multiple periods resulted in a higher risk of young adult AUD than exposure in only one period.

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Contributors

ACE and SLL designed and conducted the analyses. ACE, KKJ, KSK, and KS conceived the research questions. ACE and SLL wrote the first draft of the manuscript and all authors contributed to and have approved the final manuscript.

Conflict of Interest

The authors have no conflicts of interest to report.

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Conclusions—In this well-powered population study, there was no evidence of “sensitive periods” of exposure to national registry-ascertained parental EB with respect to impact on young adult AUD, but sustained exposure was more pathogenic than limited exposure. These findings suggest developmental timing does not meaningfully vary the impact, but rather there is a pervasive risk for development of young adult AUD for children and adolescents exposed to parental EB.

Keywords

alcohol use disorder; sensitive period; externalizing behavior

1. Introduction

Parental externalizing behaviors (EB), including substance use disorders and antisocial or criminal behavior, are strong predictors of similar outcomes in children (1–8). This risk is conferred by both genetic liability and environmental exposures, as evidenced by genetically informative studies of adoptees and twins (9–11), and by studies exploring mediation across factors (12). Alcohol use disorder (AUD), which is moderately heritable (13), falls within the spectrum of outcomes associated with exposure to parental EB; however little is known about factors that may moderate these effects, such as timing and duration of exposure. In the current study of young adult AUD, we draw on tenets from developmental psychopathology to investigate patterns and effects of exposure to parental EB during upbringing, with an emphasis on differences in risk conferred by exposure during sensitive developmental periods and by exposures that accumulate over time. A better understanding of these temporal effects can inform targeted prevention of AUD.

Sensitive developmental periods refer to life phases such as middle childhood and adolescence during which exposures to risk factors and stressors may be particularly salient. For example, sensitive periods have been examined with respect to trauma exposure and later depression (14) and post-traumatic stress disorder (15). In the case of parental EB and young adult AUD, heightened risk is expected given instability likely to be experienced by children and adolescents exposed to parental EB, the role of parental modeling of EB (16), and the stress-sensitive and dynamic neurodevelopmental processes at play during these early years (17, 18). This question has been previously addressed in the context of child physical abuse. A recent study of US young adults found physical abuse starting in adolescence increased risk for pathological drinking behaviors including AUD (19). This is noteworthy, as early childhood represents a developmental period especially sensitive to the impact of child abuse on subsequent functioning (20). However, some studies have found that abuse exposure during adolescence leads to later alcohol misuse (21, 22). With respect to parental EB exposure, previous research has demonstrated that parental AUD has both proximal and distal effects on children’s externalizing behavior (23), of which AUD is a potential manifestation; it remains unclear whether those effects differ as a function of timing of exposure.

Another important aspect of parental EB exposure concerns its duration or chronicity. Accumulated risk refers to the build-up over time of repeated/sustained exposure to AUD

risk factors. Compounding of risks engendered in early developmental stages impacts later health and development (24). This concept is similar to the *cumulative risk hypothesis* (25), although here we are examining chronic exposure to a constellation of related risk factors grouped as exposure to parental EB rather than exposure to diverse risk factors. In the study of sequelae of child abuse, chronic exposure was associated with significantly increased risk of heavy drinking and AUD, and this risk was greater than that seen for time-limited child abuse (19). This line of questioning also can be applied to the impact of chronicity of parental EB exposure on AUD risk. Children of parents with EB likely experience more sustained exposure to a variety of environmental stressors than do their peers (26). As noted above, evidence that adoptive parental EB confers risk for AUD (11, 27, 28) confirms that environmental exposure is a risk factor. Because parental EB can remit, children exposed to parental EB during only some developmental periods may be at a lower risk for later AUD than their counterparts with sustained exposure.

Exposure to multiple affected parents can also be considered a form of cumulative risk. Prior studies have examined the effects of having one versus two parents with psychopathology with respect to offspring outcomes. While some studies have reported (non-additive) interactions between maternal and paternal psychopathology (29), others have not (30, 31). Thus, clarification is needed regarding the impact of multiple affected parents.

In the current study, we examine whether parental EB impacts the likelihood of young adult AUD differentially as a function of timing and chronicity of exposure. We also test the effects of cumulative exposure from two perspectives. First, how does having one versus two affected parents impact risk of young adult AUD, and does the gender of the affected parent differentially impact risk? Second, is parental EB exposure across multiple developmental periods more pathogenic than time-limited exposure? We explore these questions using the population of Sweden, for which data are available on substance abuse and criminal behavior in parents, as well as on AUD in their children. We anticipated that having a parent exhibit EB during adolescence would have a stronger influence on AUD risk than a similar exposure during early childhood. We further hypothesized that cumulative exposure to parental EB would act as a more potent risk factor than limited exposure.

2. Materials and Methods

2.1. Sample

These analyses are based on the Swedish population. The following national registries were used: 1) the Swedish Hospital Discharge Register, which included hospitalizations for people in Sweden from 1964 through 2010, classified by the main discharge diagnosis and eight secondary diagnoses; 2) the Multi-Generation Register linking children born after 1932 to their parents; 3) the National Census Registry, which provided information on education at 5-year increments (1960–1990); 4) the Total Population Registry, which included annual data on education from 1990 to 2009; and 5) the Swedish Crime Register, containing all convictions in lower court from 1973 to 2011.

Linking was based on individual Swedish 10-digit personal identification numbers, which are assigned at birth or immigration for all Swedish residents and used in all official records

for his or her lifetime. This number was replaced by a serial number to guarantee confidentiality for all individuals. The study was approved by the ethics committee in Lund, Sweden; subject consent was waived.

As described above and previously (2, 11, 27), information from various national registries is available across different time frames, which impacts the cohorts for which specific combinations of data are available. The current analyses incorporate the risk conferred by biological parental behavior; accordingly, we were limited to cohorts for whom biological parental data was available. We therefore examined outcomes for individuals born in Sweden between 1970 and 1984, for whom data on young adult (age 19–24) AUD were available. These individuals were divided into three cohorts to account for potential differences in the social environment over time. We included individuals who did not emigrate or die before age 24 and who had two registered biological parents in the multi-generation register. No further limitations were made for the parents.

2.2. Measures

2.2.1 Outcome variable—We defined AUD from the inpatient register, which covers the young adult period for all three cohorts, using ICD codes for alcohol abuse and related disorders as described elsewhere (11). Briefly, these include codes for alcohol related disorders such as abuse and dependence (F10), alcoholic liver disease (K70), alcohol induced pancreatitis (K85.2 and K86.0), and toxic effects of alcohol (T51), among other diagnoses. The current analyses focus on AUD during young adulthood (between ages 19–24).

2.2.2. Primary predictors—The primary risk factor of interest was exposure to parental externalizing behavior. This was operationalized as a registration for AUD (as defined above); a registration for drug use disorder (also from the inpatient register), using ICD codes described elsewhere (27); or a registration for criminal behavior. Criminal behavior was identified by convictions in lower court for violent crime, property crime, or white collar crime (32). We refer to this composite measure as *parental externalizing behavior (EB)*. Note that this measure likely represents relatively severe cases with high levels of EB due to its reliance on medical and criminal registrations; more moderate forms of externalizing behavior are unlikely to lead to such registrations. Parental EB was derived separately for each developmental period of interest (child age 0–6, 7–12, and 13–18; given the absence of defined ages corresponding to developmental periods, these ranges correspond to Swedish preschool, middle school and high school), such that if a *new* parental registration was identified during a given time period, exposure to parental EB was considered to be present (vs. absent) during that period.

2.2.3. Other covariates—We included sex, cohort, and parental education in all analyses. Cohort was based on year of birth (1970–1974, 1975–1979, or 1980–1984). Parental education was determined by the highest education level of the two parents and grouped as low (compulsory school only), middle (upper secondary school), or high (university level).

2.3. Statistical analyses

We investigated the association between AUD in young adulthood and parental EB using logistic regression. Parental EB in the three developmental periods can be combined in eight ways. Letting the first position represent parental EB between age 0–6, the second between 7–12, and the third between 13–18, the eight patterns can be denoted: (0,0,0), (1,0,0), (0,1,0), (0,0,1), (1,1,0), (1,0,1), (0,1,1), and (1,1,1). These patterns are included as a categorical variable in a single logistic regression model from which odds ratios were calculated, thus minimizing the number of tests. Absence of parental EB during all three time periods was the reference group. We report odds ratios (ORs) for comparisons of these parental EB patterns. As noted above, we adjust for parental education, sex, and cohort, and, based on preliminary analyses, we also allow the effect of cohort to be modified by sex. Besides ORs we also present the predicted probabilities, based on parameter estimates.

We also study the effect of maternal and paternal EB and investigate how associations are affected if both parents exhibit EB by including an interaction term between maternal and paternal EB into the model. In all analyses we account for familial clustering by allowing for a correlation between maternal siblings under the assumption of an exchangeable correlation structure. All analyses were performed in SAS 9.3 (SAS Institute, Cary NC).

3. Results

3.1. Descriptive statistics

For the current analyses, data were available for 1,399,489 young adults (Table 1). Correlations (SE) of parental EB exposure were modest to moderate across time: $r=0.48$ (0.002) between ages 0–6 and 7–12; $r=0.53$ (0.002) between ages 7–12 and 13–18; and 0.41 (0.003) between ages 0–6 and 13–18. Individuals who had a parent with a history of EB during any developmental period were at increased risk for young adult AUD (Table 2), with the adjusted odds ratios (AORs) ranging from 2.29 to 2.44 for those with one period of exposure, increasing to AORs of 3.31 to 3.85 for those with two periods of exposure, and up to 4.84 for those exposed during all three periods. Preliminary analyses indicated that although young adult AUD was more common among men, there was no interaction between gender and exposure pattern ($p = 0.85$). Therefore, subsequent analyses included both men and women, with gender as a covariate.

3.2. Effect of timing of exposure

Next we addressed whether the effect of parental EB exposure differed as a function of timing. These comparisons were limited to children exposed to parental EB during at least one developmental period. We compared the effect of exposure during a single period to the effect of exposure during the other periods. We also compared the effects of exposure during two periods; these could be contiguous or separated by a period of parental remission. These results (Table 3) indicate that the likelihood of AUD did not differ as a function of timing of exposure. Though we observed trends suggesting that earlier exposure was more pathogenic, confidence intervals always spanned unity.

3.3. Impact of affected parent gender and multiple affected parents

We next asked whether the risk of young adult AUD increased as a function of which parent was affected, or whether two affected parents conferred additional risk compared to one affected parent. Results, shown in Table 4, demonstrate that the gender of the affected parent did not differentially impact risk. However, the increase in risk conferred by the second affected parent was less than that conferred by the first (see Table 4 interaction term).

3.4. The effects of cumulative exposure

Finally, we asked whether risk of young adult AUD increases as a function of cumulative exposure to parental EB. We compared the odds of developing young adult AUD when exposed to parental EB during 2 vs. 1, 3 vs. 1, and 3 vs. 2 time periods. Results (Table 5) demonstrate that a higher degree of exposure confers greater risk. Among those children exposed to parental EB, each period of exposure increased the child's risk of developing AUD by young adulthood by up to an additional 50%.

4. Conclusions

The current analyses assessed the impact of parental EB on young adult AUD as a function of timing and accumulation of exposure. We found that any exposure to parental EB increased risk of young adult AUD, but there was no evidence that any of the time periods examined represented a particularly sensitive period: all were similarly pathogenic. We further found that cumulative exposure to parental EB in the form of sustained exposure across multiple developmental periods significantly increased AUD risk. However, while having two affected parents conferred greater risk than having a single affected parent, the effect of the second parent was lower than that of the first. These findings suggest that parental EB acts as a risk factor for offspring AUD regardless of the stage of social and cognitive development of the child during the period of exposure. The effects of sustained exposure may be indexing parental EB severity, which could increase risk via both biological (genetic) and environmental mechanisms.

Parental EB, operationalized as substance use problems, antisocial behavior, and/or criminal behavior, is a robust predictor of alcohol problems in their children. While some component of risk is conferred biologically – i.e., children of alcoholics inherit genetic variants that increase their own risk for AUD – prior research suggests that the *environmental* exposure to parental EB may also be pathogenic. For example, a previous study of Swedish adoptees indicated that individuals whose adoptive parents had a history of AUD or criminal behavior were more likely to develop AUD themselves (11). The effect size of an adoptive parent's AUD was similar to that of a biological parent's AUD, suggesting an important role for social modeling of antisocial behavior and substance use disorders. The environmental aspect of risk, unlike that which is heritable, is potentially temporally dynamic.

The current observation that risk of young adult AUD is uniformly increased regardless of exposure timing contrasts with studies that have identified “sensitive periods” of exposure to other risk factors for later AUD, such as child abuse (19, 21, 22). One possible interpretation of this finding is that risk is independent of the child's social, cognitive, and brain

development at the time of exposure. Another plausible explanation is that a parent's externalizing behaviors may be consistent throughout their child's development, even if the behavior does not meet the relatively high clinical thresholds used for these analyses. That is, even parents whose EB only meets our threshold during one of the three time frames are likely to exhibit subthreshold behavior during the other two periods; i.e., the behavioral issues of the parent may not in fact remit entirely. This is consistent with the finding that chronicity increases risk. We are likely underestimating the effect of chronicity of exposure since we are limited to detecting severe manifestations (that is, repeated parental EB registrations across time frames). A third possibility is that the risk conferred is primarily genetic, as that would not change across development. If this were the case, we could interpret the greater risk conferred by sustained exposure to be indicative of severity: Perhaps the more severely affected parents in turn pass on higher genetic liability to their offspring.

Regardless of the timing of the exposure, parental EB is detrimental and has long-term negative impacts on child development that can manifest in serious behavior problems, including patterns of alcohol use necessitating medical intervention and treatment. That these impacts were seen as early as ages 19 to 24 in the children of parents with EB suggests that swift and early family-based intervention is warranted to help curtail the inter-generational transmission of externalizing and substance use disorders, and that these interventions are important in all developmental stages.

While the nature of the data available for this study precludes detailed testing of hypotheses regarding mechanism, prior research provides some context. For example, one study (33) found that parental AUD and antisocial behavior were related to higher levels of child EB at ages 6–8, and that these effects were mediated through family conflict, parent-child conflict, and parental depression. The effects of parent-child conflict on children's EB and parental negativity – above and beyond genetic loading for EB – have been confirmed in genetically informative samples (34, 35). Other potential mediating factors include low parental monitoring, harsh parenting, and limited communication about alcohol use (36). In addition, sustained exposure to a stressor (e.g., abuse) has been shown to impact neurodevelopment (37), which could impact AUD risk. Though not all the studies above examined young adult AUD as the outcome, the strong relationship between early EB and later AUD suggests that such findings are potentially relevant to the current study.

We note a number of limitations to the current study. First, we did not capitalize on the genetically informative nature of the data. However, by limiting our analyses to biological families only, we eliminate complication of our findings by variation in genetic correlations such as between children and their biological versus step-parents. It is possible that associations between parental EB and young adult AUD are due in part to genetic liability shared across externalizing problems. Indeed, were genetic liability the underlying factor, we would not expect to observe period-specific influences of parental EB, as genetic liability would be temporally consistent. This possibility warrants further consideration in future studies.

Second, we have not accounted for parental death, which can be a risk factor for AUD (11). Furthermore, in the absence of two parents, having a single affected parent may differentially increase risk of young adult AUD. Third, parental EB prior to a child's birth, which could be considered informative of genetic risk that might not manifest after the child's birth, could not be assessed for all cohorts, and therefore was not included as a covariate. However, results were unchanged when this variable was accounted for in analyses replicated in only the youngest parental cohort. Fourth, we did not incorporate census data, so these analyses do not account for the fact that not all children lived with both parents during all time frames included. However, we conducted *post hoc* analyses restricted to families where census data confirmed that the child lived with both parents during a given time frame, and results did not substantively differ. Fifth, data availability precluded an examination of later adult AUD.

Finally, both the risk factor and outcome likely represent the severely affected end of the spectrum given that parents with EB and young adults with AUD were ascertained through registries. With respect to EB, our approach assumes that, in the absence of a parental registration for AUD, drug abuse, or criminal behavior during a given period, the offspring was not meaningfully exposed to parental EB. This is unlikely to be a reasonable assumption as EB may not entirely remit, and is a limitation of the data. However, the children exposed to the types of externalizing behaviors that can be ascertained via population registries represent those likely to be most in need of targeted services. With respect to AUD, our method primarily identifies young adults whose AUD has resulted in medical problems (more frequently due to acute rather than chronic use). These individuals may be at increased risk for later registrations and are in need of targeted intervention. Selection of severely-affected individuals with EB or AUD may result in an underestimation of effect sizes overall, but it is important to understand the etiology of AUD in these high-risk groups to inform intervention.

Despite these limitations, there are unique and compelling features of the Swedish register data. Its comprehensive nature ensures findings represent the entire Swedish population, and the population size enables us to detect predictive factors of modest effect. Furthermore, we do not rely on self-reports, reducing error due to recall bias or sincere misconceptions about one's own behavior. Sweden's socialized health care system increases the likelihood that individuals with drug or alcohol problems receive medical care (and are thus appropriately included in the current analyses) whereas in countries with less egalitarian systems those individuals would potentially be excluded from care as a function of income/resources.

In summary, these analyses provide evidence that parental EB exposure increases risk for young adult AUD regardless of the timing of that exposure with respect to the child's developmental period. Thus, there was no evidence of "sensitive periods" of exposure to parental EB. Furthermore, we demonstrate that cumulative exposure in the form of having at least one affected parent across multiple developmental time frames increases risk. Family-based interventions to serve adults with AUD, drug abuse and criminal histories, as well as their children, are needed to help prevent the development of AUD in young adults.

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Highlights

- Parental externalizing behavior predicts offspring AUD in young adulthood
- Timing of parental EB exposure does not differentially impact AUD risk
- Sustained parental EB exposure results in higher offspring AUD rates

Table 1

Sample sizes across predictors and outcomes.

	N (% of sample)	N (%) within Young Adults with AUD
<i>Cohort</i>		
1970–1974	515,947 (36.9%)	2,553 (42.0%)
1975–1979	449,322 (32.1%)	1,729 (28.5%)
1980–1984	434,220 (31.0%)	1,793 (29.5%)
<i>Total</i>	1,399,489	6075
<i>Gender</i>		
Males	722,257 (51.6%)	3,770 (62.1%)
Females	677,232 (48.4%)	2,305 (37.9%)
<i>Parental education</i>		
Low parental education	165,675 (11.8%)	1,010 (16.6%)
Mid parental education	455,431 (32.5%)	2,495 (41.1%)
High parental education	778,332 (55.6%)	2,570 (42.3%)
<i>Parental EB</i>		
EB in mother but not father	32,516 (2.3%)	211 (3.5%)
EB in father but not mother	110,878 (7.9%)	1,073 (17.7%)
EB in both mother and father	14,364 (1.0%)	220 (3.6%)
<i>Parental EB by period^I</i>		
(0,0,0)	1,241,731 (88.7%)	4,471 (73.6%)
(1,0,0)	55,598 (4.0%)	527 (8.7%)
(0,1,0)	39,922 (3.2%)	353 (5.8%)
(0,0,1)	37,526 (2.7%)	332 (5.5%)
(1,1,0)	6,910 (0.5%)	106 (1.7%)
(1,0,1)	3,586 (0.3%)	49 (0.8%)
(0,1,1)	5,941 (0.4%)	78 (1.3%)
(1,1,1)	8,275 (0.6%)	159 (2.6%)

^IThe trio of numbers in parentheses represents the three developmental periods under investigation (ages 0–6, 7–12, and 13–18). Thus, (1,0,0) indicates a new parental EB registration when the child was age 0–6, but not when the child was 7–12 or 13–18.

Table 2

Risk of young adult AUD, based on medical registration as described in the text. Odds ratios (ORs) are presented as a function of parental externalizing behavior, by period of exposure, before and after controlling for sex, cohort, and parental education.

Period of Exposure to Parental Externalizing Behavior	Unadjusted OR(95% CI) for AUD	Adjusted OR (95% CI) for AUD	Predicted Prevalence
None	Reference	Reference	0.38%
Age 0–6	2.60 (2.38; 2.84)	2.44 (2.23; 2.68)	0.92%
Age 7–12	2.46 (2.22; 2.74)	2.29 (2.05; 2.55)	0.86%
Age 13–18	2.45 (2.20; 2.74)	2.32 (2.07; 2.60)	0.87%
Ages 0–6 & 7–12	4.10 (3.39; 4.97)	3.85 (3.16; 4.68)	1.44%
Ages 0–6 & 13–18	3.77 (2.85; 4.99)	3.45 (2.58; 4.63)	1.29%
Ages 7–12 & 13–18	3.68 (2.96; 4.57)	3.31 (2.64; 4.15)	1.24%
All 3 time periods	5.32 (4.55; 6.21)	4.84 (4.12; 5.69)	1.80%

Table 3

Comparisons of the effects of timing of exposure to parental externalizing behavior, before and after controlling for sex, cohort, and parental education.

	Comparison	Unadjusted Model OR (95% CI)	Adjusted Model OR (95% CI)
1 period	(0,1,0) vs. (1,0,0) ^I	0.95 (0.83; 1.08)	0.94 (0.82; 1.07)
	(0,0,1) vs. (1,0,0)	0.94 (0.83; 1.08)	0.95 (0.83; 1.09)
	(0,0,1) vs. (0,1,0)	1.00 (0.86; 1.15)	1.01 (0.87; 1.18)
2 periods	(0,1,1) vs. (1,1,0)	0.90 (0.67; 1.19)	0.86 (0.64; 1.16)
	(0,1,1) vs. (1,0,1)	0.98 (0.69; 1.39)	0.96 (0.66; 1.38)
	(1,1,0) vs. (1,0,1)	1.09 (0.78; 1.53)	1.11 (0.79; 1.58)

^IThe trio of numbers in parentheses represents the three developmental periods under investigation (ages 0–6, 7–12, and 13–18). Thus, (1,0,0) indicates a new parental EB registration when the child was age 0–6, but not when the child was 7–12 or 13–18. Children who were never exposed to parental EB are not included in these comparisons.

Table 4

Effect of affected mother vs. father; effect of multiple affected parents; and effects of covariates.

Predictor/Covariate	Unadjusted Model OR (95% CI)	Adjusted Model OR (95% CI)
EB in mother but not father	2.67 (2.36, 2.99)	2.49 (2.21, 2.80)
EB in father but not mother	2.70 (2.52, 2.88) ¹	2.51 (2.34, 2.68) ²
EB in mother x EB in father (interaction term)	0.60 (0.49, 0.72)	0.60 (0.50, 0.72)
Males vs. females		1.97 (1.81, 2.14)
Cohort 1975–1979 vs. 1970–1974, females		0.97 (0.87, 1.07)
Cohort 1980–1984 vs. 1970–1974, females		1.21 (1.10, 1.34)
Cohort 1975–1979 vs. 1970–1974, males		0.72 (0.67, 0.78)
Cohort 1980–1984 vs. 1970–1974, males		0.72 (0.66, 0.78)
Parental education (high vs. low)		0.63 (0.58, 0.68)
Parental education (mid vs. low)		0.94 (0.87, 1.01)

¹In the unadjusted model, the OR for having both parents affected is 4.30.²In the adjusted model, the OR for having both parents affected is 3.77.

Table 5

Odds ratios for comparisons of exposure to parental externalizing across 1, 2, or 3 developmental time frames, controlling for sex, cohort, and parental education.

	Unadjusted Model OR (95% CI)	Adjusted Model OR (95% CI)
<i>2 periods vs. 1^I</i>	1.56 (1.35; 1.80)	1.51 (1.31; 1.74)
<i>3 periods vs. 2</i>	1.36 (1.11; 1.67)	1.36 (1.10; 1.67)
<i>3 periods vs. 1</i>	2.12 (1.79; 2.51)	2.05 (1.73; 2.42)

^IChildren who were never exposed to parental EB are not included in these comparisons.