Article

Binge Drinking During Pregnancy as a Predictor of Psychiatric Disorders on the Structured Clinical Interview for DSM-IV in Young Adult Offspring

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Objective: This study explored the extent to which the high frequency of psychiatric problems reported in clinical groups with fetal alcohol spectrum disorders might also be observed in a nonclinical group of young adults and the psychiatric conditions that are related to prenatal alcohol exposure in this group.

Method: From a longitudinal prospective study beginning with interviews of 1,529 pregnant women, a birth cohort of about 500 newborns was chosen to include all of the most heavily alcohol exposed plus a sampling of the continuum of alcohol exposures from total abstinence through heavy drinking. At an average age of 25.7 years, 400 members of this birth cohort were administered valid Structured Clinical Interviews for DSM-IV (SCID), including both the SCID for axis I disorders and the SCID for axis II personality disorders.

Results: The odds of the appearance of six psychiatric disorders and traits were more than double in adults exposed to one or more binge alcohol episodes in utero. Three of these six odds ratios were uniformly stable against confounding: axis I substance dependence or abuse disorders and axis II passive-aggressive and antisocial personality disorders or traits.

Conclusions: Prenatal exposure to alcohol may be a risk factor for specific psychiatric disorders and traits in early adulthood, even in a nonclinical group.

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Prenatal exposure to alcohol causes birth defects, including fetal alcohol syndrome, fetal alcohol effects, and alcohol-related neurodevelopmental disorder, collectively referred to as fetal alcohol spectrum disorders (1). These involve abnormal development in various domains, including attention and memory, executive functioning, motor skills, learning, and judgment.

The brain is the organ most vulnerable to prenatal alcohol damage across a wide range of regions (2–13), and alcohol-related brain pathologies affect specific domains of neuropsychological and neuromotor functions (14, 15). Although mental health conditions are not a criterion for any of the fetal alcohol-related diagnoses, they have been identified in 87% and over 90% of the subjects in two independent studies of people with fetal alcohol spectrum disorders, although the subjects were not recruited into these studies specifically because of these conditions (16, 17).

Here we used the Structured Clinical Interview for DSM-IV (SCID) to quantify the psychiatric disorders and traits that exist in a nonclinical group of adults with known levels of prenatal exposure to alcohol. This work is intended as a contribution to developmental neuropsychiatry (18–20) and neurodevelopmental psychiatry (21, 22), which acknowledge the importance of early biological development in adult psychiatric etiologies.

Method

Acquisition of Study Group

In 1974–1975, 1,529 pregnant women were interviewed in mid-pregnancy regarding their prenatal use of alcohol, cigarettes, caffeine, recreational drugs, and medications. Based on a hierarchical listing of 19 alcohol use patterns and cigarette use and without the knowledge of newborn status or functioning, approximately 500 singleton children were chosen at birth for a longitudinal prospective study. The group was stratified for cigarette use across levels of alcohol use and oversampled for heavier drinkers. These women were generally at low risk of adverse pregnancy outcome; street drug use was rare except for marijuana. All mothers were in prenatal care by mid-pregnancy but were otherwise representative of the Seattle area in terms of sociodemographic characteristics (23). Eighty-eight percent of the mothers were married, 13% had not graduated from high school, and 88% reported white ethnicity; the mean maternal age was 26.5 years (range=14–45) (9% were teenagers). The children had previously provided developmental data at birth, 8 and 18 months, and 4, 7, 11, 14, 21, and 25 years.

A 25-Year Follow-Up

Across a 3-year period, 431 members of this birth cohort participated in an extended clinical research assessment that included the SCID and the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II) (24). SCID data were not collected from 29 subjects who participated by only telephone or mail, one who refused, and one whose IQ was 69. The average age of the 400 subjects who provided valid SCID data was 25.7 years (range=24.8–27.4); 53% were men; 83% reported white ethnicity, 4% were black, 2% were Asian, and 12% were of other or mixed races. IQs at age 21 years ranged from 70 to 144 with a mean of 103.

TABLE 1. Frequencies of Psychiatric Disorders and Traits in a Follow-Up of 25-Year-Olds, by Prenatal Alcohol Binge Exposure

	Total (N=400)		Subjects Not Exposed to Binge Drinking (N=329)		Subjects Exposed to Binge Drinking (N=71)			
Disorder or Trait[a]	N	%	N	%	N	%	Odds Ratio[b]	95% CI
Axis I disorders (one or more)								
Somatoform	5	1.3	2	0.6	3	4.2	7.21	1.18–44.00
Substance abuse or dependence	140	35.0	102	31.0	38	53.5	2.56	1.52–4.32
Manic	7	1.8	5	1.5	2	2.8	1.88	0.36–9.88
Dysthymia or mood	30	7.5	22	6.7	8	11.3	1.77	0.75–4.16
Depressive	154	38.5	120	36.5	34	47.9	1.60	0.95–2.68
Anxiety	117	29.3	93	28.3	24	33.8	1.30	0.75–2.24
Eating	14	3.5	11	3.3	3	4.2	1.28	0.35–4.69
Adjustment	15	3.8	12	3.6	3	4.2	1.17	0.32–4.24
Psychotic	5	1.3	4	1.2	1	1.4	1.16	0.13–10.54
Axis II disorder or trait (personality disorder)								
Paranoid	9	2.3	5	1.5	4	5.6	3.87	1.01–14.79
Passive-aggressive	23	5.8	14	4.3	9	12.7	3.27	1.35–7.88
Antisocial	27	6.8	17	5.2	10	14.1	3.01	1.31–6.89
Other	19	4.8	13	4.0	6	8.5	2.24	0.82–6.12
Depressive	32	8.0	24	7.3	8	11.3	1.61	0.69–3.76
Schizoid	24	6.0	18	5.5	6	8.5	1.59	0.61–4.17
Schizotypal	8	2.0	6	1.8	2	2.8	1.56	0.31–7.90
Avoidant	39	9.8	30	9.1	9	12.7	1.45	0.65–3.20
Mixed	26	6.5	20	6.1	6	8.5	1.43	0.55–3.69
Histrionic	10	2.5	8	2.4	2	2.8	1.16	0.24–5.60
Dependent	6	1.5	5	1.5	1	1.4	0.93	0.11–8.05
Narcissistic	12	3.0	10	3.0	2	2.8	0.92	0.20–4.31
Borderline	13	3.3	11	3.3	2	2.8	0.84	0.18–3.87
Obsessive-compulsive	65	16.3	55	16.7	10	14.1	0.82	0.39–1.69

[a] Ordered by odds ratio for alcohol exposure within axis.
[b] Odds ratios greater than 1 indicate prenatal alcohol risk. A two-tailed log-symmetric 95% CI is next to each odds ratio. Lower CI limits above 1.0 correspond to conventional significance levels of $p \leq 0.05$.

Outcomes

The SCID assesses 129 symptoms sorted into nine primary classes of axis I psychiatric disorders: depressive, manic, psychotic, anxiety, somatoform, mood, adjustment, eating, and substance (alcohol or drug) disorders. Questions are phrased in terms of "ever in your life."

The SCID-II (24) evaluates 14 personality disorders derived from responses to 107 3-point ratings for which a code of zero stands for the rating of "none," a code of 1 for "yes, subthreshold," and a code of 2 for "yes, suprathreshold." These are also evaluated for "ever in your life." The scoring software provides diagnoses, and for 12 of the 14 disorders, it also indicates maladaptation or traits that do not meet criteria for diagnosis but that are nevertheless serious enough to "interfere with life." Here we used the disorder or trait scores for each of the 12 classes of personality disorders for which they are available.

The 23 SCID classifications presented here cover all of the information available from the SCID. Each of the 23 summary scores (Table 1) is set to 1 if any disorder in the class is positive and to 0 otherwise. The general summary score is a simple count of the number of disorders and traits (from 0 to 23).

The SCID was administered privately face-to-face by one of two SCID-trained, licensed clinical psychologists (P.D.C. and J.E.H.): 394 at the University of Washington Fetal Alcohol and Drug Unit, four in private rooms reserved offsite, and two in prisons. After the procedures had been fully explained and informed consent had been obtained, SCID data were collected with software from Multi-Health Systems Inc. (North Tonawanda, N.Y.) and American Psychiatric Publishing, Inc. (Arlington, Va.). Interviewers were blind to maternal reports of prenatal alcohol use and to all previous developmental data. In a random subsample of five cases rated by both clinicians, interrater reliability was 100% agreement on the SCID diagnoses; axis II scores from the two examiners differed by two points on 2% of the reliability data and by one point on 8%.

Prenatal Alcohol Exposure

Alcohol exposure was assessed from maternal self-reports for two gestational periods: early pregnancy (before pregnancy recognition) and mid-pregnancy (around the time of the interview). The measures available included average ounces per day, monthly occasions of drinking, average drinks per drinking occasion, maximum number of drinks on any occasion, and binge episodes. The small numbers of psychiatric disorders and traits in this group precluded the dose-response explorations that would use continuous alcohol measures. For this report, alcohol is a simple dichotomy: one or more binge episodes during mid-pregnancy compared to none. A binge episode is defined as five or more drinks on at least one occasion. Seventy-one mothers of this group (17.8%) reported such binge drinking. In contrast were 150 mothers (37.5%) who abstained or drank only infrequently at low levels and 179 (44.8%) who reported light or moderate alcohol use patterns.

Other Predictors of Mental Health Problems

Of the potential predictors of mental health problems identified in a literature search (23, 25–27), 11 were available for this cohort. These included prenatal cigarette exposure, prenatal marijuana exposure, prenatal nutrition, breast-feeding, socioeconomic status, the Mother/Infant Interaction Scale (an ordinal maternal deviancy score) (28), surrogate parenting of the subject (e.g., foster care, adoption), biological family history of serious mental health problems (in first- and second-degree relatives), a history of alcohol problems in two parents and four grandparents, sex, and the subject's own cigarette smoking history. Each was used as a dichotomy in our analyses. Although current

TABLE 2. Effect Sizes of Disorders and Traits by the Presence or Absence of Potential Risk Predictor Characteristics in a Follow-Up of 400 25-Year-Olds With or Without Prenatal Alcohol Binge Exposure

	High Risk[b]			Low Risk[b]			
Predictive Factor[a]	N	Mean	SD	N	Mean	SD	Effect Size
Smokes cigarettes	117	3.06	2.55	283	1.56	1.70	0.88
Adopted, fostered, or parented by a surrogate parent	43	3.42	2.06	357	1.83	2.04	0.78
Prenatal socioeconomic status at lowest 10%	40	3.22	2.60	360	1.86	1.99	0.68
Mother-infant interaction at highest 10%	37	2.95	2.52	325	1.91	2.08	0.50
Alcohol bingeing occurred mid-pregnancy	71	2.72	2.37	329	1.84	2.00	0.44
Prenatal nicotine use	124	2.58	2.26	276	1.74	1.97	0.43
Not breast-fed	138	2.49	2.43	262	1.74	1.85	0.40
Prenatal marijuana use	69	2.65	2.48	331	1.86	1.99	0.40
Fetal alcohol syndrome, fetal alcohol effects, or alcohol-related neurodevelopmental disorder[c]	29	2.72	2.66	371	1.94	2.04	0.38
Poor prenatal nutrition	86	2.37	2.44	314	1.90	1.99	0.24
History of problems with alcohol among parent(s) or grandparent(s)	186	2.14	2.09	191	1.79	2.04	0.17
History of serious mental health problem(s) among first- or second-degree relative(s)	71	2.08	2.30	315	1.95	2.04	0.06

[a] High-risk characteristic.
[b] When group sizes do not sum to 400, the predictor variable has missing data.
[c] Refers to evaluations by project collaborators, including dysmorphologists, from birth through 7 years of age. Two of these subjects were known to have been identified with fetal alcohol spectrum disorders by the community standard of care.

smoking by the subject can be a consequence of psychiatric disorders as well as a predictor, we included it for consistency with the literature. Because these other predictors served here only for challenging the main effects of alcohol, the reader should not construe our findings as assessing the effect of these confounders with any sophistication or as testing their separate effects on psychopathology or their interactions per se.

Analysis

For each predictor, including alcohol binge exposure, we computed one version of an "effect size" for the general summary score: the mean for the high-risk group minus the mean for the low-risk group divided by the standard deviation of the low-risk group. For each of the 23 individual disorders and traits, the frequency observed in adult offspring of mid-pregnancy binge drinkers was compared to that of offspring of nonbingeing drinkers with odds ratios. Odds ratios resulted in a two-by-two table, alcohol against a disorder or a trait, by means of the ratio of the odds of the psychiatric condition in the mid-pregnancy binge exposure group to the odds in the group without bingeing. In studies with multiple discrete predictors, there are various methods for adjusting odds ratios, including multivariate cross-tabulations and logistic regressions. Because our purpose was simply to validate the alcohol effect against these possible confounders, we chose a much simpler approach: recomputation of the odds ratios in groups homogeneous for low risk on each potential confounder in turn.

Results

Table 1 reports the prevalence of each of 23 disorders and traits for the total group and separately for the bingeing and nonbingeing groups; it also tabulates the odds ratios for alcohol along with a 95% confidence interval (CI) that derives from transforming conventional symmetric intervals for log odds ratios. An odds ratio of 1 indicates no difference between the two groups. For six of the 23 scores, the odds of scoring positive were more than double for subjects exposed to one or more alcohol binges in utero: axis I somatoform disorder (odds ratio=7.21) and substance dependence or abuse disorders (odds ratio=2.56) and the axis II paranoid (odds ratio=3.87), passive-aggressive (odds ratio=3.27), and antisocial (odds ratio=3.01) personality disorders or traits and other personality disorders (odds ratio=2.24).

Table 2 shows effect sizes of 12 potential predictors for the summary SCID count. All are in the direction expected from the literature. The prenatal alcohol bingeing exposure score had the fifth largest effect size: 0.44.

A data supplement available in the online version of the *Journal* shows the odds ratios recomputed with subgroups restricted to subjects with low-risk characteristics (e.g., a nondeviant mother-infant interaction). For 16 of 23 SCID disorders and traits that were observed for more than 10 subjects in the total group, each column deletes a subgroup of subjects based on one of the other predictive characteristics. The final two columns were computed separately for men and for women. Under challenge by 11 other predictors along with gender, three of the psychiatric disorders and traits (axis I substance dependence or abuse disorders and axis II passive-aggressive and antisocial personality disorders or traits) have odds ratios that are consistently above 2.0. Even as a selection of three of 23 outcomes, these remain comfortably significant by conventional standards after Bonferroni correction of tail probabilities. Additionally, when the odds ratios for these three select relationships were replicated, comparing the 71 mid-pregnancy bingeing-exposed subjects to only the 150 offspring of abstainers and infrequent drinkers, all three odds ratios were still above 2.00.

Discussion

Clinical reports of a high frequency of psychiatric problems among patients with fetal alcohol spectrum disorders alerted researchers to the possibility of these CNS sequelae to prenatal exposure to alcohol (16, 17). Within clinical

groups of people already known to be affected by prenatal alcohol exposure, there can be reasons other than prenatal alcohol exposure for the high frequency of mental health problems. A comparison of clinical data to historical controls, such as previously published population frequencies, does not allow consideration of competing predictors or mediating causes and characteristics. Among the naturalistic studies of human teratogens, only population-based epidemiological studies, such as this one, have the resources needed to support the causal inferences we are suggesting. Prenatal exposure to alcohol may be a risk factor for specific psychiatric disorders and traits in early adulthood, even in this nonclinical group. In these exploratory analyses, we challenged the observed associations by listing competing hypotheses, and the association survives and is consistent with the known consequences of human neurocognitive deficits (23). In a prospective longitudinal study, there is obviously an implied developmental trajectory with earlier neuropsychiatric manifestations. Many neurodevelopmental characteristics of these young adults have been previously described and subsequent articles will study their relation to these adult neuropsychiatric symptoms. The effect size of alcohol in this group is commensurate with other well-known predictors of psychopathology published in the larger literature.

Study Limitations

1. Even when disorders and traits are grouped into broader DSM-IV classifications, the analyses and interpretation of this data set are hampered by low frequencies that preclude dose-response analyses.
2. Limited contact with subjects and parents necessarily focused on prenatal alcohol use and outcomes. Potential covariates were not as well measured, so subjects in subgroups in the online data supplement may be at high risk.
3. This study has no information corroborating the self-reported SCID data. However, the psychiatric characterizations used were predicted by covariates suggested by the literature for these same mental illnesses (Table 2).
4. The paucity of subjects with psychiatric disorders, such as axis II schizotypal disorder, in this group reflects the low population base rate and also the difficulty in obtaining participation from subjects with such disorders. Studies of such disorders proceed better in clinical groups, either of people with fetal alcohol diagnoses or of people with psychoses; however, such studies would sacrifice the detail of in utero exposure characterized by this prospective longitudinal study.

Passive-aggressive and antisocial disorders or traits were infrequent in women in this group, but prenatal alcohol exposure characterizes a large fraction of these subjects. Only 29 of 187 (15.5%) of the women were exposed to one or more binge alcohol episodes, but among these 29 were found three of five (60%) of the passive-aggressive disorders or traits and three of six (50%) of the antisocial disorders or traits. In other words, prenatal alcohol exposure may be a direct cause of passive-aggressive and antisocial behaviors in women of this age group.

The majority of the mothers in this group who reported mid-pregnancy binge drinking episodes would not be identified as alcohol abusers by the most common definitions of the mid-1970s when this study began, yet they represent the heaviest drinkers in this group across a broad range of drinking measures and during both early- and mid-pregnancy. The mothers characterized here as binge drinkers averaged 13 drinking occasions per month and 3.5 drinks on each of those occasions, compared to five drinking occasions per month and 1.3 drinks per occasion for other mothers. Ninety percent of those who drank in binges during mid-pregnancy also reported binge drinking in early pregnancy. So the results of this study should not be construed to apply to mid-pregnancy or mid-pregnancy binge drinking only. Follow-up parental interviews identified 17 of 66 (25.8%) mid-pregnancy binge drinkers as having had "problems with alcohol" at some time in their lives. Previous articles from this study examining continuous neurocognitive outcomes quantify alcohol exposure as a linear combination of 13 (mostly continuous) measures of alcohol consumption that has usually emphasized maternal binge behavior. Detailed examination of these alternative dose measures by outcomes showed no systematic improvement over the statistics reported here. In other words, we used mid-pregnancy binge drinking as a simple dichotomous proxy for heavy drinking. This simple binge dichotomy is as powerful in its association to these SCID scores as any other score available to us and is, furthermore, a good deal easier to measure. For this report, the choice of a simple binary indicator of one or more binge episodes during mid-pregnancy lends itself to analyses of discrete and rare outcomes and also simplifies replication by future studies.

Mid-pregnancy binge alcohol characterized 17.8% of this group but over a third of each of several disorders or traits: nine of 23 cases (39.1%) of passive-aggressive disorder or traits in this group; four of nine cases (44.4%) of paranoid disorder or traits; and 10 of 27 cases (37.0%) of antisocial disorder or traits. Yet, unlike the clinical reports that preceded this work, this study did not select subjects based on either psychiatric disorders or traits/diagnoses considered part of fetal alcohol spectrum disorders. In this nonclinical group, prenatal alcohol exposure doubled the odds of axis I substance abuse and dependence and also doubled the odds of axis II passive-aggressive disorders and traits and axis II antisocial disorders and traits. These observed odds, which withstand challenge by other predictors, are likely causal.

Clinical Implications

At present, the assessment of fetal alcohol spectrum disorders is skewed to the dysmorphological developmental disorders. Careful clinical attention should also be paid to the psychiatric presentation of adult patients with fetal alcohol spectrum disorders. Also, because fetal alcohol spectrum disorders are transgenerational conditions, adult psychiatric providers need to be alert to the risks of alcohol use problems in women of child-bearing age. The management of children damaged by prenatal exposure to alcohol is a difficult parenting assignment, irrespective of any psychiatric disorders in the parent. Conversely, clinicians assessing psychiatric disorders, such as substance abuse/dependence disorders and passive-aggressive and antisocial disorders, in young adults should consider the possibility of a prenatal alcohol etiology.

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