A COMPARISON OF PSYCHOPATHOLOGY IN CHILDREN WITH AND WITHOUT PRENATAL ALCOHOL EXPOSURE

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Research suggests that psychiatric problems may be common in children with prenatal alcohol exposure. The purpose of the current study was to examine psychiatric diagnoses in a non-clinic referred sample of 130 children ages 6 to 12 years old, with and without prenatal alcohol exposure. A standardized diagnostic interview procedure was employed, comparing children with prenatal alcohol exposure and social skills deficits to children without prenatal alcohol exposure and social skills deficits. Findings suggest that children with prenatal alcohol exposure exhibit significantly more psychopathology, including symptoms of anxiety, disruptive behaviors, and mood disorders, when compared to children without alcohol exposure.

Keywords: intellectual disability, prenatal alcohol exposure, child psychopathology, fetal alcohol spectrum disorders, fetal alcohol syndrome, psychiatric disorder

ver the past 30 years, mounting evidence about the impact of maternal alcohol consumption during pregnancy has prompted increased attention to the link between prenatal alcohol exposure and a constellation of developmental disabilities that are characterized by physical, cognitive, and behavioral impairments. These disabilities include a continuum of disorders known as Fetal Alcohol Spectrum Disorders (FASDs).⁴⁷ Fetal Alcohol Syndrome (FAS) is considered the most severe condition resulting from in utero alcohol exposure and involves characteristic facial malformations, growth deficiencies, and neurodevelopmental deficits.¹⁴ Although prevalence rates for FAS vary widely depending on the epidemiological and clinical methods used to collect information, as well as the populations being studied, one recent report estimated a national rate of 0.5 to 2 cases of FAS per 1,000 live births, with the prevalence of the entire continuum of FASDs estimated to be 1 in 100 in the United States.²⁰

Relatively recent research on structural brain changes in individuals with prenatal alcohol exposure has documented overall reductions in brain size and greater than expected reductions in the sizes of the basal ganglia, corpus callosum, and anterior cerebellar vermis.³⁹ Although changes in brain structure are particularly compelling evidence of alcohol's teratogenicity, changes in behavior caused by prenatal alcohol exposure can be equally devastating. Most behavioral research has particularly focused on impairment in overall intellectual functioning and deficits in general cognitive abilities, which have been reported in both children with FAS and those with heavy prenatal alcohol exposure who do not meet full criteria to warrant a diagnosis of FAS.³⁴ In addition to intellectual deficits, children with prenatal alcohol exposure also present with other significant neurocognitive deficits. These deficits include problems with executive functioning, learning and memory, language, attention, and information processing speed.^{16,31,32,33,34,46}

Given the significant neurocognitive deficits seen in this population, it is not surprising that psychosocial dysfunction among children with FASDs has also been consistently noted in the literature. Children with prenatal alcohol exposure have difficulty understanding social cues, exhibit indiscriminant social behavior, and have difficulty communicating in social contexts.^{21,43} Caregiver and teacher ratings of social functioning suggest that children with prenatal exposure to alcohol have poorer social skills than unexposed children, even after controlling for differences in cognitive functioning.^{35,47,48} Furthermore, studies of adolescents and adults with FASDs indicate that these social skills deficits continue into adulthood.^{27,46} Behavioral difficulties are also prevalent in alcohol-exposed children, with externalizing behaviors being particularly problematic in the classroom and at home.^{3,6,16,25,26,29,30} Moreover, as alcohol-exposed individuals approach adolescence, behavioral difficulties often increase and may include problems with alcohol and substance use, school failure, delinquency, and trouble with the law.^{37,44}

Although the pervasive neurocognitive, social, and behavioral problems typically seen in individuals with FASDs have been explored in numerous studies, psychiatric outcomes among this population are less well understood. Studies of relatively small samples reveal that psychiatric problems are common in children with prenatal exposure to alcohol.^{12,22,25,30,35,41} In one clinic referred sample of 23 alcohol-exposed children between the ages of 5 and 13 years, 87% met criteria for a psychiatric disorder. The majority of the children (61%) received a mood disorder diagnosis, 26% were diagnosed with major depressive disorder or adjustment disorder with depressed mood, and 35% met criteria for bipolar disorder.²⁵ Consistent with the findings on the presence of mood disorders in this population, a few studies have reported an increase in self-reported depressive and internalizing symptoms.^{12,23,25} The most commonly reported findings, however, suggest the increased prevalence of externalizing and disruptive behavior diagnoses.12,23,35

Although the previously cited studies have provided some insight into the psychopathology experienced by individuals with prenatal alcohol exposure, the limitations of these studies impact our ability to make generalizations from the results for a number of reasons. First, the sample sizes of the majority of these studies have been small; second, these studies typically involve clinic-referred participants, possibly leading to over-estimates of associations between psychopathology and prenatal alcohol exposure; third, with the exception of two studies,^{9,12} standardized clinical interviews have not been employed in the methodology; and fourth, these studies either lack non-alcohol-exposed control groups or rely on typically-developing unexposed controls. Considering these limitations, the purpose of the current study was to examine the association between prenatal alcohol exposure and psychiatric diagnosis in a relatively large non-clinic referred sample of children. A standardized diagnostic interview procedure was employed to compare children with and without prenatal alcohol exposure who also had social skills deficits.

Methods

Participants

All study related activities took place at the University of California at Los Angeles, Semel Institute for Neuroscience and Human Behavior. The University of California at Los Angeles and the Centers for Disease Control and Prevention Institutional Review Boards approved all procedures and a Certificate of Confidentiality was obtained from the NIAAA prior to participant recruitment. Informed consent was obtained from the parent(s) and assent from children >7 years of age.

The sample consisted of 130 children who met screening criteria for having social skills deficits. Participants were recruited from February 2003 to June 2005 through community-posted flyers and letters mailed to local health care providers (i.e., pediatricians), YMCAs, and schools. Interested families were screened by telephone to determine eligibility. Children were eligible if they were between 6 and 12 years of age, had measurable social skills deficits (\geq - 1 standard deviation below the mean) on the Socialization Domain of the Vineland Adaptive Behavior Scales (VABS),⁴⁰ and a Verbal IQ of \geq 70 on the Kaufman Brief Intelligence Test (K-BIT).¹⁵ Children were not admitted if they had major sensory or motor deficits or a past diagnosis of developmental disability or pervasive developmental disorder. See Table 1 for a comparison of children with and without prenatal alcohol exposure.

FASD Diagnosis

Participants received a physical examination to assess for the presence of the diagnostic features of FASDs according to the criteria set forth in the Diagnostic Guide for Fetal Alcohol Spectrum Disorders.² This system uses a 4-digit diagnostic code reflecting the magnitude of expression of four key diagnostic features of FAS: (a) growth deficiency; (b) FAS facial phenotype, including short palpebral fissures, flat philtrum, and thin upper lip; (c) central nervous system dysfunction; and (d) gestational alcohol exposure. Using this coding system, the study physician ranked the magnitude of expression of each feature independently on a 4-point Likert scale, with 1 reflecting complete absence of the feature and 4 reflecting the full manifestation of the feature. The study physician administered this examination after achieving 100% reliability with the senior study clinician who was trained by S. J. Astley, the co-developer of this diagnostic system. The physician was unaware of the prenatal exposure group assignment of the participants.

Alcohol Exposure Criteria

The history of prenatal alcohol exposure was obtained from the biological mothers by means of

TABLE 1. SAMPLE CHARACTERISTICS							
Variables	Total Sample (N = 130)	Alcohol-Exposed (N = 100)	Non-Exposed (N = 30)				
Ethnicity (%) White, Non-Hispanic Black, Non-Hispanic Hispanic Asian	50.0 16.9 20.0 3.1	54.0 17.0 17.0 2.0	36.7 16.7 30.0 6.7				
Mixed	10.0	10.0	10.0				
Child Gender - Males (%) Child Age in Years (M, SD)	51.0 8.50 (1.53)	51.0 8.59 (1.56)	50.0 8.35 (1.46)				
Socialization (M, SD) ^a	64.35 (8.84)	62.83 (8.04)***	69.43 (9.57)***				
Child Composite IQ (M, SD) ^b	99.39 (15.05)	97.24 (14.83)**	106.57 (13.69)**				
Biological Mother (%)	35.9	21.0**	86.7**				
Primary Caregiver Married/Partner (%)	66.4	62.8**	83.3**				
Primary Caregiver Yrs Education (M, SD)	16.45 (2.81)	16.28 (2.60)	17.03 (3.40)				
*** p<.001 ** p<.01 * p<.05 ^a Vineland Socialization Standard Score							

Kaufman Brief Intelligence Test Composite IQ

the Health Interview for Women.²² Among adopted or foster children, medical or legal record documentation referencing known alcohol exposure was used to determine the degree of alcohol exposure. In addition, reliable collateral reports by others who had observed the mother drinking during pregnancy were obtained. Because many children with prenatal alcohol exposure are often adopted or in foster care, it is often necessary to rely on such records to assess the child's history of alcohol exposure and is an accepted practice in the scientific community when making a diagnosis of FAS or related conditions.² All children in the alcohol-exposed group met criteria for ratings of 3 (some risk) or 4 (high risk). Within the control group, all children met criteria for ratings of 1 (no risk) with exposure levels of <1 standard drink (0.60 oz. absolute alcohol) throughout gestation.

Measures

Institute for Mental Health National Computerized Diagnostic Interview Schedule for Children—Fourth Edition (NIMH C-DISC-IV). The C-DISC-IV is a structured interview developed by

the National Institute of Mental Health that assesses for 36 mental health disorders for children and adolescents, using DSM-IV criteria.³⁸ The interview version conducted in this study used the parent or primary caregiver as the interview subject. The C-DISC-IV assesses for the presence of diagnoses occurring within the last four weeks (present) as well as the last year, and also assesses the level of impairment. The C-DISC-IV is organized into six different modules: anxiety disorders, mood disorders, disruptive disorders, substance use, schizophrenia, and miscellaneous disorders, with individual symptom scores for each Axis I diagnostic category. Symptom scores are derived from key stem questions that are asked of all respondents for a given diagnosis. The diagnostic interview has adequate test-retest reliability³⁸ and good concurrent criterion validity, particularly with regard to attention deficit disorders.²⁰

Data Analysis

Data analyses were conducted using SPSS Statistical Analysis software (14.0). Descriptive information comparing children with and without prenatal alcohol exposure was examined using Chi-square and independent *t*-tests. The relationship between prenatal alcohol exposure and levels of psychopathology were evaluated in separate regression analyses. Twelve Axis I psychiatric diagnosis outcome categories on the C-DISC-IV were examined: separation anxiety disorder, generalized anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder, attention-deficit/hyperactivity disorder, oppositional defiant disorder, conduct disorder, major depressive disorder, dysthymic disorder, mania, hypomania, and schizophrenia. Symptom scales provided continuous variables for each psychiatric diagnosis. Child ethnicity (1=White, non-Hispanic, 2=Black, 3=Hispanic, 4=American Indian, 5=Alaskan Native, 6=Asian, 7=mixed ethnicity), gender (1=boys, 2=girls), age, full scale IQ, socialization standard score, caregiver marital status (1=single/separated/divorced/never married; 2=married/living with a partner), education, and home placement (1=non-biological parent; 2=biological parent) were used as the primary covariates when appropriate, based on a statistically significant correlation (p<.05) with the individual psychiatric diagnostic outcomes. Prenatal alcohol exposure (0=non-exposed; 1=alcohol-exposed) was entered as the last predictor variable in each regression model. The statistical significance of each model, R^2 , and standardized beta coefficients were calculated.

RESULTS

Characteristics of Children With and Without Prenatal Alcohol Exposure

Chi-square and independent *t*-tests revealed no significant differences between children with and without prenatal alcohol exposure on child ethnicity, gender, age, or caregiver education. Significant differences were found between groups on Full Scale IQ, caregiver marital status, home placement (non-biological parent or biological parent), and socialization standard score, although all children scored in the deficit range on socialization. (See Table 1)

Comparison of Children With and Without Prenatal Alcohol Exposure on FASD Diagnosis

As expected, a Chi-square analysis comparing children with and without prenatal alcohol exposure on FASD diagnostic criteria revealed that all children in the alcohol-exposed group were classified as having an alcohol related condition; whereas, none of the children in the non-exposed group met criteria for an alcohol related diagnosis (X^2 (3, N = 130) = 130.00, p<.0001). On the basis of the 4-digit diagnostic system, 11% of children in the alcohol-exposed group were diagnosed with FAS, 43% with partial FAS (pFAS), and 46% with static encephalopathy, which is consistent with a diagnosis of alcohol related neurodevelopmental disorder (ARND) according to guidelines developed by Astley (personal communication, July 5, 2005) for converting the 4-digit code to the diagnostic categories proposed by the Institute of Medicine.42 No child in the alcohol-exposed group met criteria for alcohol related birth defects (ARBD).

Prediction of Psychiatric Symptoms

Correlations among child characteristics, prenatal alcohol exposure, and psychiatric diagnostic symptoms are presented in Table 2. Regression models are presented in Table 3. Results revealed statistically significant effects of prenatal alcohol exposure in predicting both separation anxiety disorder and generalized anxiety disorder, even after controlling for significant covariates of caregiver marital status and home placement. Prenatal alcohol exposure did not predict symptoms of obsessive compulsive disorder or post-traumatic stress disorder. Externalizing disorders, including symptoms of attention deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder, were all positively predicted by prenatal alcohol exposure, after accounting for the contributions of IQ, social skills deficits, caregiver marital status and home placement. An analysis of the symptoms related to major depressive disorder indicated that children with prenatal alcohol exposure had more depressive symptoms than those without exposure, but this effect was not statistically significant after controlling for covariates measuring socialization, caregiver marital status, and home placement. Similarly, prenatal exposure to alcohol did not predict symptoms of dysthymic disorder or schizophrenia. Exposure to alcohol prenatally was predictive of symptoms of mania and hypomania.

DISCUSSION

Children with prenatal alcohol exposure were found to exhibit significantly more symptoms of psychopathology, including anxiety disorders,

TABLE 2. CORRELATIONS												
Variable	Sep. Anxiety ^a	GAD⁵	OCD°	PTSD ^d	ADHD ^e	ODD ^f	CD ^g	MDD^{h}	Dysthymic	Hypomania	Mania	Schiz ⁱ
Alcohol exposure	.34**	.21*	.13	.12	.61**	.65**	.38**	.32**	.07	.36**	.35**	.13
Gender	06	03	13	.05	13	08	10	08	.12	01	01	07
Ethnicity	.04	.16	.06	08	06	.01	04	.08	04	08	09	05
Age (months)	.01	.16	.10	09	03	.00	.09	.00	02	04	04	.04
KBIT IQ	.01	12	.09	10	21*	21*	32**	08	14	14	16	06
Vineland Socialization	15	17	12	04	38**	28**	32**	26**	09	18*	18*	08
Caregiver marital status	13	25**	.07	09	20*	23**	06	21*	17	-08	08	.04
Home placement	31**	06	13	16	40**	46**	31**	29**	09	25**	25**	11
*** p<.001 ** p<.01 * p<.05												

^a Sep Anxiety: separation anxiety

^b GAD: generalized anxiety disorder

^c OCD: obsessive compulsive disorder

^d PTSD: post-traumatic stress disorder

^e ADHD: attention deficit/hyperactivity disorder

^f ODD: oppositional defiant disorder

^g CD: conduct disorder

^h MDD: major depressive disorder

ⁱ Schiz: schizophrenia

disruptive disorders, and mood disorders, when compared to children without exposure. Furthermore, child characteristics and environmental factors appeared to add to the prediction of psychopathology. Specifically, having a lower IQ, poorer social skills, living with a single/divorced or a non-biological caregiver placed children at greater risk.

The general findings of this study are in accordance with previous research studies, typically conducted with smaller samples, that suggest a relationship between prenatal alcohol psychopathology exposure and in children.^{12,22,23,25,30,41} However, the results of the current study extend previous findings through the use of a larger sample of non clinic-referred children with social skills deficits. In addition, the augments present study previous methodologically-limited findings through the use of structured diagnostic parent interviews, which were used to assess for a wide range of psychopathology.

With regard to specific findings, results revealed that symptoms of anxiety were significantly related to prenatal alcohol exposure. The link between fetal alcohol exposure and anxiety has been less well studied than externalizing disorders and mood disorders: however, research on early attachment behavior has demonstrated a higher prevalence of insecure attachment in children with moderate to high prenatal alcohol exposure compared to those with little or no exposure.²³ Furthermore, clinical reports describe anxiety associated with separation particularly in relation to placement outside the biological home. The current findings support these reports in that children who were not living with their biological mothers had higher levels of separation anxiety. Nevertheless, prenatal alcohol exposure was an independent

TABLE 3. PREDICTION OF PSYCHIATRIC SYMPTOMS AS A FUNCTION OF PRENATAL ALCOHOL EXPOSURE							
	F	β	B (SE)	R ² (Adjusted R ²)			
Separation Anxiety Disorder Home Placement Prenatal Alcohol Exposure	9.82***	17 .24*	-8.34 (4.93) 13.35 (5.62)	.13 (.12)			
Generalized Anxiety Disorder Caregiver Marital Status Prenatal Alcohol Exposure	6.27**	22* .17*	-9.31 (3.74) 8.35 (4.18)	.09 (.08)			
Obsessive Compulsive Disorder Prenatal Alcohol Exposure	2.20	.13	2.27 (1.53)	.02 (.01)			
Post-Traumatic Stress Disorder Prenatal Alcohol Exposure	1.73	.12	3.15 (2.39)	.01 (.01)			
Attention Deficit Hyperactivity Disorder KBIT IQ Socialization Score Caregiver Marital Status Home Placement Prenatal Alcohol Exposure	17.79***	26 19* 08 06 .50***	05 (.15) 64 (.25) -5.36 (4.53) -3.64 (5.45) 35.25 (6.29)	.42 (.39)			
Oppositional Defiant Disorder KBIT IQ Socialization Score Caregiver Marital Status Home Placement Prenatal Alcohol Exposure	20.81***	02 06 12 14 .53***	04 (.15) 22 (.26) -8.26 (4.66) -8.95 (5.59) 39.99 (6.46)	.29 (.43)			
Conduct Disorder KBIT IQ Socialization Score Home Placement Prenatal Alcohol Exposure	9.69***	21* 20* 05 .24*	19 (.08) 31 (.13) -1.50 (2.79) 7.62 (3.19)	.24 (.21)			
Major Depressive Disorder Socialization Score Caregiver Marital Status Home Placement Prenatal Alcohol Exposure	6.27***	14 17 17 .15	32 (.19) -6.89 (3.53) -6.81 (4.16) 6.98 (4.89)	.17 (.14)			
Dysthymic Disorder Prenatal Alcohol Exposure	0.56	.07	.42 (.56)	.04 (03)			
Mania Socialization Score Home Placement Prenatal Alcohol Exposure	6.32***	07 06 .30**	15 (.19) -2.15 (4.00) 13.91 (4.65)	.13 (.11)			
Hypomania Socialization Score Home Placement Prenatal Alcohol Exposure	6.54***	07 06 .30**	15 (.19) -2.41 (3.99) 13.42 (4.63)	.14 (.11)			
Schizophrenia Prenatal Alcohol Exposure	2.12	.13	1.35 (.93)	.02 (0.1)			
*** p<.001 ** p<.01 * p<.05	-	•	•				

predictor of anxiety symptoms even after controlling for home placement. These anxiety problems do not appear to ameliorate with age in that high levels of phobic anxiety are reported in alcohol-exposed adults.⁸ Even in typically developing children, anxiety and depressive symptoms are associated with a multitude of negative outcomes, such as school failure and problems with peers^{1,13} and children with prenatal alcohol exposure are already considered high-risk for these secondary disabilities.^{7,27,44,46} The additional risk associated with anxiety symptoms underscores the idea that children with prenatal alcohol exposure are prime candidates for early interventions focusing on reducing anxiety and increasing coping skills.

Not surprising, significant differences between children with and without prenatal alcohol exposure were found in the disruptive disorders categories: attention deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder. These findings are consistent with the literature on prenatal alcohol exposure that suggests long-term difficulties with attention/hyperactivity and disruptive behaviors.^{3,30,41,45}

Attention deficits among children with FASDs are well documented in the literature and corroborate the widespread presence of these problems in children exposed to alcohol prenatally.^{8,19} However, some investigators have hypothesized that the inattention and hyperactivity associated with prenatal alcohol exposure is a particular clinical subtype with an earlier onset, different clinical and neuropsychological presentation, and probable differential medication response.^{18,28} In the future, sophisticated studies of this population, such as the ones conducted by Lee et al.,¹⁸ can provide useful guidelines for addressing the specific areas of deficits in attention exhibited by children with prenatal alcohol exposure and can suggest more prescribed and focused treatments.

Findings regarding the associations between prenatal alcohol exposure and the presence of oppositional defiant and conduct disorder are also not surprising given that children with prenatal alcohol exposure have been found to be more than three times more likely to be rated as having delinquent behavior scores in the clinical range³ and have been found to have lower levels of moral maturity and higher levels of delinquency than non-alcohol-exposed controls matched on age, gender, socioeconomic status, and ethnicity.³⁷ confined at some point in their lives.45 Other findings reveal that individuals with prenatal alcohol exposure are significantly over represented in the criminal justice system, yet often go unidentified as having a FASD diagnosis.^{5,10,11} The results of the current study support the notion that disruptive behaviors that may lead to delinguency and social maladjustment can be identifiable in early to middle childhood and suggest the need for interventions with high risk children in order to prevent more serious secondary disabilities in the future. Results revealed that mood disorder symptoms were significantly higher for children

Furthermore, a study of 451 adults with prenatal

alcohol exposure found that 60% had been in trouble with the law and 50% had been legally

with prenatal alcohol exposure compared to children without exposure, suggesting that although externalizing behaviors are certainly problematic in this population, impairments associated with prenatal alcohol exposure are not limited to disruptive behaviors. A positive finding was that although children with prenatal exposure to alcohol had higher levels of depressed mood than non-exposed controls, having better social skills and living with a married biological parent seemed to ameliorate the effects of early exposure. These findings are consistent with previous reports of links between early social competence and depressive symptoms⁴ and the effects of parenting variables on the teratogenic effects of alcohol.²⁵ For example, O'Connor and Paley²⁵ found that the effects of prenatal alcohol exposure on depressive symptoms in preschool aged children were mediated by the mother-child interaction. Mothers who were more emotionally connected to their young children had children with fewer depressive symptoms compared to children whose mothers provided less positive emotional support. By understanding the transaction between parent and child characteristics, early interventions can target maladaptive parent-child relations to reduce the risk for future depression.

Finally, a positive association between prenatal alcohol exposure and symptoms of mania and hypomania were found. These findings are consistent with an earlier study of a clinical population of children in which 35% manifested symptoms of bipolar disorders.²³ These results suggest that when working with children with prenatal alcohol exposure, it is prudent to assess for the full range of Axis I symptoms. Appropriate diagnosis is essential for appropriate treatment in that the course of action would be different depending on whether or not the child had a mood disorder as opposed to attention deficit hyperactivity disorder.

There are some limitations to the current study that merit discussion. First, only children with verbal IQs of 70 or higher participated in the study, thereby eliminating children functioning in the moderate to mild range of developmental disability. However, research shows that using this cut point would allow the majority of children with exposure to be examined. For example, it has been estimated that 73% of children with FAS and 91% of children with partial FAS and ARND fall above an IQ score of $70^{.36}$ Second, the sample was composed of volunteers who identified their children as having social skills deficits which may have introduced an ascertainment bias, thus limiting our ability to generalize to populations of children who are functioning adequately both socially and emotionally. Third, interviews were conducted with parents rather than child participants. In the future, it would be informative to assess child psychopathology using self-report measures.

In spite of these limitations, study results suggest that children who have been exposed to alcohol prenatally are at high risk for developing symptoms of psychopathology. Furthermore, children with exposure to alcohol in utero tend to be overrepresented in psychiatric populations, and are frequently not identified as having central nervous system deficits associated with prenatal alcohol exposure.²⁴ Therefore, these children are often referred for mental health services, but these services may fail to take into account their unique needs when setting goals and making treatment plans.³ Thus, they may be more likely to fail to respond or under-respond to treatment. Proper diagnosis of the psychiatric problems of children with prenatal alcohol exposure is essential, as is the need to adapt existing interventions to accommodate the deficits and strengths of these children.^{17,21}

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