Heavy prenatal alcohol exposure with or without physical features of fetal alcohol syndrome leads to IQ deficits

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Objective: To assess general intellectual functioning in children with histories of heavy prenatal alcohol exposure, with or without the facial features and growth deficiencies characteristic of fetal alcohol syndrome (FAS).

Design: Forty-seven alcohol-exposed children were recruited on evaluation at a dysmorphology clinic and evaluated as part of a university research project using standard tests of IQ. Thirty-four of the alcohol-exposed patients met the traditional diagnostic criteria for FAS. The other 13 alcohol-exposed children lacked both the pattern of facial features and prenatal or postnatal growth deficiency characteristic of the diagnosis.

Results: Compared with normal control subjects matched for age, sex, and ethnicity, both groups of alcohol-exposed children displayed significant deficits in overall IQ measures and deficits on most of the subtest scores. Although those in the nondysmorphic group usually obtained marginally higher IQ scores than those in the FAS group, few significant differences were found between the two alcohol-exposed groups.

Conclusions: These results indicate that high levels of prenatal alcohol exposure are related to an increased risk for deficits in intellectual functioning and that these can occur in children without all of the physical features required for a diagnosis of FAS. They also emphasize the need for conducting a thorough history of prenatal alcohol exposure in children with intellectual deficits. (J Pediatr 1997;131:718-21)

Since fetal alcohol syndrome was identified in the United States more than 20 years ago,[1] a multitude of physical, behavioral, and cognitive characteristics have been documented in both children and animals exposed to alcohol prenatally.[2,3] The diagnostic criteria for FAS are threefold: (1) a characteristic pattern of facial features, (2) prenatal or postnatal growth deficiency, and (3) evidence of central nervous system dysfunction. Although the precise pattern of central nervous system abnormality is still under study, it has become clear that FAS represents a devastating developmental disorder with significant cognitive sequelae. However, the degree of intellectual impairment in structurally normal children of women with chronic alcoholism is unknown. Given the large percentage of children exposed to high amounts of alcohol prenatally in whom FAS is not diagnosed, it is imperative to define clearly their cognitive potential, because it is this aspect of the disorder that is most devastating. This article addresses the degree and nature of the cognitive deficits in structurally normal children of women with chronic alcoholism. That is, do these children, who lack the physical features characteristic of the FAS, have a similar degree of cognitive impairment as those who possess a pattern of malformations consistent with that diagnosis?

ANOVA	Analysis of variance
FAS	Fetal alcohol syndrome
FSIQ	Full Scale IQ
NC	Normal control [subjects]
PEA	Prenatal exposure to alcohol
PIQ	Performance IQ
SD	Standard deviation
SES	Socioeconomic status
VIQ	Verbal IQ

METHODS

To evaluate intellectual ability, 94 children were given either the Wechsler Preschool and Primary Scale of Intelligence-Revised[4] or Wechsler Intelligence Scale for Children-Revised,[5] according to their age. The children included in this study were drawn from a larger population of children under study at the Center for Behavioral Teratology, Department of Psychology, San Diego State University. Thirty-four of these children met the traditional diagnostic criteria for FAS. These children each had the characteristic facies, growth retardation, and evidence of central nervous system dysfunction (e.g., microcephaly, mental retardation, or attentional deficits). An additional 13 children had histories of significant prenatal exposure to alcohol but did not meet the traditional criteria for

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Supported in part by National Institute on Alcohol Abuse and Alcoholism grant No. AA10417.

Submitted for publication July 30, 1996; accepted Jan. 15, 1997.

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0022-3476/97/$5.00 + 0 9/21/80750

FAS. We identify this group as the PEA group. The children in this group lacked both the facial features and prenatal or postnatal growth deficiency characteristic of FAS. Although the majority had some evidence of cognitive or behavioral impairment, none were microcephalic. All of the alcohol-exposed children had been seen by one of us (K.L.J.) for dysmorphology evaluation before testing. Alcohol exposure was confirmed through maternal/relative report (62% of FAS cases; 77% of PEA cases), from birth records (6% of FAS cases), or from social services (32% of FAS cases; 23% of PEA cases). Although detailed histories (i.e., daily records) of the actual levels of exposure were typically not available, in all cases the mothers were known to be abusing alcohol and typically drank daily throughout their pregnancy.

The other 47 children in this study were normal control subjects recruited from the community. They were matched by age and sex with children in the two alcohol-exposed groups. Exclusionary criteria included the occurrence of a primary language other than English; any major medical, neurologic, or psychiatric disorder; or any physical limitation that would preclude participation. For the NC group, subjects were also screened for prenatal exposure to possible teratogens. As a whole, the NC group reported very minimal or no prenatal alcohol exposure. The children ranged in age from 4 to 16 years. Demographic data for the three subject groups are presented in Table I.

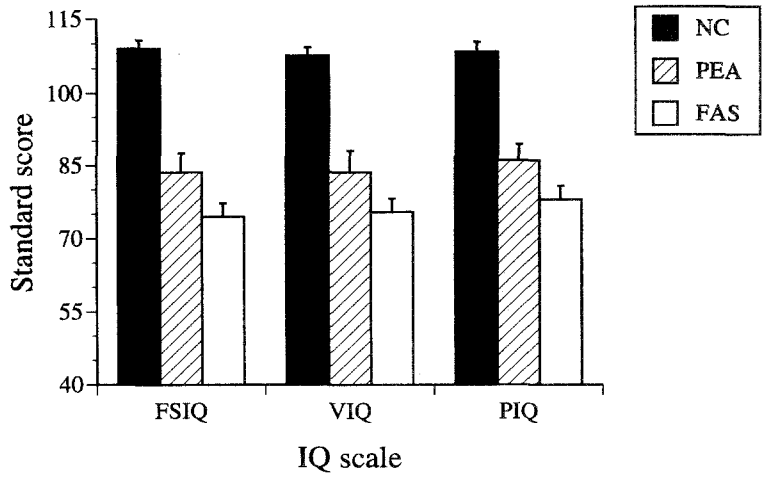

Fig. 1. Performance of children with fetal alcohol syndrome (FAS), prenatal exposure to alcohol (PEA), or matched normal control subjects (NC) on age-appropriate tests of IQ.

Table I. Demographic characteristics of study population

Group	Age (M ± SD)	Sex (Female/male)	Ethicity (% White)	Handedness (% Right)
NC	8.6 (3.8)	22:25	66.0	93.6
PEA	8.5 (4.0)	8:5	38.5	92.3
FAS	8.5 (3.8)	17:17	50.0	82.4

Chi-square test (sex, ethnicity, handedness) or ANOVA (age) revealed no differences among the groups (p values > 0.1).

RESULTS

Both Wechsler revised scales are standardized tests composed of 12 individual subtests encompassing both verbal and nonverbal abilities. Both tests provide three IQ indexes: the Full Scale IQ, Verbal IQ, and Performance (nonverbal) IQ. FSIQ scores were analyzed by a 3 × 2 analysis of variance with group (FAS, PEA, or NC) and sex (male or female) as between-subjects variables. In addition, VIQ and PIQ were analyzed by a 3 × 2 × 2 repeated measures ANOVA with group and sex as between-subjects variables and IQ scale (VIQ and PIQ) as the within-subject measure. Finally, to assess specific deficits on the subtests, the subtests were analyzed by two 3 (group) × 2 (sex) multivariate ANOVAs with follow-up univariate F tests.

For the measure of FSIQ, the ANOVA revealed a significant main effect of group ($F_{(2,88)} = 66.4$; $p < 0.001$). Because there was no main or interactive effects of sex (p values > 0.05), the data were collapsed over these variables for subsequent analyses and presentation in Fig. 1. Newman-Keuls tests revealed that the FAS and PEA groups both differed from the NC group and from each other (p values < 0.05). The mean FSIQ scores for the NC, PEA, and FAS groups were 109.0, 83.6, and 74.4, respectively.

For VIQ and PIQ, the repeated measures ANOVA revealed a significant main effect of group membership ($F_{(2,88)} = 65.44$; p values < 0.001), but no main or interactive effects of sex ($p > 0.05$). Newman-Keuls tests revealed that on both VIQ and PIQ, the NC group achieved a higher score than the two alcohol-exposed groups (p values < 0.05), which did not differ from each other. As shown in Fig. 1, the mean VIQ scores for the NC, PEA, and FAS groups were 107.4, 83.5, and 75.3, respectively, and the mean PIQ scores were 108.3, 86.0, and 77.9, respectively.

Group differences were also found on subtest scores. For the Wechsler Preschool and Primary Scale of Intelligence-Revised scale, the multivariate ANOVA revealed an overall main effect of group membership (Wilks' lambda (24, 54) = 3.28; $p < 0.001$), but no main or interactive effects of sex (p values > 0.05). Follow-up univariate F tests were conducted with alpha levels set at $p < 0.002$ to correct for familywise error. These analyses revealed group differences for all but three subtests (Picture Completion, Sentences, and Similarities). For all but one (Comprehension) of the remaining subtests, Newman-Keuls tests revealed that the NC group achieved a higher

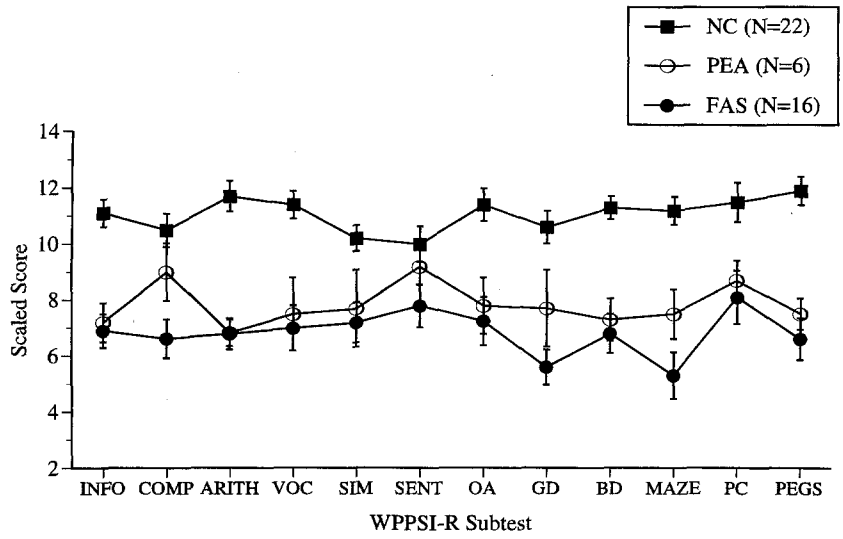

Fig. 2. Performance of children with fetal alcohol syndrome (FAS), prenatal exposure to alcohol (PEA), or matched normal control subjects (NC) on the subtests of the Wechsler Preschool or Primary Scale of Intelligence-Revised.

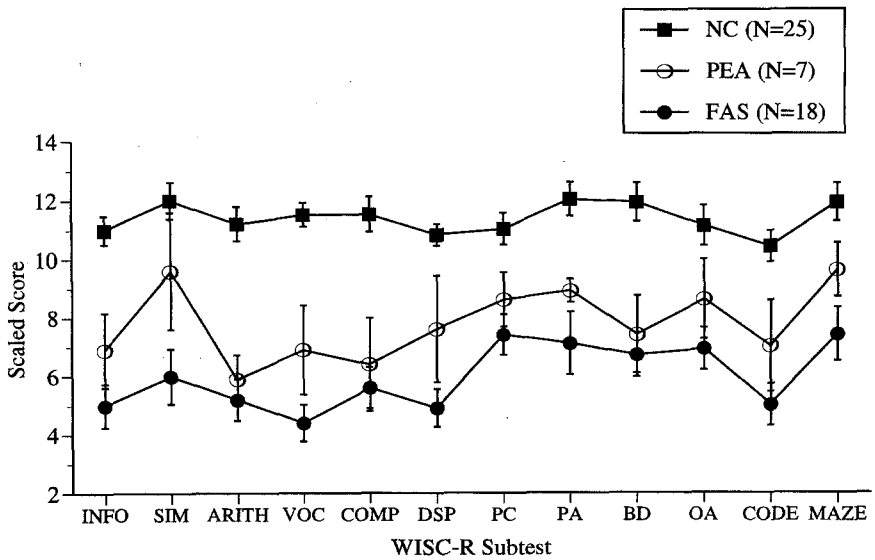

Fig. 3. Performance of children with fetal alcohol syndrome (FAS), prenatal exposure to alcohol (PEA), or matched normal control subjects (NC) on the subtests of the Wechsler Intelligence Scale for Children-Revised.

score than the two alcohol-exposed groups (p values < 0.05), which did not differ from each other. On the Comprehension subtest only the FAS versus NC group comparison was significant.

Similar results were found on the Wechsler Intelligence Scale for Children-Revised subtests. The multivariate ANOVA revealed a main effect of group (Wilks' lambda (24, 66) = 3.67; p < 0.001), but no main or interactive effects of sex (p values > 0.05). Follow-up univariate F tests revealed group differences for all subtests (p values < 0.002), and Newman-Keuls tests revealed that the FAS group performed significantly worse than the NC group on all measures (p values < 0.05). In addition, the PEA group differed from the NC group on all but three subtests (Similarities, Object Assembly, and Mazes subtests) and from the FAS group on three subtests (Similarities, Vocabulary, and Digit Span). Average subtest scores are presented in Figs. 2 and 3.

Finally, the roles of home environment and SES were evaluated in two exploratory analyses. Alcohol-exposed subjects were categorized into three types of home placements: biologic homes (49%), long-term foster or adoptive homes (34%), or other foster homes (17%). ANOVAs comparing the FSIQ scores among these three type of home placements revealed no significant differences among any of the groups (F < 1.0). For the analysis of SES, Hollingshead estimates of SES (A. Hollingshead; unpublished data, 1975) were available for 68% of the subjects. Using only this subset, a regression analysis was conducted using group and Hollingshead SES to predict FSIQ scores. This analysis indicated that although SES was marginally related to IQ on its own (p = 0.09), group was a much stronger predictor (p < 0.0001).

DISCUSSION

These data indicate that children born to women who drink heavily during pregnancy have an increased risk of cognitive impairment, even in the absence of the facial features and growth deficiencies characteristic of FAS. In this study, alcohol-exposed children, with or without a diagnosis of FAS, performed significantly worse than control subjects on measures of IQ. It is important to recognize that the PEA group, those subjects without the characteristics of FAS, is slightly less affected than the FAS group by their alcohol exposure. Although the differences between these two groups did not reach statistical significance for most measures, there was a statistically significant difference on FSIQ and a consistent tendency for the PEA group to be less affected than the FAS group on most subtests. A power analysis performed on the data indicated that a sample of 100 children in each group would be needed to determine which of the observed group (FAS vs PEA) differences are significant. Nonetheless, it is important to emphasize that the PEA group appears functionally much more similar to the FAS group, as evidenced by their similar pattern of subtest scores.

These results emphasize the need to evaluate children with histories of prenatal alcohol exposure for cognitive deficits regardless of whether they have the physical features and growth deficits charac-

teristic of FAS. In the present study, there was a wide range of IQ scores for the FAS and PEA groups, ranging from 40 to 112. The distribution of IQ scores is shown in Table II. In addition, the FSIQ scores for the PEA group ranged from 64 to 112, with a mean of 83.6. This is more than one standard deviation below the standardized average of this measure. It is also more than two SDs below the average for the NC group who were matched to the alcohol-exposed subjects on several important demographic criteria.

These results are concordant with and extend previous data showing intellectual deficits in children with histories of heavy prenatal alcohol exposure. The average IQ of the FAS subjects in this study was 74.4. In reviewing 58 cases of FAS, Abel[6] reported an average IQ of 67. Streissguth et al.[7] found that individuals with a diagnosis of FAS had a mean IQ of 66, whereas those individuals with a partial phenotype of FAS had a mean IQ of 79.5. In another article by the same group, the mean IQ was 66 for individuals with FAS and 73 for those with the partial phenotype.[8] Similar to the data set forth in our study, the FAS group was more impaired than the group without all the characteristics associated with FAS. The current study goes beyond previous data on the partial phenotype by demonstrating marked cognitive deficits in alcohol-exposed children lacking both the pattern of facial features and growth deficiency characteristic of FAS.

The extent to which this sample represents the larger population of alcohol-exposed children or conversely whether it suffers from an ascertainment bias is unknown. Although an ascertainment bias is possible, we do not believe this to be the case, because some were identified in the newborn nursery as children of alcoholic women and some subjects were obtained prospectively by a teratogen information service. In fact, a comparison of the 14 alcohol-exposed children who were originally evaluated in the first year of life, including 12 who were identified either prenatally or in the newborn nursery, revealed no difference in IQ (mean = 77.2, SD = 17.98) from the other alcohol-exposed children (N = 33) who were evaluated later in life (mean = 76.9, SD = 15.60).

Table II. IQ score distributions for study groups

Group	IQ range			
	Above average (≥110) No. (%)	Average (90-109) No. (%)	Below average (70-89) No. (%)	Intellectually deficient (≤69) No. (%)
NC	23 (48.9)	21 (44.7)	3 (6.4)	0 (0)
PEA	1 (7.7)	4 (30.8)	5 (38.5)	3 (23.0)
FAS	0 (0)	6 (17.6)	17 (50.0)	11 (32.4)

Given the number of children born to women who abuse alcohol, a clear understanding of potential outcome in these children is warranted. According to Abel,[6] 8742 children with FAS were born in the United States in 1986; however, there were 12 times that many children born to alcohol-abusing mothers whose condition was not so diagnosed. The data from this report indicate that these children are at risk of significant cognitive deficits that are likely to interfere with everyday functioning. It is important to emphasize, however, that the diagnosis of FAS is associated with a wide range of cognitive development. In the current study, six (18%) of the children with FAS and five (38%) of the children with PEA displayed FSIQ scores at or above the average range (≥90), illustrating the wide range of abilities in children exposed to alcohol (see Table II). However, just as the presence of facial features should not definitively label a child as cognitively impaired, neither should their absence suggest that no impairment exists.

In conclusion, these data indicate that in cases where there is documented alcohol abuse during pregnancy, the absence in the offspring of physical features associated with FAS does not imply the absence of intellectual compromise. Assessment of cognition and other behaviors should be considered at a young age in all children prenatally exposed to alcohol so that remediation efforts can begin as early as possible.

We thank Rachel Braithwaite, Carolyn Spencer, Kathleen Johnson, Julie Rippeth, and Catie Stern for their assistance.

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