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Measures of Maternal Alcohol Use as Predictors of Development in Early Childhood

Marcia Russell, Donna M. Czarnecki, Richard Cowan, Elizabeth McPherson, and Pamela J. Mudar

The effect of prenatal alcohol exposure on growth, dysmorphology, and cognitive development at 6 years was examined in children whose mothers had completed a self-administered questionnaire during pregnancy. Drinking patterns prior to pregnancy recognition and indications of problem drinking (IPD) were assessed. Heavier alcohol intake was associated with slower growth in height and head circumference and increased dysmorphology, as evidenced by facial features associated with fetal alcohol syndrome (FAS) and the prevalence of probable/possible fetal alcohol effects (FAE). Indications of problem drinking predicted facial features associated with FAS and cognitive deficits (i.e., lower WPPSI Verbal IQ scores and lower scores on a test of receptive language function, the Token Test). Effects of alcohol consumption on head circumference and of indications of problem drinking on Verbal IQ and Token Test scores remained significant, even after excluding children born to mothers having drinkers (over seven drinks a day) and children with probable/possible FAE. Verbal IQ was an average of 7.1 points (95% confidence interval = 0.01, 14.25) lower among children born to mothers having more than one indication of problem drinking than it was among those born to women having fewer indications; Token Test scores were 4.3 points lower (95% confidence interval = 1.38, 7.24). Although the confidence intervals for these estimates are broad in this small, heterogeneous sample, their magnitude, if confirmed, is significant given that the population standard deviation for Verbal IQ is 15, and that for the Token Test is 5.

Key Words: Fetal Alcohol Syndrome, Cognition, Growth, Dysmorphology, Screening.

THE FETAL ALCOHOL Syndrome (FAS) refers to a recognizable pattern of abnormalities observed in children born to alcoholic mothers.[1] It is diagnosed by the presence of abnormalities in each of three categories: (1) prenatal and/or postnatal growth retardation; (2) central nervous system (CNS) involvement; and (3) a characteristic face.[2] Since its description, numerous studies have documented the potential of prenatal alcohol exposure to damage the fetus, and the importance of intervening to reduce maternal drinking during pregnancy has been widely recognized.[3]

The present study was part of a program to evaluate methods for the early identification of women whose alcohol use puts their pregnancies at high risk. In 1978 and 1979, obstetric outpatients waiting for prenatal care appointments were asked to complete a self-administered questionnaire on alcohol use prior to pregnancy recognition (Prior to Pregnancy Absolute Alcohol per day, PPAA) and indications of problem drinking (IPD). PPAA was selected for evaluation because drinking patterns prior to pregnancy generally persist until pregnancy is recognized (from 6 to 8 weeks after conception), overlapping with much of the period during which embryonic development takes place.[4] In addition, drinking prior to pregnancy may provide a better measure of maternal drinking during the early weeks of pregnancy than does drinking at the time of the first prenatal examination. By then, many women have already reduced their alcohol intake,[5] and those who have not reduced their intakes may be more reluctant to report current than past heavy drinking.[6,7] IPD was selected for evaluation because it is correlated with heavy alcohol intake, and it may be associated with a tendency to continue drinking throughout pregnancy, increasing the period of prenatal alcohol exposure.[8,9]

A follow-up of pregnancy outcome indicated that PPAA predicted spontaneous abortion and lower Apgar scores, whereas IPD predicted smaller head circumference, lower birth weight, and lower Apgar scores.[10] These findings support the potential clinical utility of PPAA and IPD in the early identification of women whose alcohol use puts their pregnancies at high risk.

In the present study, the research question was extended to determine whether PPAA and IPD predicted development in early childhood. Long-term mental impairment, deficits in academic achievement, and maladaptive behavior have been reported in children of alcoholic mothers who were diagnosed as having fetal alcohol syndrome or fetal alcohol effects (FAE).[11,12] In addition, a number of prospective studies in the U.S. and Canada have assessed long-term consequences of prenatal alcohol exposure in children born to population-based samples of obstetric patients.[13] Positive relationships between prenatal alcohol exposure and dysmorphology,[14,15] lower weight,[16] shorter height and smaller head circumference,[15,16] and deficits in cognitive and neurobehavorial development,[15-20] have been reported among preschool children.

The present study was based on the hypotheses that: (1) heavy maternal alcohol consumption prior to the recognition of pregnancy and indications of problem drinking are associated with prenatal exposure to alcohol; (2) pre-

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natal alcohol exposure, as measured by PPAA and IPD, will increase the incidence of minor physical anomalies and/or alter development such that growth, general intelligence, and specific cognitive skills will be adversely affected; and (3) these effects will not be readily attributed to other potentially confounding factors such as poor postnatal health, postnatal environmental deficiencies, and familial/hereditary influences. To investigate whether effects can be attributed to the inclusion of a few severely affected children, we examined the effects of prenatal alcohol exposure on growth and cognition after excluding children born to very heavy drinkers and those diagnosed as having probable/possible FAE.

METHODS

Sample

In 1978 and 1979, a systematic sample of obstetric patients receiving prenatal care at five sites in Buffalo, New York, participated in a Women's Health Survey. Sites were selected to include patients from a broad range of socioeconomic levels. During a prenatal visit, 547 participants completed a self-administered questionnaire on the following topics: patterns of alcohol use prior to pregnancy recognition; indications of problem drinking; drug use in the month prior to pregnancy recognition; smoking; reproductive history; menstrual problems; and sociodemographic characteristics. Pregnancy outcome assessed at birth was analyzed with respect to prenatal alcohol exposure among 490 live births.[10]

The present study was based on a 6-year follow-up of 313 children. This group included all children born to abstainers, heavy drinkers (PPAA >1), or problem drinkers (IPD >1), plus a sample of light/moderate drinkers (0<PPAA<1) that was matched with heavy and problem drinkers on age, race, education, and child's sex as closely as possible. A response rate of 59% (186/313) was obtained. Children were excluded from the study if their mothers reported they had had serious postnatal health problems ($n = 8$) or if data were missing on potentially confounding factors ($n = 3$), for a final sample size of 175. The dysmorphologist was unavailable to examine 23 children; therefore, analyses of growth and dysmorphology were based on 152 subjects. To maintain comparability among the cognitive tests, data are presented for 164 children having valid information on all five measures of cognitive development; 11 children were excluded. Cognitive data were omitted for nine children who did not pass an auditory screening test, because hearing deficits may have reduced comprehension of instructions given verbally by the examiner. Data were also omitted for children not eligible to take the Token Test because they had not yet mastered the requisite concepts of shapes and colors ($n = 2$). There was no bias related to PPAA or IPD associated with any of the above exclusionary criteria.

Procedures

Matching procedures were carried out by the project director (MR); all other investigators were blind to the alcohol exposure data. Children's growth and minor physical anomalies were assessed by a pediatric dysmorphologist (EMcP). Children's hearing and cognitive tests were conducted by a graduate student in psychology (DC) who received extensive training in their administration. While children were being assessed, their mothers completed a cognitive test and were interviewed regarding their sociodemographic characteristics; the children's behavior, health history since birth, and postnatal environment; and drinking history of their children's fathers. Interviewers were matched with mothers on race. The interviewer not making the assessments greeted mothers and their children and escorted them to their respective testing/interview sites, so that staff making children's assessments were not influenced by having met the mothers and vice versa.

Alcohol Measures

Alcohol Intake (Prior to Pregnancy Absolute Alcohol, PPAA). Drinkers in the present study were defined as women who had had at least one drink in the year prior to recognizing their pregnancy, the drinking time frame established for obstetric patients. They were asked how often they had wine, and how many glasses they usually had at one time when they had wine. These quantity-frequency questions were repeated for beer and liquor. Total absolute alcohol intake was calculated after Jessor et al,[21] and, as indicated earlier, expressed in terms of average ounces of absolute alcohol consumed per day, where 1 ounce of absolute alcohol is equal to approximately two drinks. Measures of alcohol consumption based on frequency of having five or more drinks at a time were not more significantly related to pregnancy outcome measures than PPAA; therefore, further analyses employed PPAA.

Light/moderate drinking was defined as 0<PPAA<1; heavy drinking was defined as 1≤PPAA<3.5; and PPAA >3.5 was considered very heavy drinking. These definitions are based on prior research that employed a cut-off point of 1 ounce of absolute alcohol to define heavy drinking,[22] and the frequency distribution of PPAA, plotted in Fig. 1. This plot shows a marked break in the distribution of alcohol consumption, with very heavy drinkers reporting substantially larger alcohol intakes than heavy drinkers, over 16 drinks per day compared to seven or less. The very heavy drinking group also included two women who reported five indications of problem drinking, whereas most women with >1 IPD reported only two ($n = 10$) or three ($n = 2$). No one reported four IPDs.

Indications of Problem Drinking (IPD). Questions assessing indications of problem drinking were adapted from established alcoholism screening measures and tested in a sample of obstetric and gynecologic out-patients.[23] Indications selected for use in the present study were: (1) Has a friend or family member ever told you about things you said or did while you were drinking that you do not remember? (2) During the past year, have close relatives or friends worried or complained about your drinking? (3) Are you able to stop drinking when you want to? (4) Does drinking sometimes lead to problems between you and your family, that is, husband, children, parent, or close relative? (5) Do you sometimes take a drink in the morning when you first get up? (6) Do you sometimes feel the need to cut down on your drinking? (7) Have you ever gone to anyone for help about your drinking? (8) Have you ever been told by a doctor to stop drinking? Indication No. 3 was scored 1 for a negative answer; all others were scored 1 for a positive answer; scores were added for an overall IPD score. Scores over 1 were interpreted as indicating probable problem drinking.

Measures of Child Development

Measures of child development were selected to assess postnatal growth, dysmorphology, and cognitive development.

Growth, Dysmorphology. The pediatric dysmorphologist measured weight, height, and head circumference; recorded the presence of minor physical anomalies[24]; and made a clinical assessment of probable/possible FAE. The latter assessment indicates that the physical findings were consistent with FAS, but that additional information on CNS function and maternal drinking history would be required to make an FAS diagnosis. Although prenatal alcohol exposure produces features in some children distinctive enough to predict maternal alcoholism,[25] in other children findings are merely suggestive and may represent a variant of normal physiognomy or exposure to a teratogen other than alcohol. Accordingly, probable/possible FAE can be found in the absence of prenatal alcohol exposure when assessments are made without knowledge of maternal alcohol history. Indeed, estimates of the prevalence of probable/possible FAE among children of abstainers is necessary to the calculation of the relative risk for this condition attributable to prenatal alcohol exposure.[26]

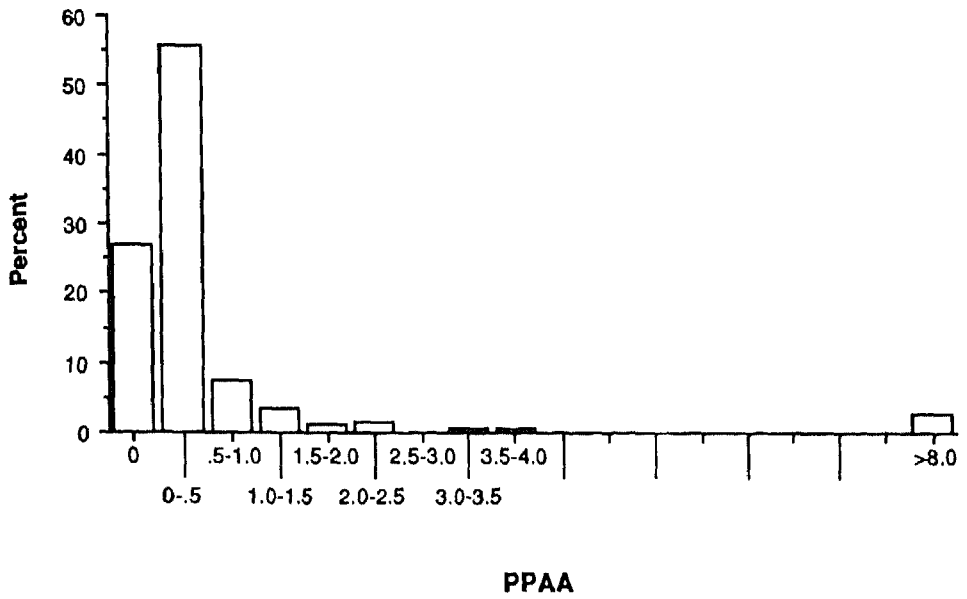

Fig. 1. Distribution of PPAA, ounces of absolute alcohol per day prior to pregnancy recognition.

Minor physical anomalies were each scored 1, and scores were added for an unweighted overall anomalies score. A score for facial features associated with prenatal alcohol exposure was based on the following features: (1) midface hypoplasia; (2) shortening of the palpebral fissures relative to inner canthal distance; (3) nose (depressed bridge and short length and anteverted tip and flat philtrum); and (4) mouth (thin upper lip and small jaw).[27] Each feature received a score of 1, and scores were added for a possible total of 4; no child received a score higher than 2 on this measure.

Cognitive Development. Intellectual development was evaluated on three dimensions: general intelligence, receptive language function, and visual-motor integration. General intelligence was assessed using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI).[28] The WPPSI provides measures of both Verbal and Performance IQ. Both are reported to further investigate previous reports indicating that prenatal alcohol exposure impairs language development.[29-31]

Receptive language function was measured using the Token Test for Children.[32] The child is asked to follow the examiner's commands to touch one or more colored tokens having simple geometric shapes (circles or squares). There are 61 commands that become progressively more difficult with respect to length and/or grammatical complexity. The Token Test assesses linguistic rather than intellectual abilities, without using difficult words and without requiring extensive memorization or verbatim repetition. Raw scores on the Token Test were transformed to a standard score scaled for a child's age, with a mean of 500 and standard deviation of 5. Normal scores range from 495 to 505; scores below 495 are considered inferior, and those above 505 are considered exceptional.

Visual-motor integration was measured with the Beery-Buktenica Developmental Test of Visual Motor Integration (VMI).[33,34] This test is designed primarily for preschool and early primary school children. Twenty-four geometric forms are arranged in order of increasing difficulty, and the child's task is to reproduce each form. The number of forms correctly reproduced provides a developmental age of VMI. The VMIs were interpreted by a clinical psychologist then on staff at Children's Hospital of Buffalo (Mark Schachter, Ph.D.). A second measure, the Draw-A-Line-Slowly test, evaluated the ability of young children to inhibit motor activity in order to perform a task according to instructions.[35,36]

Covariates

A major concern in interpreting any deficits in child development related to maternal alcohol use is whether or not these deficits could also be accounted for by parental characteristics and/or postnatal environmental factors associated with maternal alcohol use. Accordingly, a number of potentially confounding variables were assessed in the present study. As listed in Table 1, maternal characteristics examined included two poverty measures (clinic vs. private patient status and method of payment for delivery, public assistance vs. private pay/insurance); marital status (married vs. not married); race (white vs. black); whether or not the child's father or a father figure was present in the home; a measure of maternal IQ, the Vocabulary score from the Weschler Adult Intelligence Scale-Revised (WAIS-R), which has a correlation of 0.85 with Full-Scale IQ[37]; socioeconomic status (SES), based on the Hollingshead 2-factor index of social position,[38] which employs occupation and education (highest value, assessed for each child's mother and father or father figure if the latter were present in the home); age; number of cigarettes smoked per day; frequency of taking psychoactive drugs with the potential for nonmedical use in the month prior to pregnancy recognition[10]; and rate of weight gain during pregnancy (grams per week).

Paternal drinking was assessed at the time of the 6-year follow-up. Mothers were asked whether their child's father had ever had problems with alcohol, and how many days in a year he had 11 or more drinks at the time of their pregnancy in 1978 and 1979. The latter question was repeated for five to 10 drinks, and the two estimates were added to obtain an estimate of the days per year the child's father had five or more drinks.

Three dimensions of the postnatal environment were assessed, quality of the child-rearing environment, family emotional atmosphere, and family stability. All measures depended on maternal self-report. The quality of the child-rearing environment was measured using the Home Screening Questionnaire (HSQ).[39] It is a parent-answered screening questionnaire based upon the Home Observation for Measure of the Environment (HOME) Inventory. The HOME requires a home visit, but the HSQ does not. Assessment of the family emotional atmosphere was based on three measures of family characteristics developed for a national survey of families.[40] The measures are family strengths (pride and accord), family satisfactions, and the Family Adaptability and Cohesion Evaluation Scale (FACES II). Family stability was assessed in terms of life events. Our measure, a 27-item unweighted life event scale, was developed using previous instruments[41,42] as guides. Events are summed from birth to the time of the interview to provide an overall score. An additional measure of postnatal environment was provided by the number of months of nursery school attended by the child.

Child's gestational age, sex, and age at testing were also taken into consideration.

These sample characteristics are summarized with respect to PPAA

Table 1. Sample Characteristics, According to Maternal Drinking Prior to Pregnancy Recognition (PPAA) and Indications of Problem Drinking (IPD)

	PPAA				IPD		
	Abstainer (n = 46)	Not Heavy (n = 111)	Heavy (n = 13)	Very Heavy (N = 5)	≤1 (n = 161)	>1 (n = 14)	Total (N = 175)
Maternal characteristics							
Clinic patients (%)	84.8	52.3	61.5	100.0***	61.5	78.6	62.9
Receiving public assistance (%)	63.0	40.5	46.2	100.0**	46.6	71.4	48.6
Not married (%)	56.5	36.0	38.5	100.0**	41.0	71.4*	43.4
Black (%)	69.6	33.3	30.8	40.0***	41.0	64.3	42.9
Single parents (%)	47.8	31.5	61.5	80.0*	37.9	57.1	39.4
WAIS-R vocabulary score	27.9 ± 16.8	40.9 ± 16.3	38.5 ± 19.1	32.4 ± 5.0***	37.6 ± 17.5	30.6 ± 12.7	37.1 ± 17.3
Age in years	22.7 ± 5.0	26.2 ± 5.1	26.7 ± 5.8	21.8 ± 0.8***	25.2 ± 5.2	25.6 ± 5.8	25.2 ± 5.3
SES, Hollingshead 2-factor index	4.2 ± 1.0	3.6 ± 1.3	3.8 ± 1.6	4.8 ± 0.4**	3.8 ± 1.3	4.1 ± 1.3	3.8 ± 1.3
Smoking (cigarettes per day)	3.1 ± 7.0	5.4 ± 8.6	4.1 ± 6.4	14.6 ± 12.7*	4.5 ± 8.0	9.7 ± 11.1*	4.9 ± 8.3
Drug use (times/month)	0.0 ± 0.0	3.2 ± 13.9	9.8 ± 34.9	0.4 ± 0.9	2.8 ± 14.9	3.1 ± 10.6	2.8 ± 14.5
Pregnancy weight gain (g/week)	336.1 ± 139.1	356.3 ± 131.4	313.2 ± 205.2	311.8 ± 53.5	348.2 ± 142.0	326.7 ± 83.5	346.5 ± 138.2
Paternal characteristics							
Ever had alcohol problems (%)	21.7	24.3	46.2	40.0	27.3	7.1	25.7
Frequency, 5+ drinks/year	36.0 ± 95.6	65.0 ± 115.4	170.5 ± 160.5	135.4 ± 167.2**	69.1 ± 121.6	46.6 ± 100.5	67.3 ± 120.0
Postnatal environment							
Home Screening Questionnaire Score	41.1 ± 5.2	44.2 ± 4.9	42.3 ± 6.3	41.2 ± 4.9**	43.4 ± 5.1	40.9 ± 5.7	43.2 ± 5.2
Family strengths	46.8 ± 8.7	47.5 ± 6.4	47.1 ± 7.8	46.8 ± 7.7	47.3 ± 7.1	47.1 ± 7.1	47.3 ± 7.1
Family satisfactions	50.3 ± 9.3	50.2 ± 9.0	48.9 ± 13.1	50.6 ± 8.6	50.2 ± 9.3	49.3 ± 10.2	50.1 ± 9.4
FACES II	1.6 ± 0.7	1.6 ± 0.7	1.5 ± 0.5	1.8 ± 0.4	1.6 ± 0.7	1.6 ± 0.7	1.6 ± 0.7
Months of nursery school	9.8 ± 9.8	14.6 ± 8.8	14.6 ± 9.7	6.0 ± 5.5**	13.2 ± 9.2	12.4 ± 11.1	13.1 ± 9.3
Number of life events	11.2 ± 7.4	9.2 ± 6.6	10.2 ± 6.4	9.4 ± 3.4	9.6 ± 6.8	11.5 ± 5.9	9.8 ± 6.8
Child characteristics							
Gestational age in weeks	40.0 ± 2.5	40.1 ± 2.1	39.9 ± 2.3	39.2 ± 1.3	40.1 ± 2.2	39.6 ± 2.1	40.0 ± 2.2
Male (%)	39.1	48.6	61.5	60.0	46.0	64.3	47.4
Age at testing in months	75.1 ± 2.3	74.5 ± 2.3	73.8 ± 2.5	73.2 ± 1.3	74.6 ± 2.3	74.2 ± 2.8	74.6 ± 2.3

Percent or mean ± SD as indicated.
* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, analysis of variance.

Table 2. Principal Components Analysis for Covariates

Variables	Component Loadings								h^2
	1	2	3	4	5	6	7	8	
Clinic patients	0.85								0.78
Receiving public assistance	0.85								0.77
WAIS-R vocabulary score	−0.84								0.75
Not married	−0.81								0.69
SES, Hollingshead 2-factor index	0.79								0.77
Maternal race	0.78								0.78
Home Screening Questionnaire Score	−0.66								0.64
Maternal age	−0.62								0.60
Single parent	0.55								0.55
Family strength		0.88							0.81
Family satisfaction		0.84							0.81
Paternal alcohol problems			0.88						0.80
Paternal drinking frequency, 5+ drinks/year			0.87						0.81
Child's sex				0.73					0.60
Child's age				−0.71					0.61
Maternal smoking					0.81				0.70
Number of life events					0.56				0.63
Months of nursery school						0.79			0.71
FACES II						−0.63			0.62
Weight gain during pregnancy (g/week)							0.74		0.68
Gestational age in weeks							0.57		0.54
Drug use (times/month)								0.91	0.87
Eigen value	5.41	1.94	1.93	1.31	1.31	1.31	1.21	1.10	
% variance	24.6	8.8	8.8	6.0	6.0	6.0	5.5	5.0	
Cumulative % variance	24.6	33.4	42.2	48.2	54.2	60.2	65.7	70.7	

.though the use of matching in the sampling design
. between light/moderate and heavy drinkers and
and without >1 IPD, abstainers and very heavy
ffer from light/moderate and heavy drinkers on
:s and two measures of the postnatal environment.
:quency of heavy drinking was positively associated
lrinking.
y small sample size, including this large number of
.n the analyses would have reduced the power and
r estimation concerning the partialed relationships
hol exposure and the developmental outcomes.[43,44]
omponents analysis (PCA) was employed to reduce
ıles to a manageable number.[43] PCA with varimax
ght readily interpretable components, which ac-
:he variability in the 22 measures. Factor loadings
ırized in Table 2. The first component, accounting
variability, summarized maternal intelligence and
ıaracteristics. The second component tapped the
'ironment. The third component measured paternal
/ior. Child characteristics made up the fourth com-
; composed of stress factors. The sixth component
al environment, and the seventh consisted of preg-
inal component was comprised of a single measure
ctive drug use. The rationale for the principal com-
s pragmatic, rather than theoretical; however, the
factors correspond to meaningful constructs supports
)proach.
fect of PPAA and IPD on child development was
ıalysis of covariance.[43,44] Tests for linear trends were
A[43,44]; and findings obtained for probable/possible
dependent variable, were confirmed using multiple
To determine whether components not included in
nfounders, the 22 covariates included in the principal
s were entered into regression analyses after the eight
of the covariates made an additional significant
variability in child development measures; therefore,
)onents were used to adjust for potentially confound-
'esent analyses.

RESULTS

:an measures of dysmorphology, growth, levelopment are summarized according to PPAA and IPD in Table 3. PPAA was associated with significant positive linear trends in the number of facial features associated with FAS ($p < 0.05$) and the proportion of children diagnosed as having probable/possible FAE ($p < 0.05$). Having >1 IPD was associated with significantly more FAS facial features ($P < 0.10$; given that the direction of the difference is in the hypothesized direction, this is equivalent to a significance level of $P < 0.05$ for a one-tailed test). The mean number of FAS facial features was approximately twice as high among children born to very heavy drinkers or women with >1 IPD as it was among women drinking less or having fewer IPDs. The proportion of children diagnosed as having probable, possible FAE was twice as high among children of heavy drinkers as it was among children of abstainers or light/moderate drinkers, and approximately four times higher among very heavy drinkers.

Significant negative linear trends in height ($p < 0.10$) and head circumference ($p < 0.05$) were also related to PPAA. Data on size at birth were missing for nine children; however, adjusting for size at birth in the children for whom data were available had very little influence on estimates of size at age six. Compared with children of abstainers ($n = 143$), on average children of heavy or very heavy drinkers were 3.9 cm shorter (95% confidence interval = 0.9, 7.0; $p = 0.013$); weighed 2.3 kg less (95% confidence interval = −0.6, 5.2; $p = 0.118$); and had head circumferences 1.3 cm smaller (95% confidence interval = 0.4, 2.1; $p = 0.004$). No significant differences in growth were associated with indications of problem drinking.

There were no significant linear trends in cognitive development associated with PPAA. However, Verbal IQ scores ($p < 0.10$) and Token Test scores ($p < 0.05$) were

/elopment by Maternal Drinking Prior to Pregnancy Recognition (PPAA) and Indications of Problem Drinking (IPD), Means and (Standard Errors) Adjusted for Covariate Components

	PPAA				IPD	
	Abstainer	Light/Moderate	Heavy	Very Heavy	≤1	>1
152)	(*n* = 39)	(*n* = 97)	(*n* = 11)	(*n* = 5)	(*n* = 139)	(*n* = 13)
ınt)	0.5 (0.10)	0.6 (0.06)	0.7 (0.18)	1.1 (0.27)**	0.5 (0.05)	0.9 (0.17)*
malies (count)	7.2 (0.50)	6.8 (0.30)	6.7 (0.88)	9.1 (1.31)	6.9 (0.24)	7.6 (0.82)
FAE (% yes)	8.0%	10.2%	18.9%	38.6%†	10.6%	17.8%
	119.5 (0.83)	117.7 (0.50)	115.8 (1.50)	115.8 (2.22)*	118.0 (0.41)	117.6 (1.40)
	23.2 (0.83)	22.8 (0.50)	21.3 (1.50)	21.3 (2.21)	22.7 (0.41)	23.0 (1.37)
;e (cm)	51.5 (0.24)	51.3 (0.14)	50.5 (0.43)	50.0 (0.63)**	51.2 (0.12)	51.2 (0.40)
ed for birth						
	(*n* = 34)	(*n* = 94)	(*n* = 10)	(*n* = 5)	(*n* = 130)	(*n* = 13)
	119.1 (0.87)	117.7 (0.49)	115.1 (1.53)	115.4 (2.17)*	117.8 (0.41)	118.0 (1.37)
	23.0 (0.82)	22.8 (0.46)	20.5 (1.45)	21.1 (2.03)	22.6 (0.38)	23.2 (1.27)
ce (cm)	51.5 (0.24)	51.3 (0.14)	50.4 (0.43)	50.0 (0.60)***	51.2 (0.12)	51.3 (0.39)
ent (*N* = 164)	(*n* = 43)	(*n* = 106)	(*n* = 11)	(*n* = 4)	(*n* = 151)	(*n* = 13)
	107.8 (1.91)	107.7 (1.16)	111.8 (3.62)	101.1 (6.01)	108.3 (0.94)	101.8 (3.30)*
ıce IQ	100.7 (1.85)	101.9 (1.12)	99.9 (3.51)	101.7 (5.82)	101.3 (0.91)	102.7 (3.21)
scale)	498.0 (0.83)	498.8 (0.51)	499.9 (1.58)	496.6 (2.63)	498.9 (0.41)	495.6 (1.43)**
gration (per-	39.5 (3.72)	40.3 (2.26)	29.5 (7.06)	32.4 (11.72)	39.5 (1.85)	35.8 (6.51)
vly (seconds)	35.7 (2.76)	32.1 (1.68)	28.3 (5.24)	26.2 (8.69)	32.9 (1.37)	28.8 (4.82)

< 0.05; *** $p < 0.01$, analysis of covariance; PPAA, test for linear trend.
iple logistic regression; test for linear trend.

significantly lower among children born to women with >1 IPD than among women with ≤1 IPD.

To evaluate whether these findings can be attributed to the inclusion of a few severely affected children, analyses were repeated omitting children born to very heavy drinkers and those diagnosed as having probable/possible FAE (Table 4). Inasmuch as the diagnosis of probable/possible FAE was based heavily on dysmorphic features, dysmorphology was no longer significantly related to PPAA or IPD with cases of probable/possible FAE omitted from the analysis. Growth retardation was also less evident, although when data were adjusted for birth size, there was still a significant linear decrease in head circumference ($p < 0.05$) associated with PPAA. Although there was a general tendency for mean measures of cognitive development to be slightly higher in the restricted sample, there was no change in the pattern of findings. Cognitive development was not related to PPAA, but mean Verbal IQ ($p < 0.05$) and Token Test scores ($p < 0.01$) were significantly lower among children born to women with >1 IPD.

DISCUSSION

Findings in the present study indicated that alcohol intake prior to pregnancy recognition was associated with a higher mean number of facial features associated with FAS, a higher prevalence of probable/possible FAE, shorter mean height, and smaller mean head circumference in children at age six. Having >1 indication of problem drinking was associated with a higher mean number of FAS facial features and lower Verbal IQ and Token Test scores. Excluding children of very heavy drinkers and those diagnosed as having probable/possible FAE reduced the effect of PPAA on dysmorphology and growth, although mean head circumference was still negatively associated with PPAA when adjusted for head circumference at birth. However, these exclusions enhanced the significance of lower Verbal IQ and Token Test scores associated with >1 IPD.

We hypothesized that PPAA would measure heavy drinking early during pregnancy. Given that dysmorphic features occur in the first trimester, the positive relationship between PPAA and measures of dysmorphology support this hypothesis. Interpretation of the relationship between PPAA and growth retardation in terms of trimester of prenatal alcohol exposure is somewhat more complex. Much of prenatal growth takes place during the second and third trimesters; therefore, intrauterine growth retardation is thought to reflect the influence of exposure during the latter stages of pregnancy. Thus, failure to observe an effect of PPAA on birth length or head circumference at birth[10] suggested that PPAA was not sensitive to heavy alcohol use in the second and third trimesters. The present observation, that head circumference and height are significantly related to PPAA after controlling for size at birth, indicates reduced capacity for postnatal growth. Day et al.,[16] reported slower postnatal weight gain and growth in height among children whose mothers had an average of more than one drink per day during their third trimester of pregnancy. Women drinking in the third trimester also drank, more heavily on average, during the first and second trimesters, making it impossible to differentiate between effects of third trimester drinking and heavier drinking earlier or throughout pregnancy.[16] However, they also cited research in mice, which found postnatal growth retardation in the absence of retarded intrauterine growth associated with alcohol exposure late in gestation.[46] These studies suggest PPAA may be useful in predicting alcohol use later in pregnancy as well as during the first trimester.

Table 4. Child Development by Maternal Drinking Prior to Pregnancy Recognition (PPAA) and Indications of Problem Drinking (IPD), Means and (Standard Errors) Adjusted for Covariate Components. Excludes children of very heavy drinkers and children with probable/possible FAE

	PPAA			IPD	
	Abstainer	Light/Moderate	Heavy	≤1	>1
Dysmorphology ($N = 132$)	($n = 37$)	($n = 86$)	($n = 9$)	($n = 122$)	($n = 10$)
Facial features (count)	0.5 (0.10)	0.5 (0.06)	0.5 (0.20)	0.5 (0.05)	0.8 (0.18)
Minor physical anomalies (count)	6.8 (0.45)	6.4 (0.28)	6.1 (0.87)	6.5 (0.23)	6.6 (0.81)
Growth ($N = 132$)					
Height (cm)	119.9 (0.85)	118.0 (0.53)	117.1 (1.66)	118.5 (0.44)	118.6 (1.56)
Weight (kg)	23.6 (0.88)	23.2 (0.55)	22.2 (1.71)	23.2 (0.45)	23.7 (1.58)
Head circumference (cm)	51.6 (0.22)	51.5 (0.14)	50.8 (0.43)	51.5 (0.11)	51.7 (0.40)
Growth (Also adjusted for birth size; $N = 123$)	($n = 32$)	($n = 83$)	($n = 8$)	($n = 113$)	($n = 10$)
Height (cm)	119.6 (0.90)	118.1 (0.53)	116.5 (1.75)	118.3 (0.44)	119.0 (1.53)
Weight (kg)	23.4 (0.86)	23.2 (0.51)	21.0 (1.68)	23.0 (0.42)	23.9 (1.46)
Head circumference (cm)	51.7 (0.23)	51.5 (0.13)	50.6 (0.44)**	51.5 (0.11)	51.7 (0.39)
Cognitive development ($N = 146$)	($n = 41$)	($n = 96$)	($n = 9$)	($n = 135$)	($n = 11$)
WPPSI Verbal IQ	108.0 (1.90)	108.0 (1.18)	114.7 (3.95)	109.0 (0.97)	101.8 (3.46)**
WPPSI Performance IQ	100.6 (1.85)	102.1 (1.15)	101.2 (3.86)	101.5 (0.95)	103.4 (3.39)
Token Test (age-scale)	498.4 (0.80)	499.0 (0.49)	501.0 (1.66)	499.3 (0.40)	495.0 (1.42)***
Visual-Motor Integration (percentile)	39.0 (3.83)	41.3 (2.38)	27.5 (7.98)	40.1 (1.99)	36.9 (7.07)
Draw-A-Line Slowly (seconds)	34.8 (2.83)	31.8 (1.76)	26.4 (5.88)	32.4 (1.46)	30.4 (5.19)

* $p < 0.10$, ** $p < 0.05$; *** $p < 0.01$, analysis of covariance; PPAA, test for linear trend.

e effect of PPAA on head circumference
ınt even after children born to very heavy
se having probable/possible FAE were
: analysis suggests that the dose of alcohol
t growth may be less than that causing
rmations, and that offspring of drinkers
r growth deficiency without dysmorphic
to observe cognitive deficits associated
phology and growth deficiencies attrib-
somewhat surprising. However, the sam-
l heterogeneous, and large standard errors
or the adjusted means of the cognitive
dingly, the power of the study to detect
:ive functioning associated with PPAA is

on that indications of problem drinking
Verbal IQ and Token Test scores suggests
problem drinkers are at risk for deficits
ıctioning in the absence of growth defi-
ɔrphic features, as was also reported for a
of FAS.[47] Our earlier study of newborns
was associated with smaller head circum-
birth weight, and lower Apgar scores.[10]
: at birth has been correlated with slower
ɔpment[48] and an increased risk of mental
Thus, the fact that IPDs predicted small
ence at birth is consistent with the current
t IPDs predict cognitive deficits. Failure to
deficiencies in children at age six suggests
ɹn these parameters of development took
cognitive development lagged behind.
ample, adjusted mean Verbal IQ scores for
ɔthers with >1 IPD were normal, and the
s overlapped considerably with the range
hildren of mothers who had ≤1 IPD. The
the observed mean deficit can be appreci-
ɔnsidering the implications of a shift in the
ɨf Verbal IQ scores to the left, i.e., toward
In population samples VIQ scores are nor-
ted with a standard deviation of 15 points.
ɜtribution were seen for children of mothers
D, their risk of having a VIQ more than one
ation below the population mean (i.e., less
ld be over two times greater than that for
others having <1 IPD. The lower scores on
ɜst parallel the lower Verbal IQ scores and
ɜistent with previous reports that prenatal
ɹure impairs language development.[30,31]
ɔothesized that IPD would predict a tendency
ıeavy drinking during the second and third
was assumed that women having >1 IPD
subset of women drinking heavily prior to
:cognition. However, few women were high
.A and IPD, indicating that women with >1
t a subset of women high on PPAA. Failure
/smorphology and growth retardation among
children born to women with >1 IPD tends to validate the lack of correspondence between PPAA and IPD. Thus, having >1 IPD appears to be associated with drinking patterns insufficient to produce dysmorphology or growth retardation, but sufficient to produce cognitive deficits. It may be that relatively low intakes of alcohol among women having indications of problem drinking pose a risk because they are sustained throughout pregnancy, they are associated with binges during critical periods of CNS development, and/or they interact with some other vulnerability factor.

The fact that PPAA and IPD appear to identify different populations of women whose children are exposed to alcohol prenatally warrants further investigation. Obviously, it is possible to drink heavily without experiencing the types of problems included in our survey. In studies of alcohol screening methods in obstetric and gynecologic patients, it was found that heavy drinkers tended to be younger, and they were more likely to be unemployed and not attending school.[23] This and other studies[9,50] have documented an association between heavy drinking by women and heavy drinking by their mates. Thus, life styles may accommodate or even foster heavy drinking rather than create interpersonal problems, and young women may not have been drinking heavily long enough to have developed alcohol-related health problems. In such cases, self-reported alcohol consumption is a more sensitive indicator of prenatal alcohol exposure than indications of problem drinking.

It is less easy to understand how a respondent could have more than one indication of problem drinking without drinking heavily. One of the most likely explanations for this reporting pattern is that some women are willing to report indications of problem drinking, but underreport their alcohol consumption. Underreporting of alcohol consumption during pregnancy has been documented by a number of researchers[6,51,52]; whereas, indications of problem drinking was reported more reliably.[52] Although this tendency may have operated during the present study, as indicated above, if it were simply a matter of denial, one would expect to see higher rates of dysmorphology and growth retardation associated with IPD. Another possibility is that women experienced indications of problem drinking in the past, but were drinking less at the time of the index pregnancy. However, an investigation revealed no predominance of past IPDs among light/moderate drinkers having more than one IPD. Finally, it may be that some women drinking relatively low average amounts of alcohol may experience problems because they are more vulnerable to its effects than others, and this vulnerability may extend to the fetus. Definitive study of these possibilities awaits the development of more objective measures of alcohol consumption.

It would be useful to know more about the levels of alcohol use associated with delays in child development. Developmental delays associated with prenatal alcohol

56. Sokol RJ, Smith M, Ernhart CB, Baumann R, Martier SS, Ager JW, Morrow-Tlucak M: A genetic basis for alcohol-related birth defects (ARBD)? Alcoholism 13(2):343, 1989 (abstr)

57. Sokol RJ, Martier SS, Ager JW: The T-ACE questions: Practical prenatal detection of risk-drinking. Am J Obstet Gynecol 160(4):863–870, 1989

58. Russell M, Martier SS, Sokol RJ, Jacobson S, Jacobson J, Bottoms S: Screening for pregnancy risk-drinking: TWEAKING the tests. Alcoholism 15(2):368, 1991 (abstr)

59. Ewing JA: Detecting alcoholism: The CAGE questionnaire. JAMA 252:1905–1907, 1984

60. Selzer ML: The Michigan Alcoholism Screening Test: The quest for a new diagnostic instrument. Am J Psychiatry 127(12):1653–1658, 1971