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*Original contribution*

# Binge alcohol consumption by non-alcohol – dependent women during pregnancy affects child behaviour, but not general intellectual functioning; a prospective controlled study

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## Summary

Effects of binge ethanol consumption during early gestation on child neurodevelopment have not been elucidated. To study whether binge drinking affects cognitive abilities and behavior of exposed children, a prospective observational study comparing 51 children exposed to binge drinking during the first trimester of pregnancy to 51 children not exposed to any teratogens was conducted. The children's physical development, intelligence, language abilities and behavior were assessed.

Temperament test results showed that children exposed *in utero* to maternal binge drinking displayed a greater degree of disinhibited behavior and that this behavior was associated with early drinking variables. Although binge alcohol drinking by non-alcohol-dependent women during the first trimester of pregnancy does not appear to affect intelligence or cognitive and language development of young children, binge drinking in pregnancy does increase the likelihood of certain behavioral characteristics that might predispose these children to later behavioral dysfunction.

*Keywords:* Ethanol; binge drinking; pregnancy; child development; temperament.

## Introduction

Fetal alcohol syndrome (FAS) refers to the triad of birth defects (Jones and Smith, 1973) that include a common craniofacial dysmorphology, prenatal and postnatal growth deficiency, and central nervous system (CNS) abnormalities and dysfunction (Clarren and Smith, 1998). FAS occurs in 0.5 to 3 per 1,000 live births and may be as high as 10% in some native communities where drinking is a common lifestyle event. By all accounts, FAS is considered to be the most common teratogenically-induced (non-hereditary) form of mental deficiency throughout the western world and it leads to reduced intelligence (Conry, 1990), attention disorders (Nanson and Hiscock, 1990; Coles et al., 1997), various neuropsychological deficits (Kaemingk and Paquette 1999; Mattson et al., 1996; Kodituwakku et al., 2001a; Kodituwakku et al., 2001b), sleep disorders and behavioral problems. May and Gossage (May and Gossage, 2001) found an overall prevalence of FAS of 0.5 to 2 cases per 1000 births in the United States.

The Fetal Alcohol Spectrum Disorder encompasses FAS, partial FAS, alcohol-related neurodevelopmental disorder (ARND) and alcohol-related birth defects (Stratton et al., 1996). ARND, which involves CNS dysfunction in the absence of the facial or growth abnormalities, may in fact be much more frequent than FAS (Sampson et al., 1997). Although children with ARND look and grow normally, some can have even worse outcome than children with FAS. In both conditions, a set of characteristic primary disabilities as well as severe and debilitating lifelong secondary disabilities including mental illness and trouble with the law are common (Streissguth et al., 1996).

Although alcohol teratogenicity can occur at any stage of pregnancy, there is some evidence that early exposure

to a large volume of alcohol may be particularly harmful (Clarren et al., 1992). However, as this observation is based on co-relational evidence, there is clearly a need to conduct long-term developmental cohort studies directly investigating the effects of gestational binge drinking on children's physical and neurobehavioral development. This is especially relevant because binge drinking, which is defined as the consumption of five or more standard drinks per a single occasion, is a common pattern of drinking among young non-alcoholic women and the association between alcohol intoxication, unprotected sex, and unplanned pregnancies is an area of major social concern. Of greater concern is the fact that among American women between 18 and 44 years, binge drinking appears to be rising and has increases from 0.7% of pregnancies in 1991 to 2.9% in 1995 (Ebrahim et al., 1999; Serdula et al., 1991). Therefore, there is clearly a need to investigate the consequences of this phenomenon. The objective of the present study was to determine whether binge alcohol consumption in early pregnancy by non-alcoholic women affects abilities and behavior in preschool offspring. This was accomplished through a prospective case-matched study comparing children of women who reported binge alcohol drinking during early pregnancy with matched controls, who were never exposed to alcohol during pregnancy.

## Method

### *Participants*

Two groups of mother-child pairs were recruited from the Motherisk Program, an information and consultation service for women, their families and health professionals regarding exposure to drugs, chemicals, radiation and infectious agents during pregnancy and lactation. One group of children was the offspring of women who contacted the program specifically for counseling following binge alcohol drinking during pregnancy. Information on elicit drug and alcohol use, brand of ethanol, number of drinks (glasses, bottle) per day, per week, per month, number of drinks per one occasion and number of binge events after conception were collected when the women called Motherisk inquiring about the risk of alcohol drinking in their current pregnancy.

Women who met the inclusion criteria were invited to the clinic, where they were directly counseled by a team physician who collected extensive data regarding medical and obstetric history, medications, nutritional status, smoking and drinking patterns prior to conception and during pregnancy. A standardized, validated Motherisk questioner was used to assess parental life style, including questions on parental anthropometry (maternal and paternal weight and height), maternal exposure to toxins, heat, or extreme physical activities. Information on illicit drugs and alcohol use, brand of ethanol, number and mode of drinking, number of binge events after conception, duration of drinking during the index pregnancy and the gestational age at discontinuation of drinking. This information was collected when the women originally called Motherisk.

All women were recontacted 7 to 9 months after delivery to verify drinking patterns and record information about illnesses during pregnancy, delivery, perinatal and postnatal complications, and child developmental milestones. Women with conditions or exposure that might adversely affect fetal outcome were excluded.

Between 1987 (when Motherisk began) and 1997, 92 eligible women called the Motherisk program regarding concern about at least one episode of binge alcohol drinking in early gestation. None were alcohol-dependent or had a condition known to adversely affect fetal outcome. Out of 92 potential participants, 12 were lost to follow-up, 7 reported miscarriage, and 3 declined to participate. Of the remaining 70, 11 were excluded due to exposure to known teratogens such as anticonvulsants, retinoids, warfarin, and 9 reported additional patterns of drinking in addition to binge events for a final sample of 50 women and their 51 offspring (one set of twins).

The comparison group consisted of 51 children from mothers who had contacted the Motherisk Program during the same period of time regarding their exposure to a substance or condition not known to harm the fetus such as acetaminophen, oral penicillin, or dental x-rays who sought counseling following. Using the Motherisk database, these women were matched on a case-by-case basis for age, socioeconomic status (SES), smoking habits, and time of conception with women in the study group. Children were also matched for age in order to receive the same set of test instruments.

The study was approved by the Hospital for Sick Children's Research Ethics Board. Informed consent was obtained from all participating women.

### *Tests and measures*

Depending on the child's age, the Bayley Scales of Infant Development – Third Edition (Bayley, 1993), the McCarthy Scales of Children's Abilities (McCarthy, 1972), or the Wechsler intelligence Scale for Children-III Full Scale IQ (Wechsler, 1991) were administered and the global cognitive composite score for each test was used. The Bayley was given to children up to 36 months of age, the McCarthy up to age 7, and the WISC-III to children beyond 7 years of age. On the Bayley, only the Mental Development Index items were administered. In addition to the Bayley MDI score, the Cognitive Facet score which provides the age at which an infant or toddler is achieving cognitively was determined. On the McCarthy, both the global scales and individual subtest scores were determined. The latter were scored as *z*-scores based on test norms.

All children were assessed for language using the Reynell Developmental Language Scales (Reynell, 1985). This test provide separate indices for expressive language and language comprehension, both of which are expressed as z-scores (mean = 0; SD = 1.0).

All parents completed an age-appropriate temperament test from the Carey series (Fullard et al., 1978) using the Toddler

Temperament Scale for children from 1 to 3 years of age and the Behavioral Style Questionnaire for older children. These two tests were designed so that comparable scales can be combined across tests. These tests each evaluate 9 unique temperament characteristics provided as independent scales: activity level, regularity of routines, approach/withdrawal, adaptability, intensity of response, mood, persistence, distractibility, response threshold. Each scale was converted to a percentile score with a higher value reflecting a more positively perceived behavior. As a rule, the 50$^{th}$ percentile represents the average for the population.

For mothers, maternal IQ was determined using an abbreviated version of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) based on the Vocabulary and Block Design subtests. Socioeconomic status (SES) was determined using the Hollingshead Four Factor Index (Hollingshead, 1975) while maternal stress was assessed using the Parenting Stress Index (PSI) (Abidin, 1995). The maternal drinking variables were the number of binges and number of drinks per binge. For each case, an alcohol index reflecting the number of drinks multiplied by the number of binges and divided by 100 was computed.

### *Procedures*

Physical examination by a team physician aimed at morphological signs of FAS. All children were subsequently assessed in the Psychology Department at The Hospital for Sick Children by an experienced psychometrist who was masked to the nature of the intrauterine exposure and supervised by a clinical psychologist. After obtaining informed consent, the examiner tested the child followed by the mother. The mother completed the study questionnaires during the same meeting.

## Statistical analysis

Groups were compared using t-tests. The Bonferroni test was used to correct for multiple comparisons within tests. All statistical tests were two-tailed. Multiple regression analysis was conducted to determine the effects of potential confounders on the outcome measures.

## Results

In the binge-drinking during group, the number of binge episodes ranged from 1 to 20. Thirty-four women (68%) reported 1 to 3 binges, four (8%) reported 4 to 5 binges, and 12 (24%) reported 6 or more binges. Most women consumed 5 to 6 drinks per binge. All women in the study group remembered the dates of drinking events. Ninety-one percent discontinued binging between 4 and 8 weeks of gestation, while the remaining 9% continued drinking up until 12 weeks of pregnancy. The time of contacting the Motherisk program was slightly earlier for mothers in the binge-exposed group than the comparison group (days from last menstrual period: $65.4 + 31.3$ versus $80.9 + 44.8$, $p < 0.05$). The groups did not differ in terms of age at conception, prevalence of cigarette smoking, gravidity, parity and rates of spontaneous or therapeutic abortions. There were no cases of reported sexual transmitted diseases, malnutrition, or severe nausea and vomiting of pregnancy. The women in both groups received prenatal vitamins supplementation, which is the standard of care in Canada. Pregnancy weight gain ranged from 4 to 30 kg, and the mean weight gain was higher among women in the study group (17.6 vs. 13.4 kg). 26 women in the study group versus 20 in control group smoked cigarettes and 8 versus 2 women in the control group smoked marijuana. Marijuana smoking was discontinued when pregnancy was diagnosed as well as number of cigarettes smoked per day was cut down. The mothers in both groups had similar mean IQ values and SES scores (Table 1).

The groups did not differ in child characteristics, including gestational age, birth weight and physical characteristics (Table 2). None of the children in either group displayed a cluster of facial anomalies consistent with Fetal Alcohol Syndrome.

In each group, 26 children were assessed with the Bayley, 22 with the McCarthy and 3 with the WISC-III. As shown in Table 3, the groups obtained similar scores

Table 1. Maternal characteristics[a]

| | Study group | Comparison group | P |
|---|---|---|---|
| Age at conception (yr) | 33.4 ± 4.4 | 34.4 ± 4.5 | 0.2 |
| Cigarette smoking | 5.8 ± 8.8 | 5.0 ± 7.6 | 0.6 |
| IQ | 100.7 ± 10.5 | 99.6 ± 12.3 | 0.6 |
| SES[b] | 40.7 ± 14.0 | 43.7 ± 10.9 | 0.2 |
| Gravidity | 2.0 ± 1.0 | 2.2 ± 1.2 | 0.5 |
| Parity | 0.5 ± 0.7 | 0.7 ± 0.8 | 0.1 |
| Spontaneous abortion | 0.22 ± 0.50 | 0.25 ± 0.60 | 0.4 |
| Therapeutic abortion | 0.35 ± 0.60 | 0.2 ± 0.4 | 0.1 |

[a] Presented as Mean ± SD.
[b] SES – Socioeconomic Status.

Table 2. Children's physical characteristics[a]

| | Study group | Comparison group | P |
|---|---|---|---|
| Gestational age (wk) | 39.9 ± 1.8 | 39.5 ± 1.7 | 0.2 |
| Birth weight (g) | 3390.0 ± 609.3 | 3376.0 ± 565.0 | 0.9 |
| Weight (%ile) | 60.6 ± 24.9 | 57.9 ± 31.1 | 0.6 |
| Height (%ile) | 55.2 ± 24.8 | 64.0 ± 25.1 | 0.08 |
| Head circumference (%ile) | 51.8 ± 20.3 | 56.6 ± 22.9 | 0.3 |

[a] Presented as Mean ± SD.

Table 3. Children's tests results[a]

| Test | Cohort | Mean | Standard deviation | t | P | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | lower | upper |
| Bayley | | | | | | | |
| MDI | binge | 95.71 | 21.30 | −0.551 | 0.584 | −13.106 | 7.457 |
| | control | 98.54 | 15.70 | | | | |
| PDI | binge | 93.15 | 12.29 | −1.405 | 0.166 | −10.475 | 1.849 |
| | control | 97.46 | 9.88 | | | | |
| Facet Screen (month) | | | | | | | |
| Cognitive | binge | 29.43 | 15.42 | −0.628 | 0.532 | −9.331 | 4.881 |
| | control | 31.65 | 9.72 | | | | |
| Language | binge | 26.25 | 9.81 | −1.718 | 0.092 | −10.380 | 0.804 |
| | control | 31.04 | 10.67 | | | | |
| McCarthy | | | | | | | |
| GCI | binge | 104.26 | 27.53 | −0.921 | 0.362 | −18.889 | 7.047 |
| | control | 110.18 | 12.58 | | | | |
| Verbal | binge | 56.20 | 12.95 | 0.573 | 0.570 | −4.841 | 8.659 |
| | control | 54.27 | 8.74 | | | | |
| Perceptual | binge | 56.91 | 9.54 | −0.581 | 0.564 | −6.503 | 3.594 |
| | control | 58.36 | 6.83 | | | | |
| Quantitative | binge | 53.36 | 12.18 | −0.057 | 0.955 | −6.575 | 6.211 |
| | control | 53.55 | 8.52 | | | | |
| Memory | binge | 52.36 | 10.04 | −0.048 | 0.962 | −5.892 | 5.619 |
| | control | 52.41 | 8.84 | | | | |
| Motor | binge | 53.36 | 9.84 | 0.197 | 0.845 | −5.464 | 6.646 |
| | control | 52.77 | 10.06 | | | | |
| Subtests (z-scores) | | | | | | | |
| Blocks | binge | 0.12 | 0.91 | −1.252 | 0.218 | −0.710 | 0.166 |
| | control | 0.39 | 0.47 | | | | |
| Puzzles | binge | 0.64 | 0.96 | 1.203 | 0.236 | −0.234 | 0.924 |
| | control | 0.30 | 0.94 | | | | |
| Picture Memory | binge | 0.07 | 0.99 | −1.421 | 0.163 | −0.992 | 0.172 |
| | control | 0.48 | 0.92 | | | | |
| World Knowledge | binge | 0.58 | 0.10 | −0.274 | 0.786 | −0.704 | 0.536 |
| | control | 0.66 | 1.04 | | | | |
| Numbers | binge | 0.93 | 1.92 | 1.557 | 0.130 | −0.218 | 1.613 |
| | control | 0.23 | 0.18 | | | | |
| Tapping | binge | 0.71 | 0.97 | −0.465 | 0.644 | −0.660 | 0.413 |
| | control | 0.84 | 0.79 | | | | |
| Verbal memory I | binge | 0.01 | 0.89 | −0.062 | 0.951 | −0.530 | 0.498 |
| | control | 0.03 | 0.78 | | | | |
| Verbal memory II | binge | 0.12 | 0.10 | 0.385 | 0.702 | −0.519 | 0.762 |
| | control | −0.00 | 0.10 | | | | |
| Leg coordination | binge | 0.14 | 0.22 | 1.026 | 0.311 | −0.324 | 0.994 |
| | control | −0.20 | 1.15 | | | | |
| Arm coordination | binge | −0.08 | 0.68 | −0.752 | 0.456 | −0.712 | 0.326 |
| | control | 0.12 | 0.97 | | | | |
| Imit action | binge | 0.01 | 0.97 | 0.169 | 0.866 | −0.536 | 0.634 |
| | control | −0.04 | 0.95 | | | | |
| Draw a design | binge | 0.35 | 0.63 | 0.235 | 0.815 | −0.362 | 0.458 |
| | control | 0.30 | 0.72 | | | | |
| Draw a child | binge | 0.83 | 1.07 | 0.506 | 0.615 | −0.423 | 0.707 |
| | control | 0.69 | 0.77 | | | | |
| Numerical memory I | binge | 0.11 | 0.77 | 0.069 | 0.946 | −0.468 | 0.501 |
| | control | 0.09 | 0.18 | | | | |
| Numerical memory II | binge | 0.40 | 1.26 | −0.485 | 0.631 | −1.158 | 0.710 |
| | control | 0.63 | 1.74 | | | | |
| Fluency | binge | 0.94 | 1.29 | 1.612 | 0.116 | −0.136 | 1.1897 |
| | control | 0.42 | 0.84 | | | | |

(*continued*)

Table 3 (*continued*)

| Test | Cohort | Mean | Standard deviation | t | P | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | lower | upper |
| Counting | binge | 0.40 | 0.96 | −0.649 | 0.520 | −0.721 | 0.370 |
| | control | 0.58 | 0.82 | | | | |
| Opposite | binge | 0.65 | 1.11 | −0.706 | 0.484 | −0.804 | 0.387 |
| | control | 0.86 | 0.83 | | | | |
| Grouping | binge | 0.55 | 0.98 | −1.158 | 0.253 | −0.831 | 0.225 |
| | control | 0.85 | 0.73 | | | | |

[a] Presented as Mean ± SD.
MDI – Mental Developmental Index.
PDI – Psychomotor Developmental Index.
CGI – Global Cognitive Index.

on the three intelligence tests (Table 3). The binge-exposed children performed comparably to controls as preschool and school-age children. On the McCarthy, the binge group scored similar to controls on all scales as well as subtests. The number of subtests in which the alcohol-exposed children scored above controls was identical to the number on which the controls scored higher (9 for each). There were no patterns favoring controls above binge and vice versa. The three children in each group tested with the WISC-III attained Full Scale IQs in the normal range that were in fact slightly but not significantly higher for those in the binge group.

On the Reynell Developmental Language, children in both groups scored comparably on the Expressive and Receptive Language scales. On the temperament questionnaires, the groups differed on only one of the nine temperament scales, reflecting the significantly higher scores of children exposed to binge drinking than controls on the ''Approach'' scale. An examination of individual items on this scale revealed a much higher propensity of the binge group to like to approach the unfamiliar (e.g., a stranger) than the control group.

Of the 50 women who binged, 38 (76%) reported 1–5 binges while 12 (24%) reported 6 or more such episodes. Dichotomizing this group by number of binges revealed no differences on any indices of intellectual, cognitive or language development, whereas children exposed to 6 or more binges differed from the others on 3 of the 9 temperament scales. The scales differentiating children within the Binge group were Approach, Adaptability and Distractibility (Fig. 1), with those in the higher binging group being more willing to approach the

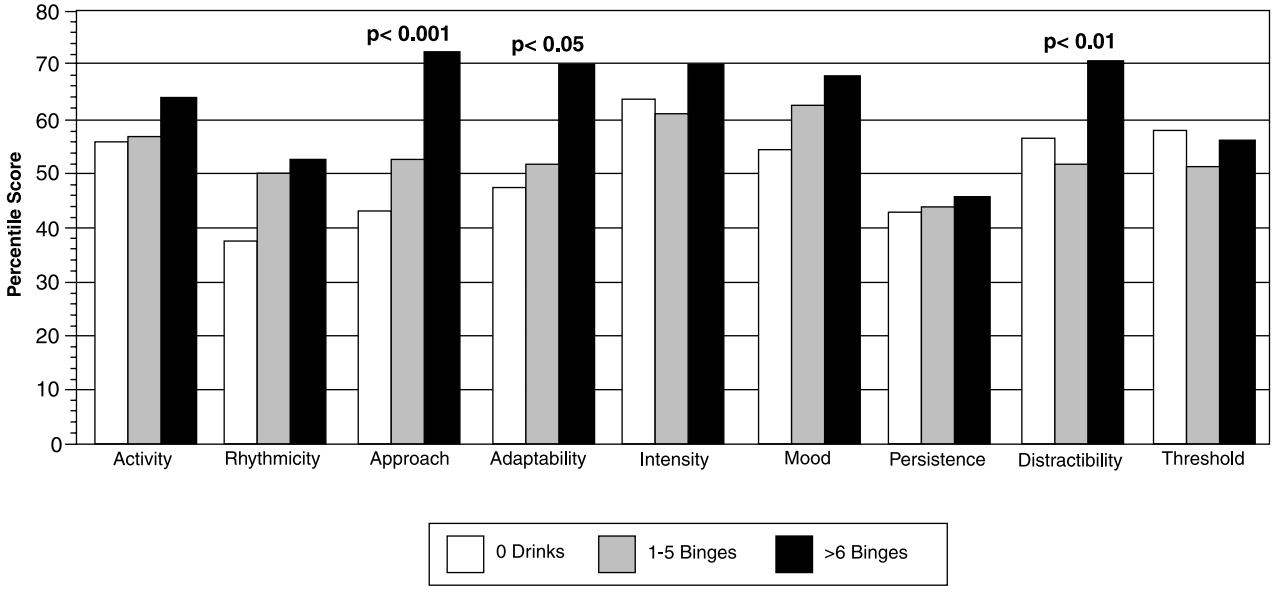


Fig. 1. Temperament scale percentile scores by binge frequency

Table 4. Multiple regression predicting behavioral outcome

| Predictors | B | St. Er | $\beta$ | t | P | 95% Confidence Interval for B | |
|---|---|---|---|---|---|---|---|
| | | | | | | lower bound | upper bound |
| Adaptability | | | | | | | |
| Maternal IQ | 0.38 | 0.29 | 0.14 | 1.30 | 0.196 | −0.20 | 0.95 |
| SES | −0.08 | 0.24 | −0.04 | −0.33 | 0.745 | −0.56 | 0.40 |
| PSI | −0.34 | 0.09 | −0.37 | −3.74 | 0.000* | −0.52 | −0.16 |
| GA | 0.50 | 1.61 | 0.03 | 0.31 | 0.758 | −2.71 | 3.70 |
| Number of binges | 1.50 | 0.50 | 0.30 | 3.03 | 0.003* | 0.52 | 2.49 |
| Approach | | | | | | | |
| Maternal IQ | −0.03 | 0.28 | −0.01 | −0.11 | 0.916 | −0.59 | 0.53 |
| SES | −0.15 | 0.24 | −0.07 | −0.65 | 0.517 | −0.63 | 0.32 |
| PSI | −0.09 | 0.09 | −0.10 | −0.99 | 0.326 | −0.27 | 0.09 |
| GA | −2.67 | 1.58 | −0.18 | −1.69 | 0.095 | −5.81 | 0.47 |
| Number of binges | 1.69 | 0.49 | 0.36 | 3.48 | 0.001* | 0.74 | 2.66 |
| Distractability | | | | | | | |
| Maternal IQ | 0.33 | 0.28 | 0.14 | 1.20 | 0.240 | −0.22 | 0.88 |
| SES | −0.22 | 0.23 | −0.11 | −0.94 | 0.350 | 0.68 | 0.24 |
| PSI | 0.22 | 0.09 | −0.26 | 2.52 | 0.001* | 0.05 | 0.39 |
| GA | −0.01 | 1.54 | −0.00 | −0.01 | 0.100 | −3.07 | 3.05 |
| Number of binges | 0.54 | 0.47 | 0.12 | 1.13 | 0.260 | −0.41 | 1.48 |

SES – Socioeconomic Status.
PSI – Parenting Stress Index.
GA – Gestational Age.
* – Statistically significant result.

unfamiliar, more adaptable and less distractible. An examination of the mothers' specific responses on these scales revealed that the high-frequent-binge exposed children were overly friendly, more willing to go to strangers, more easy-going and unflappable. Their high scores on the distractibility scale (suggesting non-distractibility) in fact reflected more an inability to disengage from an ongoing task than to become distracted.

To evaluate the influence of potential maternal confounders and drinking characteristics on children's cognitive and behavioral outcome, regression analyses were conducted on IQ combined across tests, language test indices and scores for the three temperament scales showing effects of drinking patterns on Approach, Adaptability and Distractibility (Fig. 1). The independent variables were maternal IQ, SES, parent stress, gestational age as well as an index of maternal drinking measured as the number of binges, number of drinks per binge and alcohol index entered into separate regression analyses. The results revealed that while none of these independent variables predicted the cognitive or language scale results, drinking was observed to be a significant predictor of the Approach and Adaptability temperament scales (Table 4) and maternal stress was a significant predictor of Distractibility. Mothers who reported more stress saw their children as less distractible than those reporting less stress.

All three drinking indices (number of binges, number of drinks per binge and the alcohol index) were found in separate regression analyses to predict Approach, Adaptability and Distractibility accounting for 16%, 16% and 15% or the variance respectively. The number of binges was the strongest predictor of the three, ($F = 3.48$, $p < 0.001$). While a similar pattern was observed for Adaptability, maternal stress additionally accounted for a substantial proposition of the variance. Mothers reporting a greater number of binges (followed by number of drinks per binge and the alcohol index) and mothers reporting less stress were more likely to consider their child as adapting easily to new situations.

## Discussion

The present study, which examined children exposed to one or more episodes of binge-alcohol drinking during early gestation, represents the first prospective cohort investigation involving non-alcoholic mothers. The majority of women were ''social'' drinkers concerned about one or more binge episodes prior to learning that they were pregnant. These women had excellent recall of

dates of exposure and the number of drinks and were highly motivated to disclose all needed health details. Because binge drinking before knowing one is pregnant is a common scenario, considering that 50% of North American pregnancies are unplanned, and periodic binge drinking is associated with social events among women of reproductive age, this study provides timely information about an important public health issue. Our control sample involving women who were similarly ascertained but did not drink during their pregnancy adds further strength to this research.

The major research on binge-exposure emanates from Seattle where a long-term longitudinal prospective study was conducted on a cohort of women followed during pregnancy and their children have now been studied into adulthood (Streissguth et al., 1991). This cohort study characterized binge behavior as part of a continuum of other forms of alcohol consumption and it included not only women who binged but those who drank regularly and continuously throughout pregnancy (Streissguth et al., 1990; Streissguth et al., 1989). Our cohort, by contrast, included only women who reported binge drinking early in the pregnancy and no other forms of alcohol exposure subsequently. None of our patients was determined by interview to be alcohol-dependent and all reportedly ceased drinking by the end of the first trimester.

We found that children exposed to binge-drinking *in utero* did not differ on any of the indices of any global indices of intellectual functioning or in their language development. In contrast, however, the children in our study group differed behaviorally from controls in that they displayed greater than expected social disinhibition in comparison to controls. They were described by their mothers as being more than normally willing to seek out strangers and unfamiliar surroundings and engage in more disinhibitory behavior than controls. In addition, when we stratified the binge-exposed group by number of binges, the results indicated that children exposed to more than six binges early in the pregnancy were more likely to show this pattern of behavior. The regression analyses confirmed a similar association with drinking indices, indicating that children exposed to more drinking episodes were more adaptable than normal in new situations, less wary of strangers and less fearful of change.

Evidence from animal studies suggests that even a single binge exposure is sufficient to produce neurotoxic effects (Bonthius and West, 1990; West et al., 1990; West et al., 1987). Although obvious difficulties arise when extrapolating data from animal studies to humans, a major advantage of animal models is the elimination of confounders such as socioeconomic status and family background factors, smoking habits, illicit drug use, genetic factors, etc. In animals, binge alcohol effects are adversely associated with maternal peak blood alcohol concentrations and not total volume consumed. Since binge drinking results in rapid achievement of high peak blood alcohol concentrations (BAC), which are the function of both dose and rate of consumption, the high BAC peaks following a binge require a longer time for the fetus to eliminate ethanol than the same amount ingested over a longer time period (Bonthius and West, 1990).

Clarren et al., using a primate model, simulated the typical once-per-week binge-drinking pattern in humans and showed that weekly administration of toxic doses of ethanol throughout gestation was capable of producing facial anomalies, growth deficiency and central nervous system dysfunction (Clarren et al., 1988). Of particular interest, behavioral abnormalities were seen in these animals, even in the absence of physical anomalies. Furthermore, Clarren et al. found that early gestational exposure produced more severe and debilitating cognitive abnormalities than did later (Clarren et al., 1992) while binge drinking appeared to affect behavior to a greater degree than learning ability (Clarren and Astley, 1992; Clarren et al., 1987). These results therefore corroborate our present findings of apparent adverse behavioral effects following exposure in early pregnancy.

To date, human studies exploring the impact of maternal binge-alcohol exposure on the offspring have yielded contradictory results. Some retrospective studies have shown no adverse effects on children exposed to moderate and binge alcohol consumption in utero (Jones et al., 1984; Tolo and Little, 1993).

O'Callaghan and colleagues reported that light and moderate alcohol consumption in early or later pregnancy had no independent effects on weight or head size at birth or at 5 years. Binge drinking in early pregnancy was not associated with restricted head circumference, and there was no modifying effect by concurrent cigarette use during early pregnancy (O'Callaghan et al., 2003). Other investigators have reported adverse effects including FAS-features from a single first-trimester binge episode (Lipson et al., 1983). Maier and West (Maier and West, 2001) concluded that children of binge – drinking mothers exhibited especially severe cognitive and behavioral deficits. However, some of the studies reviewed by them were limited by vague definitions of binge drinking, potential recall and reporting

biases, failure to record chronic alcohol consumption among the mothers who binged, and indirect measurement of neurodevelopmental outcome.

Steissguth and her colleagues found that in 7.5-year old children, early binge drinking was the strongest predictor of poorer attention and memory skills as well as behavior factors such as increased distractibility and poor organization (Olson et al., 1992; Streissguth et al., 1990). As mentioned previously, this study did not directly examine the effects of binge-exposure in non-alcohol-dependent women, and included women who exhibited other patterns of alcohol consumption in addition to binge. In contrast, when the sample was studied at 18 to 24 months of age, Olson (Olson, 1994) and colleagues reported no adverse effects of binge drinking on cognitive development. While our findings are generally consistent with Olson's, indicating only a mild delay on early outcome, our additional findings showing a significant effect of binge exposure on the child's disinhibitory behavior is unique and suggests a greater need to evaluate early behavioral than cognitive characteristics of these children, particularly as this behavior may be the precursor of the attention and behavioral observations noted by Streissguth at a later age. Because our study was based on accurate reports collected short time (days or number of weeks after the drinking event), and due to the fact that the women were concerned about potential effects on the fetus, they most likely gave the accurate information and recall bias was minimal. We used the definition of binge as 5 or more drinks per one occasion. Women who consumed alcohol between binge events or drank 3 or more drinks every day, or those who had less then 5 per occasion were excluded. Women who were not able to recall accurately their drinking events were excluded as well.

Our findings, which address the serious concerns of a large group of women who binge before knowing they have conceived and do not continue to drink once pregnancy is confirmed, signify that subtle behavioral teratogenesis with or without accompanying physical abnormalities does occur following gestational exposure to binge drinking, especially if the number of early binges exceeds 6 episodes. By examining mothers whose only drinking pattern was binging alcohol, we provide confirmatory evidence indicating a potentially adverse effect of such drinking on certain aspects of child development. While our findings suggest that global IQ is not compromised, selective cognitive abilities that may be especially vulnerable to early heavy alcohol exposure (e.g., attention, inhibitory control), deserve further follow-up with detailed neuropsychological tasks once the children are older.

There are several limitations to the present study that must be acknowledged. While we observed that the binge-exposed group was more affected in terms of temperament than cognitive abilities, we lack behavioral measures on the mother. Our design did not address the possibility that the behavioral styles observed in children exposed to higher numbers of binges are due to alcohol per se, or they reflect maternal temperament, which in turn could have influenced her drinking behavior during early pregnancy. While the multivariate analysis showed that extent of drinking (number of binges, number of drinks per binge) predicted the critical temperament features, it is possible that mothers who were themselves more disinhibited and hence more willing to take risks, drank more in early pregnancy. Also, as our sample of children was relatively young, we were limited by the ability of the test to assess subtle cognitive dysfunction in depth. The existing literature suggests that the impact of alcohol becomes clearer as children grow older and as task demands increase. While we did test a few older children, the numbers were too small to make meaningful comparisons. It is possible that at the time of testing, the abilities most affected by binge alcohol consumption had not yet emerged in the children presently studied.

In summary, binge drinking by nonalcoholic women in early pregnancy may contribute to selected behavioral difficulties in children of preschool and school age but does not appear to affect global IQ, language, or other aspects of cognitive development. As a group, children exposed to binge drinking perform solidly within the normal range on all cognitive tests. Our finding that the binge-exposed children demonstrated indiscriminate approach to new stimuli or people suggests that temperament may be a sensitive measure for studying the effects of *in utero* binge drinking and that certain underlying behavioral traits may be modulated by binge alcohol consumption in early pregnancy. In light of findings that these behavioral characteristics may predispose these children to later psychopathology (e.g. ADHD), studies of similar cohorts at a later age may provide critical information on the long-term behavioral consequences of early intrauterine binge exposure.

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