THE LONG-TERM NEUROCOGNITIVE CONSEQUENCES OF PRENATAL ALCOHOL EXPOSURE: A 14-Year Study

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Abstract—Prenatal alcohol exposure, at doses not generally associated with maternal alcohol problems, produces a broad array of neurocognitive deficits in offspring even in the absence of effects on growth and morphology. This report presents a summary of neurobehavioral, growth, and morphology findings from long-term follow-up of a birth cohort of 500 from a population-based study that has revealed attention, memory, and information processing deficits from birth through 14 years. Also observed (from school age through 14 years) have been problems with antisocial and delinquent behaviors, and classroom learning and behaviors; some of these problems may be secondary to earlier neurocognitive disabilities. Continuing research in behavioral and neurobehavioral teratology provides important opportunities for the neurosciences and for improved health of future generations.

In 1973, fetal alcohol syndrome (FAS) was identified as a birth defect presumed to be caused by prenatal alcohol exposure because the physical findings were observable at birth and the birth mothers of the first children so identified were chronic alcoholics (Jones & Smith, 1973). In the subsequent 25 years, alcohol has been irrefutably established as a teratogen through thousands of experimental animal studies, the whole field of neurobehavioral teratology has emerged (Riley & Vorhees, 1986), and hundreds of studies have demonstrated the comparability of the neurobehavioral findings from human and animal research on the short- and long-term consequences of prenatal alcohol exposure (Table 1; Driscoll, Streissguth, & Riley, 1990).

Although FAS has been identified as the most frequent known cause of mental retardation, clinical work proceeded slowly because of the subtleties of establishing the clinical diagnosis (Streissguth, 1997). FAS is diagnosed by the coexistence of three features: prenatal-onset growth deficiency, a characteristic pattern of dysmorphological characteristics read most explicitly in the face, and evidence of central nervous system (CNS) dysfunction. But the diagnostic process has not been readily incorporated in clinical practice, and thousands of individuals remain undiagnosed.

Hundreds of experimental animal studies have shown that the brain is the organ that is the most vulnerable to prenatal alcohol exposure (Goodlett & West, 1992) and that CNS effects can last a lifetime (Dumas & Rabe, 1994). However, no specific and unique clinical markers that are suitable for the detection of individuals with the CNS effects of prenatal alcohol exposure have emerged. The Institute of Medicine (Stratton, Howe, & Battaglia, 1996) recently suggested the new term alcohol-related neurodevelopmental disabilities (ARND) to describe children who were prenatally exposed to alcohol and have variable CNS effects but lack the physical features of FAS. Defining ARND poses a challenge for neuroscientists and clinicians that should not go unnoticed.

The magnitude of the public-health problem posed by prenatal alcohol exposure is clear from two recent studies based on empirical and clinical methods. The first concluded that the incidence and prevalence of FAS and ARND combined is almost 1 out of 100 live births (Sampson et al., 1997). The second documented the costly secondary disabilities, such as school or job difficulties, experienced by individuals with FAS and other fetal alcohol effects as they attempt to pursue lives handicapped by primary CNS disabilities that frequently go unrecognized (Streissguth, Barr, Kogan, & Bookstein, 1997).

The present article describes findings from the Seattle Longitudinal Prospective Study (a population-based study ongoing since 1974) that demonstrate broad and variable CNS effects of prenatal alcohol in a primarily low-risk population conceived before general awareness of alcohol’s adverse effects on pregnancy outcome and the later lives of children and adolescents. We propose using this accruing body of knowledge as a basis for developing tools that detect individuals affected by prenatal alcohol exposure, whatever their age.¹

METHOD

Two hospitals with demographic characteristics representative of the Seattle area were selected for study (Table 2). So that alcohol effects could be studied in the absence of competing risks, only women enrolled in prenatal care by the 5th month of pregnancy were eligible. The screening interviews from 1,529 consecutive consenting women revealed a fairly low-risk lifestyle in relation to a variety of factors that could relate to their offsprings’ health, including diet, drugs, medications, caffeine, alcohol, smoking, family history, and environment. The follow-up birth cohort of approximately 500 infants represented an oversampling of the heavier drinkers and smokers from the original 1,529 mothers, along with others representing a variety of drinking patterns, including abstaining (Table 3). In this sample, 18% used marijuana (2% used other street drugs), 12% had not graduated from high school, and 8% were on welfare.

¹. This article extends prior reviews of this study, most recently, Streissguth, Bookstein, and Barr (1996). A full list of reports from the study is available from the senior author.
The primary independent variable, alcohol, was assessed via a quantity-frequency-variability interview with additional questions regarding having more than five drinks per occasion, intoxications, and problems with drinking. Drinking during two time periods was assessed: during pregnancy and prior to pregnancy or recognition of pregnancy (see Streissguth, Bookstein, Sampson, & Barr, 1993, for details). The majority of mothers were white, married, middle class, and well educated, although a broad range of socioeconomic and racial groups was represented (Table 2). Heavier drinkers did not differ from the rest of the mothers in terms of nutrition, maternal weight gain, prenatal care, or other pregnancy risk factors such as diabetes, renal disease, thyroid abnormality, or rubella.

Children in the follow-up cohort were examined on the first 2 days of life, at 8 and 18 months, and at 4, 7, and 14 years. Parents were interviewed at each examination; teacher evaluations were obtained at 8 and 11 years. All examinations were conducted blind, without the examiner knowing subjects’ exposure history, living conditions, or previous scores. Follow-up has been excellent, with at least 82% of the original follow-up birth cohort included at each assessment. There has been no differential loss of heavily exposed subjects.

Data analyses from the first 4 years of life involved multiple regression analyses of single outcomes against single alcohol predictor variables. Analyses from 7 years onward have incorporated partial least squares (PLS), a method of data analysis that permits the simultaneous assessment of relations among multiple alcohol predictor scores and multiple outcome scores. PLS is better suited than multiple regression or other alternatives to the complex multifactorial data generated in human behavioral teratology studies such as ours (Bookstein, Sampson, Streissguth, & Barr, 1996). In teratology studies, a PLS analysis typically yields a dose latent variable, or LV (here, alcohol), and a response LV (here, outcomes) for each study (Sampson, Streissguth, Barr, & Bookstein, 1989; Streissguth, Bookstein, Sampson, & Barr, 1989; Streissguth et al., 1993). The specification of the pair of LVs, and their relationship, demonstrates the salience of the prenatal alcohol scores for the outcomes under consideration, and similarly, the salience of these outcomes for prenatal alcohol exposure. The alcohol LV, which is computed as a linear combination of all the prenatal dose measures, is very stable over the whole range of outcome ages examined in the present study.

Data on possible confounds were obtained prenatally and prospectively at each succeeding examination. Now exceeding 150, these variables include maternal nutrition and use of all drugs and medications during pregnancy, sociodemographic and education characteristics of the family, mother–child interactions, major life stresses in the household, childhood accidents, hospitalizations and illnesses, education experiences of the child, and many others (Streissguth et al., 1993).

All findings reported here have been evaluated in terms of potential confounds. Correlations between the many covariates in the database and the outcome LVs were examined. Then covariates associated with both the alcohol LV and the outcome LVs were examined in regression analyses to see the extent to which they altered the estimated effects of alcohol dose. Scatter plots and partial residual plots were routinely examined.

### Table 1. Comparable behavioral effects following prenatal alcohol exposure in humans and animals

<table>
<thead>
<tr>
<th></th>
<th>Humans</th>
<th>Animals</th>
</tr>
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<tbody>
<tr>
<td>Hyperactivity, reactivity</td>
<td>Increased activity, exploration, and reactivity</td>
<td>Decreased attention</td>
</tr>
<tr>
<td>Attention deficits, distractibility</td>
<td>Inhibition deficits</td>
<td>Decreased attention</td>
</tr>
<tr>
<td>Lack of inhibition</td>
<td>Impaired associative learning difficulties</td>
<td>Altered gait</td>
</tr>
<tr>
<td>Mental retardation, learning difficulties</td>
<td>Impaired habituation</td>
<td>Poor coordination</td>
</tr>
<tr>
<td>Reduced habituation</td>
<td>Impaired habituation</td>
<td>Poor coordination</td>
</tr>
<tr>
<td>Perseveration</td>
<td>Developmental delay</td>
<td>Developmental delay</td>
</tr>
<tr>
<td>Feeding difficulties</td>
<td>Feeding difficulties</td>
<td>Altered auditory potentials</td>
</tr>
<tr>
<td>Gait abnormalities</td>
<td>Poor fine and gross motor skills</td>
<td>Poor state regulation</td>
</tr>
<tr>
<td>Poor fine and gross motor skills</td>
<td>Poor state regulation</td>
<td>Poor state regulation</td>
</tr>
<tr>
<td>Developmental delay (motor, social, language)</td>
<td>Developmental delay</td>
<td>Developmental delay</td>
</tr>
<tr>
<td>Hearing abnormalities</td>
<td>Altered auditory potentials</td>
<td>Poor state regulation</td>
</tr>
<tr>
<td>Poor state regulation</td>
<td>Altered auditory potentials</td>
<td>Poor state regulation</td>
</tr>
</tbody>
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Note. Reprinted by permission of the publisher from Driscoll, Streissguth, and Riley (1990).

### Table 2. Maternal and household characteristics: Screening sample versus follow-up cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Screening sample (N = 1,529)</th>
<th>Follow-up cohort (N = 464)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>86%</td>
<td>88%</td>
</tr>
<tr>
<td>Married</td>
<td>87%</td>
<td>87%</td>
</tr>
<tr>
<td>Middle class</td>
<td>81%</td>
<td>81%</td>
</tr>
<tr>
<td>Prenatal vitamins taken during pregnancy</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>Prenatal care received by 5th month</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Mean educational level</td>
<td>13.8 years</td>
<td>13.7 years</td>
</tr>
<tr>
<td>Mean number of children in household</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Median annual income (at age 14)</td>
<td>—</td>
<td>$45,000</td>
</tr>
</tbody>
</table>

Note. All statistics except for median family income reflect maternal or household characteristics at the time of the prenatal interview in 1974–1975. Number of children excludes the cohort child.
RESULTS

The neurobehavioral effects of prenatal alcohol summarized here have been measured in this study from the first day of life through 14 years. The observed effects of alcohol on offspring are dose dependent, generally without a threshold, and are more salient for binge-type maternal alcohol use than for other measures of use. Self-reported drinking prior to recognition of pregnancy is generally more salient for these outcomes than drinking in midpregnancy, but the two are highly correlated. The results reported are not attributable to such potential confounds as exposures to other drugs, smoking, or social and demographic factors (Streissguth et al., 1993). For details of specific analyses, see the original scientific reports from which this overview derives. Streissguth et al. (1993) lists those reports pertaining to the first 7 years of life.

This study measured three types of outcomes across the life span: neurobehavioral deficits, growth, and alcohol-related physical anomalies. At birth, all three were related to prenatal alcohol exposure. After 8 months of age, alcohol effects on height, weight, and head circumference were no longer observable (Sampson, Bookstein, Barr, & Streissguth, 1994). Alcohol-related facial dysmorphic features were detected at birth and at 4 years from “blind” clinical examinations and at 7 years from facial photographs (Streissguth, Bookstein, & Barr, 1996). By 14 years, effects of prenatal exposure to alcohol were no longer detectable in the face. Alcohol effects on neurobehavioral deficits, however, have not attenuated over time, and a rich body of data for the first 14 years of life has accrued.

On Day 1, the Brazelton Neonatal Behavior Scale was administered blind to 417 infants. Prenatal alcohol exposure was related to poorer habituation, indicating difficulty “tuning out” redundant stimuli, and to poorer response modulation (Streissguth, Barr, & Martin, 1983). Alcohol was also related to other CNS responses, including increased head turning to the left, increased tremulousness, increased hand-to-face movements, increased time with eyes open, and decreased bodily activity (Streissguth et al., 1993). On Day 2 of life, prenatal alcohol was related to longer latency to suck and lower sucking pressure obtained on a pressure-transducer measure of nonnutritive sucking (Streissguth et al., 1996). These early neurobehavioral findings indicated that even before the infants left the hospital, they had measurable effects of prenatal alcohol exposure.

At 8 months of age (but not at 18 months), prenatal alcohol exposure was related to small decrements in mental and motor development measured on the Bayley Scales of Infant Mental and Motor Development (Streissguth, Barr, Martin, & Herman, 1980). At 4 years, prenatal alcohol exposure was related to decreased attention and longer response latency on a computerized vigilance test (Streissguth, Sampson et al., 1994), longer latency to correct errors (suggesting slower central processing time) and poorer fine motor performance on the Wisconsin Motor Steadiness Battery, poorer gross motor performance (especially on balance; Barr, Streissguth, Darby, & Sampson, 1990), and IQ decrements on the Wechsler Preschool and Primary Scale of Intelligence (Streissguth, Barr, Sampson, Darby, & Martin, 1989).

At 7 years, prenatal dose was associated with decrements on the Wechsler Intelligence Scale for Children—Revised (WISC-R), particularly Arithmetic and Digit Span subtest scores, and with arithmetic deficits on the Wide Range Achievement Test—Revised (Sampson et al., 1989). In the domain of vigilance, prenatal dose predicted deficits of several sorts in the Continuous Performance Test (CPT) vigilance scores, notably errors of commission on the AX task and standard deviation of reaction time throughout (Streissguth, Sampson, et al., 1994), longer latency to correct errors (suggesting slower central processing time) and poorer fine motor performance on the Wisconsin Motor Steadiness Battery, poorer gross motor performance (especially on balance; Barr, Streissguth, Darby, & Sampson, 1990), and IQ decrements on the Wechsler Preschool and Primary Scale of Intelligence (Streissguth, Barr, Sampson, Darby, & Martin, 1989).
son, et al., 1994). Other consequences of prenatal exposure include poorer performance on tests of spatial memory and integration, verbal memory and integration, flexible problem solving, and perceptual motor function, and on examiners’ ratings of distractibility, organization, and flexibility in problem solving (Streissguth, Bookstein, et al., 1989).

By the end of the second grade, heavier prenatal alcohol exposure was associated with an increased chance that a child would be in special programs and classes at school. The children were also rated by teachers on standardized rating scales as not well organized, lacking tactfulness, and having poor grammar, poor word recall, and poor attention in the classroom (Sampson et al., 1989). At 11 years, alcohol-related effects emerged in continuing teacher reports of processing and reasoning problems, as well as ratings of distractibility, impersistence, and restlessness. Prenatal alcohol exposure was also related at age 11 to poorer academic achievement, as reflected in teacher ratings (of reading, arithmetic, written expression, spelling, and overall learning) and lower national percentile scores (especially for arithmetic and total achievement; Carmichael Olson, Sampson, Barr, Streissguth, & Bookstein, 1992). Teacher ratings of classroom attention at 11 years, in the fifth and sixth grade, were predicted by the 7-year vigilance LV $r = .36$. Teacher ratings also predicted the 14-year vigilance LV $r = .42$. Although poor vigilance characterized some subjects across the entire exposure range, high alcohol exposure appeared to vitiate any possibility that the adolescent would score in the very best range for vigilance (i.e., make very few errors; Streissguth, Bookstein, Sampson, & Barr, 1995).

At 14 years, prenatal alcohol exposure was related to poorer performance on laboratory measures of attention, memory, phonological processing, and arithmetic (Streissguth, Sampson, et al., 1994). The same alcohol LV associated with neurobehavioral outcomes at earlier ages had highest saliences for standard deviation of reaction time and errors of commission on AX measured on CPT Vigilance, for a complex letter-cancelation test, and for a demanding spatial memory test called the Stepping Stone Maze. The attention-memory LV at 14 years correlated .67 with the neurobehavioral LV salient for prenatal alcohol exposure from birth to 7 years. Word Attack, a test thought to measure a more biological aspect of linguistic skill than reading skill, and the Arithmetic subtest of the WISC-R each revealed an approximately 1/3-SD decrement in performance at exposure levels of more than 1.5 drinks per occasion on average (Streissguth, Barr, et al., 1994). Ten out of 11 children of heavier drinkers who had low Arithmetic scores at 7 years continued to have low Arithmetic scores at 14 years.

A recent report from this study (Carmichael Olson et al., 1997) showed that prenatal alcohol exposure (essentially the same alcohol LV as discussed earlier) is related to learning and behavior problems self-reported by adolescents and observed by parents and in ratings by research examiners. These observations include projecting a subtle impression as a “bad kid” to the research examiner; antisocial and delinquent behaviors; early use of tobacco, alcohol, and other drugs; poor academic progress; partaking of special programs for the learning disabled; and low grades in mathematics. Examiners’ ratings salient for prenatal alcohol exposure in these teenagers included high impulsivity and problems with organization, especially under stress—behaviors similar to those attributed to these subjects by a different set of examiners 7 years earlier. Clearly, the cognitive and neurobehavioral deficits measured earlier had an impact on classroom learning and behavior as the children matured.

**REFERENCES**


Neurocognitive Consequences of Prenatal Alcohol


