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Journal of Communication Disorders 38 (2005) 279–302

Journal of
**Communication
Disorders**

Prenatal alcohol and cocaine exposure: Influences on cognition, speech, language, and hearing

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Received 1 December 2004; received in revised form 11 February 2005; accepted 11 February 2005

Abstract

This paper reviews research on the consequences of prenatal exposure to alcohol and cocaine on children's speech, language, hearing, and cognitive development. The review shows that cognitive impairment, learning disabilities, and behavioral disorders are the central nervous system manifestations of fetal alcohol syndrome (FAS), and cranio-facial abnormalities are also present. Delays in language acquisition, as well as receptive and expressive language deficits, are commonly reported. The cranio-facial abnormalities of FAS, which sometimes include cleft palate, make the child prone to otitis media with effusion and conductive hearing loss. The family environment in which one or both parents is a heavy alcohol user presents challenges to a child with normal intelligence, but may be especially deleterious to the child with mental retardation.

Prenatal exposure to cocaine results in subtle cognitive disabilities when measured at 4 years of age. The cognitive effects may be ameliorated by a stimulating and sensitive care-giving environment. A small, deleterious "cocaine-effect" is also seen in speech and language development. The child with prenatal exposure to cocaine may be considered at increased risk for language delay or disorder. There is no evidence that prenatal cocaine exposure by itself is a risk factor for sensorineural hearing impairment, although auditory evoked potentials from the brainstem and cortex suggest some abnormalities in central auditory processing, at least during the newborn period.

The strong effect of the home environment for ameliorating the effects of prenatal cocaine-exposure suggests that a family-focused approach for cognitive, language, and social-emotional habilitation would be beneficial to all.

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Learning outcomes: The learner will be able to describe the major features of fetal alcohol syndrome and how they relate to speech, language, hearing, and cognitive disorders. The learner will review the literature and determine research needs with respect to language, speech, and hearing among infants and children with fetal alcohol syndrome. Similarly, the learner will distinguish the outcomes of prenatal alcohol-exposure from those of prenatal cocaine-exposure. The learner will summarize the controversy regarding the possible stigmatization of cocaine-exposed infants. The learner will summarize the speech, language, and hearing effects of prenatal cocaine-exposure.

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1. Introduction

Before the United States declared a war on terrorism, they had declared wars on drugs and poverty. There is an insidious synergy between the effects of poverty and drugs and alcohol on the developing infant. Those in poverty have little or no access to prenatal care, or treatment for addiction. Poverty, poor nutrition, and lack of prenatal care lead to high-risk conditions for the infant, including premature birth with low birth weight. While addiction to drugs or alcohol does not recognize income levels, when combined with poverty, the teratogenic effects of addictive substances, such as cocaine, alcohol, and nicotine, may be exacerbated.

In this review, the consequences of prenatal exposure to alcohol and cocaine on children's speech, language, hearing, and cognitive development will be summarized. The emphasis of this review will be on studies published within the past 10 years. Although more infants are exposed prenatally to nicotine than alcohol, and more to alcohol than to cocaine, it appears that funding for research on cocaine babies hit a peak during the late 1980s and into the mid-1990s, and thus we have a substantial literature on this subject. It is only within the last few years, however, that research has been completed on the longer term outcomes of children who experienced prenatal cocaine-exposure. Another emphasis of this review will be on what has been learned about the consequences of this exposure on speech, language, hearing, and cognition when measured in the pre-school or early elementary school years.

The questions asked in this review are:

- (1) Does prenatal alcohol-exposure (PAE) or prenatal cocaine-exposure (PCE) cause speech, language, hearing, and cognitive delays, or dysfunction?
- (2) What are the specific effects of PAE and PCE on speech, language, and hearing?
- (3) What environmental factors may exacerbate the effects of PAE and PCE?

1.1. *The effects of parental alcohol use*

Fetal alcohol syndrome (FAS) or fetal alcohol effects (FAE), the manifestation of the teratogenic effects of alcohol on the developing fetus, are recognized in 0.5–3 in 1000 live births (Kenner & D'Apolito, 1997), although a higher rate is reported in some native American populations (Centers for Disease Control and Prevention, 1997) and among the indigenous people of Australia (O'Leary, 2004). FAS is seen in infants, whose

mothers had a history of chronic, daily, heavy alcohol use, or frequent, heavy, intermittent alcohol use (O'Leary, 2004), including binge drinking. The features of FAS include facial dysmorphism, specifically, short palpebral fissures, epicanthal folds, a broad nasal bridge, flattened midfacies, short upturned or beak-like nose, thin upper lip or vermilion border, smooth filtrum, micrognathia, and a hypoplastic maxilla. Microcephaly, abnormal palmar creases, intra-uterine, and postnatal growth retardation are also features of this syndrome. Cognitive impairment, learning disabilities, and behavioral disorders are the central nervous system manifestations of FAS. The three criteria necessary for assigning a diagnosis of FAS include: (1) growth retardation; (2) central nervous system involvement; (3) facial features of short palpebral fissures, thin upper lip, and elongated, flattened mid-face (O'Leary, 2004; Weinberg, 1997).

Fetal alcohol effects may be evident in infants and children with prenatal exposure to alcohol, but who have only some of the features of FAS. Alcohol-related neurodevelopmental disorder (ARND) and alcohol-related birth defects (ARBD) have also been proposed to describe conditions in the infant that are related to maternal drinking during pregnancy (American Academy of Pediatrics, 2000). FAS, FAE, ARND, and ARBD may result in lifelong disability in cognitive, behavioural, and psychosocial domains.

Fetal alcohol-exposure is one of the leading causes of mental retardation. Studies in humans and in experimental animals have established that maternal use of alcohol affects fetal brain development (Weinberg, 1997) and its chemical, endocrine, and immunological function. Anatomical abnormalities include incomplete cortical development, enlarged ventricles, absent, or underdeveloped corpus collusum, and cerebellar changes. Alcohol itself is a toxin to the fetus, as is its major metabolite, acetaldehyde. Alcohol can cause a direct effect on cells and can also cause damage due to hypoxia and disturbances in prostaglandin physiology.

There is now some evidence that genetic factors, inherited maternally or paternally, can contribute to the fetal susceptibility to alcohol damage (Weinberg, 1997). It is thought that the father's use of alcohol may alter his genetic material inherited by the fetus and provide another source of variability and severity in FAS. In addition, it appears that maternal age also plays a role. The risk of functional impairment in the offspring increases by two- to five-fold when maternal age is greater than 30 years (O'Leary, 2004).

Both pre- and postnatal conditions accompanying exposure to alcohol can exacerbate the risk for poor developmental outcomes. Smoking, caffeine-use, maternal malnutrition during pregnancy and lack of prenatal care will put the fetus at higher risk for abnormal development. Parental alcohol use before, during and after pregnancy is also associated with stressors, such as economic instability, lack of consistent caregiving, physical, and emotional neglect, and increased rates of family violence and abuse (Weinberg, 1997). There is also an interaction with family income, with a higher incidence of FAS in lower socio-economic groups. This may be due to the cumulative effects of poor nutrition and genetic factors, including a history of intergenerational maternal alcoholism among those of lower socio-economic status (SES) (O'Leary, 2004). Racial differences in the incidence of FAS have been explored, however, there is no evidence that race, when it can be untangled from poverty, plays a role in the susceptibility of the fetus for FAS/FAE.

1.2. PAE and cognitive disorders

Exposure to alcohol during fetal development can cause mental retardation, which, among children with FAS, is in the mild to borderline range, or 60–85 IQ points. Studies of Caucasian middle-class children, and also of African–American children of lower SES, found that IQ scores were lower among those who received moderate to heavy alcohol-exposure during prenatal development compared to non-exposed controls, but were still in the average range, and remained stable (did not improve) over the long-term (Weinberg, 1997). Learning disabilities resulting from PAE have been described in both human and experimental animal models. Specific to humans, disabilities and/or weaknesses have been found in arithmetic skills, spatial memory, and integration, verbal memory, attention, problem-solving, grammar, information retention and comprehension, and reading.

Weinberg (1997) reminds us that while a child with FAS/FAE may present what appear to be good superficial speech skills, deficits in language may underlie poor peer relationships and thus, be a primary cause of the significant behavioral and social problems evident in these children. The behavioral problems of children, adolescents, and adults with PAE, including impulsivity, aggression, inattention, and problems with social interaction, are beyond the scope of this review, but are pervasive and disabling (O’Leary, 2004; Weinberg, 1997). These behavioral deficits have been posited to be due to frontal lobe damage from PAE. For the child with FAS, FAE, ARND, or ARBD, the cognitive and behavioral deficits appear to be more common than specific speech and language disorders.

1.3. Speech and language effects of PAE

Weinberg (1997) cites the Abkarian (1992) and Institute of Medicine (1996) with respect to language functioning in children with PAE:

“There is a paucity of studies in this very important area.”

Early studies had very limited sample sizes. Shaywitz, Caparulo, and Hodgson (1981) described the language and behavioral characteristics of two children with developmental language delay as a result of FAS/FAE and Becker, Warr-Leeper, and Leeper (1990) provide a description of oral motor, articulatory, short-term memory, grammatical, and semantic abilities for eight North American Indian (Ojibway) children with FAS. They attempted to define areas of language function specific to FAS, taking into account the affected children’s cognitive abilities. Qualitative differences were found in articulation abilities and language structure.

Because prenatal alcohol-exposure can cause structural and functional brain abnormalities, resulting in cognitive impairment, it is no surprise that children with FAS demonstrate delay in language acquisition and/or receptive and expressive language deficits (Church & Kaltenbach, 1997). Most reports describing children with FAS include some language measure, but there are few studies focusing specifically on language. Another confounding issue is that a good portion of the language studies were conducted using native American and African–American children, for whom racially and culturally biased test methods could influence results. In general, the syntactic and semantic language domains are affected in these children. Verbal learning and memory function deficits

measured in children with FAS (Becker et al., 1990; Mattson, Riley, Delis, Stern, & Lyon-Jones, 1996) will certainly compromise language development and ability.

1.4. PAE and hearing

The strongest evidence for the effects of alcohol on the developing auditory system comes from studies using rodents (Strasnick & Jacobson, 1995). Ethanol is an ototoxic agent in both the mature and immature animal. Sensorineural hearing loss has been found in 18–20% of the offspring C57BL/6 mice who were fed ethanol during pregnancy (Church & Kaltenbach, 1997). The auditory brainstem response (ABR) was used to document threshold elevation and abnormalities in latency, consistent with such a hearing disorder. In addition, there was histological evidence of damage to outer hair cells. Cell death in the otic placode has been observed in alcohol-exposed mouse embryos (Kotch & Sulik, 1992), suggesting that such exposure may cause damage to the cells that develop into the auditory nerve. Thus, alcohol can cause both sensory and neural effects during development.

There are very limited data on the relationship between FAS and sensorineural hearing loss (SNHL) in humans. Pooling data from two geographically separate clinics (in Denver and Detroit), 10 out of 36 (28%) children with FAS demonstrated SNHL (Church & Kaltenbach, 1997). The rate of SNHL in this group of patients was the same as that for other children with cranio-facial anomalies, such as those with Trisomy-21 or sub-mucous cleft-palate. Twelve of the 36 subjects in this study had a cleft-palate, but SNHL was present for only two of those 12 children, whereas SNHL was present in a greater percentage of FAS children who did not have an overt or sub-mucous cleft. The pure tone audiograms most often showed mild-moderate high frequency impairment, consistent with the fact that alcohol is an ototoxic agent. Church and Kaltenbach (1997) hypothesize that FAS is a syndrome of the neuroectoderm, characterized by malformations of brain tissue, ocular abnormalities, SNHL, and other sensory disorders. These problems occur together, because the tissues involved arise from the embryonic ectoderm.

Cranio-facial anomalies are a distinguishing feature of FAS, and recurrent otitis media with effusion (OME) is common among those with such anomalies. Recurrent OME is also associated with high rates of conductive hearing loss. Church and Kaltenbach (1997) reported conductive hearing loss due to recurrent OME in 83% of the children with FAS who were part of the Denver–Detroit cohort. Sixteen of the 36 children in the Denver–Detroit cohort were born with a cleft palate, and OME was persistent in 14 (87%) of these children. Yet recurrent OME was also apparent in 16 out of 20 (80%) children without cleft palate in the Denver–Detroit FAS cohort. The high rate of recurrent OME among children with FAS is likely due to eustachian tube dysfunction, another aspect of the cranio-facial dysmorphism.

So-called central auditory-processing deficits may also be recognized as a result of prenatal alcohol-exposure. The pups of Sprague–Dawley rat dams, fed a diet in which 40% of the calories came from alcohol, exhibited prolonged ABR latencies (Church & Kaltenbach, 1997), particularly for later peaks of the ABR, suggesting some delay in neural transmission. While these pups eventually “caught up” to the control groups in terms of ABR transmission times, the results suggested a risk factor of delayed brainstem auditory pathway development. In another study, however, there were persistent delays of the ABR

inter-peak intervals in the offspring who had only modest or moderate PAE. These prolonged inter-peak latencies lasted into the rats' adulthood, suggesting a permanent deficit in brainstem myelin or synaptic efficiency for these animals. Other studies in the rat model indicate abnormalities in function at the level of the auditory cortex, with reduced glucose utilization (Vingan, Dow-Edwards, & Riley, 1986).

In a small group of children with FAS ($N = 12$) tested using methods that tap central auditory processes, all showed "clinical" abnormalities (Church & Kaltenbach, 1997). The test battery consisted of the dichotic Competing Sentence Test (CST) and a test of word recognition with ipsilateral competing noise (WRIN). The investigators suggested that performance deficits found for the CST were due to inefficient transmission of information across the corpus collosum; dys- and agenesis of the corpus collosum is a feature of FAS.

Church and Kaltenbach (1997) suggest that it may be these central auditory pathway abnormalities, a "central hearing impairment" that is the basis of some language and learning deficits observed in children with FAS/FAE:

"Such a hearing disability can make language seem chaotic and incomprehensible and can lead to speech and language pathology, inattention, learning problems, and disruptive behaviors" (p. 508).

The problem of treating central auditory-processing disorder, a condition that defies objective definition and an evidence-based, rational intervention plan, is beyond the scope of this review. Language stimulation/enrichment programs and classrooms that have a well-controlled acoustic environment (i.e., enhanced signal-to-noise ratio through the use of listening technologies) will help most children, including those with FAS.

Certainly, early detection and intervention for hearing and language deficits accompanying FAS, FAE, ARND, and ARBD will lead to the best outcomes. Universal newborn hearing screening programs are generally designed to screen for moderate or greater impairment, and so the infant with the stigmata of FAS, at higher risk for mild-moderate hearing impairment, may need to be targeted for diagnostic assessment on the basis of risk factors, rather than the result of a general newborn screening test. Likewise, intervention for cognition and language should be undertaken on the basis of the infant's high risk for developmental disorder.

2. Cocaine

2.1. *Biologic effects of cocaine on the developing fetus*

Cocaine is a psychoactive substance. Cocaine inhibits the post-synaptic re-uptake of catecholamines, dopamine, and tryptophan, and blocks sodium ion permeability, resulting in an anesthetic effect (Chiriboga, 1998). Cocaine metabolites benzoylecgonine and benzoynorecgonine also have powerful pharmacologic effects, and are, like cocaine, neurotoxic.

Cocaine and its metabolites cross the placenta to the fetus. Cocaine affects the maternal cardio-vascular and autonomic systems, and thus has an indirect effect on the fetus. The

cocaine that crosses the placenta can affect the fetal cardio-vascular and autonomic systems directly.

Cocaine use during pregnancy causes uterine vasoconstriction, which is linked to spontaneous abortion, abruptio placenta, stillbirths, fetal distress, meconium staining, and pre-mature delivery (Chiriboga, 1998). Low birth weight and smaller head circumference is a common outcome of prenatal cocaine-exposure (PCE). Prenatal cocaine-exposure has been associated with microcephaly, vascular insults, such as stroke, seizures, and frank brain malformation, including agenesis of the corpus callosum and encephalocele. Neurobehavioral examination of the cocaine-exposed neonate reveals impaired organizational state, depressed sensorium, hypertonia, and coarse tremor, and irritability, including excessive startle (Chiriboga, 1998).

Chiriboga (1998) proposed a model by which cocaine may exhibit effects on long-term neurodevelopmental outcomes. Fetal cocaine-exposure can cause increased concentration of post-synaptic monoamines that can alter dendritic arborization. Cortical dysgenesis and impaired neuropil growth follow-on from the aberrant dendritic arborization, resulting in restricted fetal head growth and the small head size found in multiple studies of cocaine-exposed newborns. The small head size is thus an indicator for impaired long-term neurodevelopment, in that it reflects the cortical dysgenesis and deficient neuropil.

2.2. Growth, development, behavior, and cognitive effects of prenatal cocaine-exposure

The effects of PCE on longer term developmental outcomes have been the subject of intense scrutiny by the popular press, legislators, the criminal court system, the medical community, and even some peer-reviewed research papers. Frank, Augustyn, Knight, Pell, and Zuckerman (2001) completed a meta-analysis of peer-reviewed papers published between 1984 and 2000 pertaining to longer term developmental outcomes for infants and children with PCE. Abstracts or non-reviewed proceedings of scientific meetings were excluded, and only those studies that had prospectively recruited samples in which the examiners were masked as to the child's exposure status, and did not include a large number of poly-drug-exposed children, were included. Out of 74 papers, 36 met these criteria.

Seven studies measured physical growth and included 699 PCE children and 1186 non-exposed (NE) children. Height, weight and occipital-frontal head circumference (OFC) were measured, with some studies taking measures as early as 8 weeks, and one at 6 years. Five of seven studies showed there was an effect of cocaine on one or more measures of physical development, although the study with the longest term outcome measurement, but a small cohort of PCE children ($N = 28$), showed no effect at 6 years (Richardson, Conroy, & Day, 1996). In other studies, height, weight, and OFC were abnormal among the exposed cohort when measured as late as 3 years of age. Frank et al. (2001) point out that there was also prenatal tobacco and alcohol-exposure in these samples, and that these can cause similar effects.

Fourteen studies evaluated cognitive development using standardized measures, such as the Bayley Scales of Infant Development (BSID), the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R), Wide Range Achievement Test-Revised (WRAT-R) and the Stanford-Binet Intelligence Scale (SBIS). Assessment ages ranged from 3 months up to 6 years. Five studies involving 404 exposed children showed an effect, while nine other studies, with 834 exposed children, did not.

Frank et al. (2001) analyzed the extant literature to determine if cocaine, by itself, had an effect on growth and cognitive outcomes. In general, the meta-analysis demonstrated that cocaine, by itself, cannot be shown to have a deleterious effect on physical growth and cognitive development. Yet, many of the analytical models used in the study controlled for or estimated the effect of other substances on the same outcome variables. The problem is that cocaine-exposure does not occur in isolation, it occurs in a milieu that can include poverty, poor nutrition, and prenatal care and use of other teratogenic substances. The outlook of the Frank et al. group is that the teratogenic effect of cocaine has been blown out of proportion by the popular press and some policy-makers (Zuckerman, Frank, & Mayes, 2002). They suggest that cocaine is no more or less teratogenic than other substances, including tobacco and/or alcohol. They further suggest that the prosecution of women on the basis of using cocaine-during pregnancy is a not-so-subtle form of racism, propped-up by bad science, and media hyperbole.

Since the Frank et al. (2001) study was published, newer findings emerged. Covington, Nordstrom-Klee, Ager, Sokol, and Delaney-Black (2002) evaluated height and weight at 7 years for a cohort of children prenatally exposed to drugs, including cocaine, alcohol, and tobacco. This was a prospectively studied cohort; however, one distinguishing feature was that the mothers were enrolled in the sample during pregnancy and received prenatal care. There were 231 children in the PCE group and 309 in the control, NE group. Multiple regression analyses revealed that prenatal exposure to cocaine was a significant predictor of birth weight and length even after control for maternal age and weight, gestational age, exposure to alcohol, and tobacco. Alcohol- and tobacco-exposure were also significant independent predictors of birth weight, and length. Birth weight and length decreased with increased exposure to cocaine, alcohol, and tobacco.

At 7 years of age, prenatal exposure to cocaine, alcohol or tobacco did not prove to be independent predictors of weight ($p = 0.073$), although all exposures together accounted for a significant amount of variance in height ($p = 0.017$) (Covington et al., 2002). When the results for children born to mothers older than 30 were considered, exposure to cocaine was an independent predictor of child height, but not of weight. Children born to women over 30 who used cocaine during pregnancy were four times more likely to fall below the 10th percentile for height, compared to controls.

Long-term cognitive outcomes for children with prenatal cocaine-exposure have recently been published (Singer et al., 2004). In this research, the outcomes at 4 years of age were evaluated using the Wechsler Preschool and Primary Scales of Intelligence-Revised. As in the previous studies reviewed, there was a non-exposed (NE) control group ($N = 186$) for comparison to the prenatally cocaine-exposed (PCE) group ($N = 190$). All infant/mother dyads were enrolled at birth, and the parent was paid for participation. The infants had been previously evaluated at 6, 12, and 24 months of age. All assessments were carried out by examiners, who were masked as to the child's cocaine-exposure status.

Maternal characteristics were evaluated for both groups. The majority of both groups were African-American women of low-income status, from the same geographic area (Cleveland, OH). Women who used cocaine during pregnancy were older, less likely to be married or to have completed high school, had lower vocabulary scores, higher psychological distress scores and had higher usage of alcohol, tobacco, and marijuana than did women who did not use cocaine during pregnancy. The cocaine-exposed infants were

of lower gestational age, birth weight, head circumference, and length than the non-exposed, control group infants. Significantly, 95% of the control group infants were in the care of their biological mothers, compared to only 55% of the cocaine-exposed infants. The majority of the children who were not with the biological parent had been in their current home situation for at least 2 years. Using the current living situation of all participants, The Home Observation for Measurement of the Environment (HOME) scores for the non-exposed and exposed children did not differ when measured at 4 years. Similarly, the language scores for the primary caregiver at 4 years did not differ between groups.

A linear regression model was used to analyze the results and adjust for confounding variables. Using these models, there was no significant effect of PCE on full-scale IQ scores, the verbal score or the performance IQ measures. There were some cocaine-exposure effects seen on several sub-scales of the Wechsler, including those for arithmetic, object assembly, and information. There was an interaction of cocaine-exposure with sex for the arithmetic scores; only boys were affected.

The quality of the care-giving environment was the strongest predictor of outcome. There was a significant interaction between cocaine-exposure and foster or adoptive care. The children in foster or adoptive care had higher scores than cocaine-exposed children in biological maternal or relative care. The foster/adoptive caregivers had higher vocabulary scores than the biologic or relative caregivers. The HOME scores were higher for the foster/adoptive homes. The PCE children in foster/adoptive care had verbal, performance and full-scale IQs equivalent to the NE children, and significantly higher than PCE living with the biologic mother or a relative. The irony of this finding is that the children in foster/adoptive care had *greater* prenatal cocaine-exposure as measured by the biologic mother's report of drug use during pregnancy. Thus, the most severely exposed children were also those who were placed in foster/adoptive care, and benefited from the treatment/intervention of growing up in a more stimulating, language proficient home environment. PCE children in foster or adoptive care did not differ from NE controls in the likelihood of mental retardation (IQ < 70), but cocaine-exposed children in maternal or relative care had the highest rate of mental retardation (25%). PCE children, regardless of caregiver status, were less likely to have IQ scores greater than 100 than were NE children.

In summary, the Singer et al. (2004) findings were that PCE is associated with increased risk for specific cognitive impairments and a lower likelihood of obtaining an above average IQ when measured at 4 years of age. They cite the limited range of cognitive functions assessed by the WPSSI-R as one drawback of the study. They also note that some exposure effects may have been masked by the high number of PCE infants who were placed in more environmentally stimulating homes. The strong effect of the home environment on ameliorating the effects of prenatal cocaine-exposure suggests that drug treatment and education for the mother, as well as a family-focused approach for cognitive, language, and social-emotional habilitation would be beneficial to all.

2.3. *Speech and language in children with PCE: a review of the literature*

Mentis and Lundgren (1995) undertook a detailed evaluation of discourse-pragmatic abilities, syntactic, and semantic development in five toddlers with prenatal cocaine-exposure and in five children from the same community who did not have cocaine-

exposure. The mean age of this sample was 2 years 4 months, with a range of 2 years 2 months to 2 years 6 months. A language sample comprised the data for the analysis of discourse-pragmatic, syntactic, and semantic abilities. The language sample included 15 min of free and 15 min of structured play between the subject and the investigator. Those involved in the analysis were not masked as to whether or not the toddler was cocaine-exposed, and so observation bias cannot be ruled-out. Topic-Coherence Analysis (Mentis, 1991) and the Pragmatic Protocol (Prutting & Kirchner, 1987) were used to evaluate the discourse-pragmatic aspects of language. Syntax was analyzed in terms of mean length of utterance (MLU) and the Language Assessment, Remediation and Screening Procedure (LARSP) (Crystal, Fletcher, & Garman, 1989). Vocabulary diversity, the number of different words used in a sample of 100 utterances, and “relational semantics” (Retherford, 1993) were measured to indicate semantic development.

The Topic Coherence Analysis revealed statistically significant differences for PCE and NE toddlers in the categories of “new information,” “no new information,” and “problematic utterances”. PCE toddlers had fewer instances of new information and greater instances of no new information than did the NE toddlers. None of the NE toddlers were observed to display inappropriate pragmatics when evaluated using the Pragmatic Protocol. In contrast, all five of the PCE toddlers had two or more inappropriate ratings for different pragmatic parameters, such as topic maintenance, repair/revision, and intelligibility.

There were no statistically significant differences in MLU for PCE and NE toddlers. Finer-grained analysis of syntax showed that NE toddlers had higher developmental clause structure scores and produced more noun phrases than did the PCE toddlers. The two groups did not differ in terms of the number of different words used nor did they differ in terms of semantic roles and grammatical categories or communication routines used.

The sensitive and thorough description of discourse-pragmatics completed by Mentis and Lundgren (1995) indicated a qualitative difference in language usage by PCE toddlers, rather than delayed development. The investigators noted that environmental factors were considered to have a strong influence on the results obtained. The PCE child with the most severe language problems had been homeless for long periods of time, and his mother, who was also his caregiver, had a prolonged illness. Three other PCE children were being raised by their grandmothers, and only one PCE child had been raised in a drug-free environment. Significantly, two PCE children had also experienced failure to thrive and were human immunodeficiency virus (HIV) positive. It was not possible, therefore, to attribute the language differences among PCE toddlers to prenatal cocaine-exposure alone, but to the generally adverse and interactive conditions of poverty, illness, addiction, and family disruption, along with prenatal exposure to other toxic substances, such as tobacco, alcohol, and marijuana.

Standardized tests of speech and language development also reveal problems for children prenatally exposed to cocaine and other drugs. Johnson, Seikel, Madison, Foose, and Rinard (1997) used the Sequenced Inventory of Communicative Development (SICD Revised Edition), the BSID and the Peabody Picture Vocabulary Test-Revised (PPVT-R; to evaluate language in a group of 24 children with multiple drug and cocaine-exposure (MD + C). In addition, the HOME was used to assess the home environment in which language development was taking place. A control group of 24 children, who had no

prenatal drug-exposure (NE), matched by age and sex to the MD + C group, were also tested with the same measures. The mean age of all the children was 30 months and ranged from 14 to 50 months. The speech-language pathologists conducting the testing, which took place in the child's home, were blinded with respect to the child's medical history, that is, prenatal drug-exposure.

There were significant differences between MD + C and NE children on the SICD receptive and expressive processing profiles. The MD + C group scored lower on these profiles than did the NE group, and males scored lower than females. The mean age equivalent receptive score for the MD + C group was 25.7 months, and for the NE group, it was 30.3. The mean age equivalent expressive score was 24.3 months for the MD + C group and 30.5 for the NE children. In general, the age equivalent scores for receptive and expressive language matched the chronological age in the NE group, but were several months behind for the MD + C group. The BSID also revealed significant differences, with the NE group scoring at 120.00 and the MD + C group at 95.3, with no significant effect for gender, and no group-by-gender interactions. Only 10 children from both groups were old enough (>30 months) for the PPVT-R. There were no differences in performance for the MD + C and NE groups on this measure.

The demographic data for the two groups were also examined for differences, including age at time of testing, the number, and duration of OME bouts, maternal age, SES scores, results of the HOME-scale analysis and birth weight. Only birth weight was statistically significant, with average birth weights for MD + C infants 869 g less than for the NE group. The fact that most of the MD + C mothers did not receive prenatal care was thought to be associated with the finding of lower birth weights in these children.

The investigators used the standard criteria for determining eligibility for special services in the state of Washington when analyzing the test scores. Only one child in the NE group qualified for services using these criteria, but 45.8% of children in the MD + C group were eligible according to the standard criteria. The investigators noted that only one child from the MD + C group had been referred for services prior to participation in the study.

Johnson et al. (1997) speak of a "cumulative synergistic effect" of prenatal poly-drug-exposure (including cocaine, alcohol, tobacco, and marijuana), poor prenatal care, lower birth weight, the ill-effects of living with a drug-impaired parent, and other uncontrolled variables that could influence language development. One strength of the study was that the groups did not differ in terms of SES or HOME scores as the MD + C toddlers had been in a drug-free environment, since the age of 11 months owing to their placement in foster homes.

In a second study, the research team evaluated phonology in the MD + C and NE groups (Madison, Johnson, Seikel, Arnold, & Schultheis, 1998). A phonological analysis of a 100-utterance language sample was undertaken, using the first 50 words. The analysis included tabulating the following: (a) number of different processes (from a list of 16, such as addition of initial consonant, fronting, palatalization, syllable simplification); (b) number of production of all processes; (c) utterances produced to obtain 50 words; (d) unintelligible words. The groups differed with respect to the number of productions of all processes, with a mean of 14.4 for the MD + C group and 8.7 for the NE group. The groups did not differ in terms of unintelligible words, however. The MD + C group had more instances of assimilation, cluster reduction, fronting, and syllable simplification than did the NE group.

This is the only study of prenatally poly-drug-exposed toddlers that focused specifically on phonology. It provides further evidence that the constellation of factors affecting overall language development in MD + C pre-schoolers may also exert a specific effect on phonology.

Additionally, [Koren et al. \(1998\)](#) showed that infants with PCE, even when adopted into upper-middle SES families, show a deficit in verbal comprehension and expressive language as evaluated by the Reynell language test.

In contrast, [Hurt, Malmud, Betancourt, Brodsky, and Giannetta \(1997\)](#) showed no difference in language function between PCE infants and a control group consisting of children from a similar, low socio-economic background. Enrollment in the study was at birth, and the infants were seen at 6-month intervals for evaluation of growth and development. At 2.5 years, the Preschool Language Scale was administered as well as the BSID. There were 76 cocaine-exposed and 81 control children tested, giving sufficient statistical power to detect a difference as small as 0.5 SD. As in the [Johnson et al. study \(1997\)](#), the cocaine-exposed infants had lower weights and head circumference at birth; in addition, these infants in the [Hurt et al. study \(1997\)](#) were born at a slightly younger gestational age than were the control infants. Otherwise, there were no maternal or neonatal characteristics that differed between the two groups. It may be that the language test at such a young age (mean = 31 months), and among children of low SES, is not sensitive enough to detect differences in language development. In both the cocaine-exposed and control groups, the equivalent (language) age scores for all sub-tests were slightly below chronological age. It could also be that the care-givers (we do not know whether it was the biologic mother or not) who enrolled in the study to provide their infants with ongoing growth and developmental assessment, and who were dedicated to it for 2.5 years, are also more likely to be providing a supportive language environment, more like that of a household untouched by the illness of addiction.

[Delaney-Black et al. \(2000\)](#) evaluated expressive language development in a group of prenatally cocaine-exposed infants. This study has many strengths, including its prospective cohort design. Mothers were enrolled in a prenatal care program on the basis of their use of or abstinence from alcohol, cocaine or tobacco. The mothers of all children in the study received prenatal care.

Two groups of children were tested at age 6 years: 186 with PCE and 272 with non-exposed controls (NE). Children were tested at 6 years of age using the Arizona Articulation Proficiency Scale. A spontaneous language sample was also evoked and analyzed for total number of words, number of word types, type token ratio, number of turns, number of words uttered per turn, number of utterances per number of turns, and mean length of utterance. In addition, a number of maternal, neonatal, and socio-economic variables were obtained.

There were significant differences in maternal age, tobacco, alcohol, and marijuana use among PCE mothers and NE mothers. The PCE mothers were nearly 5 years older than NE mothers and had higher rates of other substance use.

Statistically significant differences at the $p \leq 0.001$ level were found for weight, length, head circumference at birth, and gestational age. The children with cocaine-exposure were lighter, shorter, had smaller heads and were born slightly earlier than their non-exposed cohorts. Family demographic data obtained at 6 years showed that the mothers did not vary

in terms of income, marital status, parent education, or socio-economic status. More NE children had their biologic mother as a caregiver than did PCE children, and more PCE parents reported current drug-exposure than did NE parents.

The language analysis revealed no significant differences between PCE and NE children. There were, however, children in both groups who demonstrated low language abilities, defined as having type token ratio less than 0.424 and fewer than 97 different word types. The low language group ($N = 57$) and the normal language ability group ($N = 401$) differed significantly with respect to maternal use of cocaine and tobacco, with 63.2% of mothers of low language ability children reporting cocaine use during pregnancy as opposed to 37.4% in the normal language group. The low language ability mothers also reported smoking 11.9 cigarettes/day, as opposed to 8.0/day for the normal language group. Maternal income was significantly lower in the low language group, and maternal language abilities, as measured by the Peabody Picture Vocabulary Test indicated lower scores for mothers of children with low language (mean score = 71.7) compared to the mothers of children with normal language (mean score = 75.7, $p = 0.06$).

All participants in this study were African-American, and the mothers of all participants received prenatal care at the same clinic. It has been suggested that the mothers of PCE infants who enrol in such a study, for which they also received prenatal care, may not be representative of the population of pregnant women who use cocaine, alcohol, and tobacco during pregnancy. Perhaps this is one reason why, at first glance, it appeared that the two groups did not differ in terms of expressive language. But, when the children with the lowest language abilities were evaluated, the rate of maternal cocaine use was much higher, with 67% of mothers of low language children reporting cocaine use.

The influence of PCE on language development was also determined by the Miami Prenatal Cocaine Study (Morrow et al., 2003). Infants were studied prospectively, and longitudinal measures of language were taken. There were 250 PCE infants and 214 non-exposed (NE) infants enrolled. The groups were homogeneous in terms of racial and demographic characteristics. As in the other studies, the PCE infants were born at lower weight, with smaller head circumferences and at a younger gestational age. Maternal characteristics differed; the mothers of PCE infants were less likely to have prenatal care (although 83% of PCE mothers reported prenatal care in contrast to 93% of NE mothers), had fewer prenatal visits, were more often unemployed and older than their NE counterparts.

The BSID were used to document language from 4 to 24 months of age, at 4-month intervals, and the Clinical Evaluation of Language Fundamentals-Pre-school was used at 3 years of age. The first finding was that a larger percentage of children with PCE had scores that were two standard deviations below the standardized sample mean. Multi- and co-variate factorial techniques were used to discern the “cocaine effect” on language. Even when potentially confounding variables are accounted for, such as child gender, maternal use of other substances, prenatal care, maternal age, employment and education, and whether the biological mother was the primary caregiver, there was a statistically significant effect of cocaine-exposure on language development. These deleterious effects were most pronounced for the 18-month and 3-year assessments. Consideration of neonatal factors, such as birth weight and head circumference “attenuated” the estimated cocaine effect on language, as birth weight and language scores were positively correlated.

The effects of poverty and unemployment were seen in the language development of both PCE and NE children. Language scores for all children declined over time, and at 3 years, the CELF-P standard score for both groups was below 80, based on an age normal of 100. This effect was not seen in the measures of cognitive functioning, that is, cognitive function did not decline with age, although language and cognitive function were obviously related, overall.

Morrow et al. (2003) remind us that the infant with prenatal cocaine-exposure is likely to experience “cumulative risk,” not only from the biological effects of cocaine, but also from the postnatal environment of poverty and living with a parent with a substance use problem. They also explain that although the “cocaine effect” on language is subtle, when considered on a population basis, the costs for providing special education for those affected are huge. Similarly, even a subtle deficit at 3 years may fester into larger problems in reading, writing, and academic performance. Thus, early intervention may be recommended for infants born into poverty and parental drug use.

2.4. Hearing and auditory nervous system effects of cocaine

Acute and gestational exposures to cocaine appear to have specific effects on the auditory nervous system. Acutely cocaine-intoxicated macaque monkeys have prolonged absolute and inter-peak components latencies of the auditory brainstem response (ABR) (Jacobson, Bedford, Eisele, & Turner, 1985). These prolonged latencies suggest both peripheral and central auditory system dysfunction. Elevated ABR thresholds and abnormal latency versus signal level functions have also been observed in cocaine-intoxicated rats (Gritzke & Church, 1988), results consistent with a cochlear hearing impairment, suggesting an ototoxic effect. Rat pups with PCE have delayed maturation of the auditory brainstem response (Church, Crossland, Holmes, Overbeck, & Tilak, 1998). Glucose metabolism in auditory nuclei may also be diminished by PCE (Burchfield, 1995).

The ABR findings in human newborns with PCE are similar to those in experimental animals. ABRs show prolonged inter-peak latencies (Cone-Wesson & Spingarn, 1993; Cone-Wesson & Wu, 1992; Salamy, Eldredge, Anderson, & Bull, 1990; Shih, Cone-Wesson, & Reddix, 1988). In Cone-Wesson and Spingarn (1993), a group of control neonates without cocaine-exposure was matched on the basis of gestational age and birth weight to PCE neonates. This was done, because birth weight is typically smaller and gestational age earlier among prenatally exposed infants. ABRs were tested in all infants using a click stimulus, presented at rates of 10, 33, and 89/s. ABR latency for components waves I, III and V were measured. There were no effects of cocaine-exposure status on wave I latency, but there were for waves III and V. This finding indicates that cochlear and eighth nerve function was not affected by prenatal exposure to cocaine. The prolonged latencies for later peaks of the ABR are consistent with central nervous system effects of cocaine, because waves III and V are dependent upon the integrity of brainstem auditory nuclei including the cochlear nucleus (wave III), superior olive and inferior colliculus (wave V). The waves I–V inter-peak latencies were prolonged for PCE infants in comparison to NE infants at all stimulus rates tested. In addition, the waves I–V inter-peak latency differences, as a function of exposure status, increased with stimulus rate. This would suggest that newborns with PCE have increased susceptibility to neural adaptation,

possibly due to neurotransmitter depletion causing synaptic inefficiency or because of immature myelination. Cocaine is known to disrupt neurotransmitter function at brainstem levels, but it is not known whether cocaine affects myelin formation, or whether this may be due to poor maternal nutrition.

Anoxia may be a factor resulting in prolonged ABR latencies. Cocaine causes vasoconstriction of the placenta, thereby decreasing blood flow to the fetus. Prolonged or repeated incidents of fetal anoxia or hypoxia can impair the central nervous system, and the brainstem auditory system is particularly sensitive to oxygen deprivation (Borg, 1997; Hall, 1964).

Low-birth-weight babies and those with intra-uterine growth retardation also show delayed or aberrant brainstem development, as indicated by prolonged ABR inter-peak latencies (Salamy, 1984). Even though Cone-Wesson and Spingarn (1993) used a control group matched for gestational age and birth weight to the PCE infants, those with exposure had greater latency aberrations. This suggests even further delayed or incomplete brain development compared to other developmentally compromised infants.

The behavioral analog of prolonged ABR inter-peak latencies is still unknown, but it is a commonly used indicator for central auditory nervous system dysfunction. Prolonged inter-peak latencies have been correlated with delay or abnormality in language development (Cone-Wesson, Kurtzberg, & Vaughan, 1987; Mason & Mellor, 1984; Murray, 1988).

Even though ABRs have been routinely used to test hearing in young infants for at least 20 years, there are no reports of an increased rate of sensory hearing impairment in PCE infants. Indeed, there is only one long-term outcome study in cocaine-exposed children that considered hearing function. Morrow et al. (2003) report behavioral audiometry results at age 3 years in their study of language among cocaine-exposed infants. Play or visual reinforcement audiometry was used to assess hearing function. Abnormalities for both ears were reported at the same rate (3%) for both non-exposed and exposed children, although cocaine-exposed had double the rate of unilateral abnormalities (6%) compared to the control group. The severity and type of abnormalities detected were not reported.

3. ABR and AMLR binaural interaction components

Auditory-processing disorders are commonly thought to be the basis of some language and learning problems and may have their basis in subtle dysfunction or frank infarct of the central auditory nervous system. Electrophysiological tests of the auditory system, as well as utilizing evoked potentials from the brainstem and cortex may prove useful in the assessment of the neural substrates for complex auditory tasks.

One such method is to use stimulus paradigms dependent upon central auditory function, such as for binaural hearing. For example, complex auditory skills, such as localization or separation of a signal from noise, rely upon the comparison of incoming signals from the two ears. Tests of central auditory function often employ binaural, dichotic stimulus paradigms. This may also be done electrophysiologically. The binaural interaction component (BIC) is one such electrophysiologic method. In this test, each ear is tested monaurally, and then the ears are stimulated binaurally. The difference

between the binaurally evoked response and the summed monaural responses results in a difference waveform, and the peaks evident in this derived waveform are known as BICs. The perceptual analog of BIC is auditory fusion and lateralization (Furst, Eyal, & Korczyn, 1990; Furst, Levine, & McGaffigan, 1985; McPherson & Starr, 1995). BIC abnormalities have been found in children with a history of auditory deprivation from transient hearing loss caused by otitis media with effusion (Gunnarson & Finitzo, 1991), children in whom ABR inter-peak latencies may be abnormal, and in children who also demonstrate abnormalities in perceptual tests of central auditory function (Hall & Grose, 1993). The presence of the ABR wave V binaural interaction component has been used to discern children with abnormalities on perceptual tests of central auditory processing with 76% sensitivity and specificity (Delb, Strauss, Hohenberg, & Pinkert, 2003).

3.1. A neonatal ABR and AMLR investigation

Binaural interaction components for ABR and for the auditory middle latency response (AMLR) were derived from 65 PCE neonates and from a control group of 100 NE neonates (some infants participated in both ABR and AMLR binaural interaction tests). The findings in the full-term control infants have been published previously (Cone-Wesson, Ma, & Fowler, 1997). The PCE infants had a mean birth weight of 2575 g and a mean gestational age of 36 weeks. Seven infants in the cocaine-exposed group were born at 33 weeks gestational age, and they were not tested until they had reached at least 36 weeks. The remaining infants were tested within 22–96 h post-delivery. All infants passed an ABR screening test prior to admission to the study. Informed consent was obtained prior to participation and all procedures were reviewed and approved by the Los Angeles County-University of Southern California Medical Center Institutional Review Board.

ABR and AMLR were evoked using click and toneburst stimuli at 500 and 4000 Hz, presented at levels of 70 dB nHL. The stimuli were presented monaurally to the right and left ears and then, binaurally. Further details of the recording and data-analysis methods and instrumentation can be found in Cone-Wesson et al. (1997).

3.2. Results

First, ABRs in response to clicks and tonebursts were considered. Infants in the cocaine-exposed group ($N = 44$) had longer waves I–V inter-peak latencies for clicks when compared to the control group ($N = 67$), replicating the results of Cone-Wesson and Spingarn (1993) and Shih et al. (1988). The I–V inter-peak latency for the cocaine infants was 5.4 ms, while it was 4.7 ms for the control infants ($F = 18.854$, d.f. = 1, 53, $p < 0.01$). It was not possible to measure inter-peak latencies for toneburst evoked responses, as waves I and III were infrequently obtained for this stimulus condition.

Inspection of the ABR waveforms in response to clicks revealed that cocaine-exposed infants appeared to have a large wave III relative to wave V. This relative amplitude difference was significant. The wave III:wave V amplitude ratio was 1.3 for PCE infants and 0.9 for NE infants.

BICs for waves III and V were measured. Click-evoked BICs for wave III were judged present more often for the PCE group than for the NE group. These results are summarized

in Fig. 1. On average, for all three stimuli, wave III BIC was present for 65% of the cocaine-exposed infants and for only 46% of the control infants. This difference in BIC incidence was statistically significant ($X_2 = 4.118, p < 0.05$).

A different trend is seen for ABR component wave V. Considering the presence of wave V over all stimulus conditions, 79% of NE control group infants had wave V BIC, as did 65% of PCE infants. This difference in occurrence did not reach statistical significance ($X_2 = 3.0, p = 0.08$). The distribution of wave V components, present as a function of stimulus condition and exposure status, is shown in Fig. 1.

AMLRs are generated at the level of the thalamus and primary auditory cortex. The component Pa, occurring with a latency of around 30 ms, is generated at the level of the primary auditory cortex. Generators for negative trough preceding Pa, labeled Na, and for the negative trough following Pa, labeled Nb, are less certain, although it appears that Na may represent auditory nervous system activity at upper brainstem and thalamic sites. In this study, the latencies and amplitudes of Na, Pa, and Nb were measured in response to clicks and tonebursts presented monaurally and binaurally.

AMLRs were obtained from 50 NE and 47 PCE infants. Click-evoked AMLRs were present for over 94% of infants, regardless of cocaine-exposure status. There were some differences as function of test stimulus, however, with only 76% of infants with a Pa component for 500 Hz, and 84% for 4000 Hz. There were latency differences as a function of exposure status, although these were not systematic. In response to clicks, cocaine-exposed infants had shorter Na latencies in comparison to controls, but latencies did not differ for other components. Latency differences for Na, Pa, and Nb were found only in response to 500 Hz tonebursts, with exposed infants having prolonged latencies in comparison to the control group ($F = 9.4, d.f. = 1170, p < 0.05$). There were no exposure-status-related differences in AMLR component amplitude.

Click-evoked BICs for PaNb were present for 66% of control infants and only 33% of cocaine-exposed infants (Fig. 1). The 500 Hz toneburst evoked PaNb–BICs for 62% of controls and 41% of cocaine-exposed infants, but for 4000 Hz, the trend was reversed with 64% of exposed infants having BICs, whereas only 54% of control infants had a Pa–BIC.

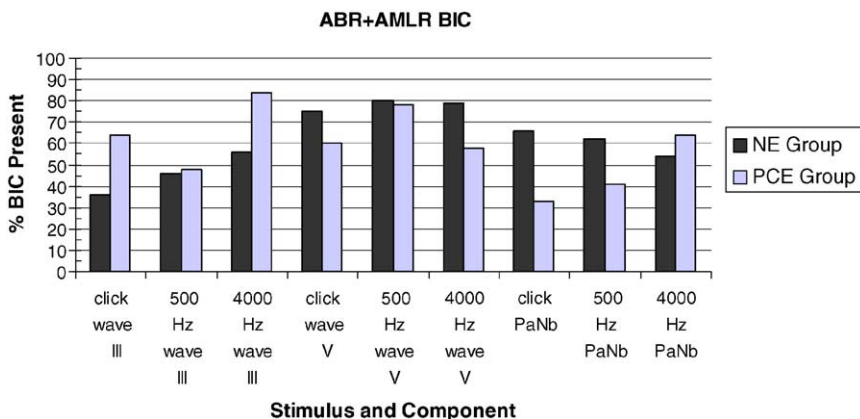


Fig. 1. Distribution of BIC components present as a function of stimulus condition.

In general, prenatal cocaine-exposure appeared to decrease the likelihood of having evidence of binaural interaction at the level of the cortex, but this was statistically significant only for the click-evoked responses.

ABR and AMLR grand mean waveforms were created by summing and averaging all waveforms from all participants. These are shown in Fig. 2, for click stimuli. The enlarged wave III for cocaine-exposed infants is evident in response to clicks (Fig. 2A). A wave III BIC is evident for PCE infants in Fig. 2A, but the wave V BIC is absent, reflecting the lower occurrence of this component among these infants.

Robust AMLRs are seen for all infants in the summed monaural and binaural waveforms (Fig. 2B). Although the component is not absent, the PaNB BIC waveform for the PCE group is of lower amplitude than for the NE infants.

3.3. Discussion

This is the first report of cortically evoked potentials in PCE neonates. It is also the first report of BICs in newborns at risk for neurologic compromise owing to PCE. The study confirmed the finding that cocaine-exposed neonates have prolonged ABR I–V inter-peak latencies, sometimes interpreted as “brainstem transmission time,” indicating some synaptic inefficiency or delayed brainstem myelination. A new finding was the abnormal wave III:wave V amplitude ratio found in cocaine-exposed infants. Wave III is generated at the level of the cochlear nucleus and superior olivary complex. Cocaine blocks the reuptake of dopamine, a neurotransmitter in the auditory nervous system. Might this cause a

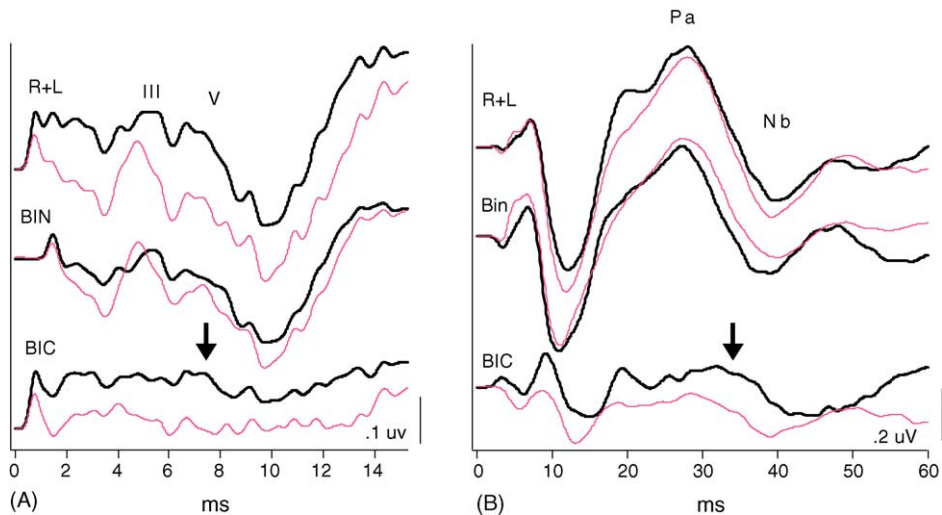


Fig. 2. ABR and AMLR grand mean waveforms for click-evoked responses. The heavy lines indicate the responses from the NE control infants, and the light lines indicate the responses from the PCE infants. The summed monaural (R + L), binaural (Bin) and derived BIC waveforms are shown. The summed monaural waveform is the response obtained by adding together the waveforms from right and left ear tests. The binaural waveform is the response obtained when stimuli are presented binaurally. The BIC is derived by subtracting the Bin waveform from the R + L waveform.

hyper-excitability at this level of the auditory system—or is the large wave III evidence of “dis-inhibition” of some inhibitory circuit? It is not possible to determine the mechanism on the basis of these data, and there are no experimental animal data that have shown this finding. Like the prolonged waves I–V inter-peak latencies, the enlarged wave III amplitudes appear to be evidence of a central, rather than peripheral effect of cocaine on the auditory nervous system.

BIC is diminished in cocaine-exposed infants at both the brainstem (ABR wave V) and cortical (AMLR) levels. ABR–BIC has been associated with binaural fusion and appears to relate to the ability of the brainstem auditory system to encode inter-aural timing differences on the order of microseconds (Furst et al., 1990). The neurons at the superior olive and inferior colliculus are particularly sensitive to inter-aural timing differences, and these are the nuclei primarily involved in the generation of wave V. The presence of ABR–BIC in neonates is affected by stimulus frequency (Cone-Wesson et al., 1997), and as shown in this study, by prenatal cocaine-exposure status. ABR–BIC is sensitive to subtle types of auditory system impairment, such as that caused by auditory deprivation from conductive hearing loss. But, it is not possible to use the absence of BIC as a clinical marker, because BIC is absent in a fairly substantial proportion of control group neonates. The absence of BIC for a larger proportion of cocaine-exposed infants supports the idea that there are subtle neural transmission, integration or fusion differences in these infants.

While some latency differences as a function of cocaine-exposure status exist for the AMLR, these appeared to be frequency-specific. The lower prevalence of click-evoked AMLR–BIC for cocaine-exposed infants was the only evidence of cortical auditory system effects. The AMLR is likely a post-synaptic dendritic potential, and less dependent upon neural synchrony than is the ABR. The neurons of the primary auditory cortex responsible for Pa do not have neurons that are specifically “tuned” for certain inter-aural timing differences as are brainstem neurons. But, differences between PCE and control infants were still ascertained by examining AMLR–BIC. The distribution of AMLR–BIC among cocaine-exposed infants was very different than for ABR–BIC, and this suggests evidence of specific differences in function at the level of the cortex, rather than simply the reflection of the differences detected at lower levels of the auditory nervous system.

Auditory evoked potentials measured in newborns offer a means for evaluating the infant at an early age, and thus separate the effects of gestational drug exposure from postnatal environmental, behavioral, socio-emotional and cognitive factors. There is clear evidence from these studies that cocaine-exposure causes change in the function of the auditory nervous system. The persistence of these abnormalities and how they relate to behavioral or perceptual abilities is not yet known.

4. Summary and conclusions

The questions posed at the beginning of this review were to determine if prenatal alcohol- and cocaine-exposure affected speech, language, hearing, and cognitive development, to describe the specific nature of the delays or disorders, and to determine if there were any exacerbating environmental conditions. FAS occurs in infants whose mothers had a history of daily, heavy alcohol use, or intermittent alcohol use, such as binge

drinking. Cognitive impairment, learning disabilities, and behavioral disorders are the central nervous system manifestations of FAS, and cranio-facial abnormalities are also present. Because prenatal alcohol-exposure can cause structural and functional brain abnormalities resulting in mental retardation, delays in language acquisition as well as receptive and expressive language deficits are commonly reported, although there are few studies that have focused specifically on the speech and language characteristics in children with FAS. The cranio-facial abnormalities of FAS, which sometimes include cleft palate, make the child prone to otitis media with effusion and conductive hearing loss. The rate of sensorineural hearing loss in children with FAS is similar to that of groups with other cranio-facial disorders, although an ototoxic effect of PAE has been shown in experimental animals. The family environment in which one or both parents is a heavy alcohol user presents challenges to a child with normal intelligence, but may be especially deleterious to the child with mental retardation.

Some have questioned whether prenatally cocaine-exposed infants exhibit any lasting, significant effects on speech, language, hearing or cognition that can be attributed strictly to the drug itself and its teratogenicity (Frank et al., 2001). Early research focused on the physical and cognitive development of PCE infants had shown a significant effect of such exposure, but long-term, prospective studies of children with PCE obtained conflicting results. The longer term (i.e. 4–7 years) outcomes appear to show subtle, but statistically significant effects. Height, but not weight, is related to PCE, especially for children born to mothers over 30 years of age (Covington et al., 2002). Subtle cognitive effects are also seen, such as in arithmetic, object assembly, and information (Singer et al., 2004). PCE effects on cognition may be masked by the caregiving environment, with children who received the greatest prenatal exposure placed in adoptive or foster homes in which the care-giver has higher educational achievement than the biological parent or relative.

Speech and language effects of PCE have been measured in prospectively studied cohorts (Delaney-Black et al., 2000; Morrow et al., 2003). In general, a small “cocaine effect” can be assayed from careful, multi-variate analysis methods. More importantly, when other variables are allowed to interact with PCE, such as concomitant exposure to alcohol, tobacco, and marijuana, lack of prenatal care, and other maternal characteristics, greater effects are seen. PCE does not occur in isolation from other risk factors for speech, language, and cognitive delay, or disability. It is therefore plausible to consider the child with PCE at “cumulative risk” (Morrow et al., 2003) for language delay or disorder.

There is no evidence that PCE by itself is a risk factor for sensorineural hearing impairment. ABRs measured from neonates with PCE show prolonged waves I–V inter-peak latencies, interpreted as an abnormality of central auditory function, specifically, neural transmission time within the brainstem. Binaural interaction components measured at brainstem and cortical levels indicate differences between PCE and NE newborns. These are likely related to the effect of cocaine on synaptic function within the auditory nervous system, similar to that causing the prolonged inter-peak latencies. Both prolonged inter-peak latencies and absent or diminished binaural interaction components have been associated with central auditory-processing disorders when evident in older children (Delb et al., 2003; Hall & Grose, 1993).

The strong effect of the home environment for ameliorating the effects of prenatal cocaine-exposure suggests that a family-focused approach for cognitive, language and social-emotional habilitation would be beneficial to all.

Acknowledgements

Dr. Ellen Ma, Manager, Infant Auditory Research Laboratory, The Los Angeles County-University of Southern California Medical Center, assisted with ABR and AMLR data collection and analysis. Dr. Julia Wunderlich, the University of Melbourne, Australia, also assisted with ABR and AMLR data analysis. The ABR and AMLR binaural interaction experiment reported herein was supported by a grant from the March of Dimes Birth Defects Foundation. Mr. Matt Metzger, B.S., assisted in the preparation of this manuscript.

Appendix A. Continuing education questions

- (1) Which of the following is not a feature of FAS:
 - (b) epicanthal folds;
 - (c) hypoplastic maxilla;
 - (d) microcephaly;
 - (e) pre-auricular pits and auricular skin tags;
 - (f) flattened mid-facies?
- (2) The following pre and postnatal conditions may contribute to the developmental delay and behavioral problems experienced by children with FAS:
 - (a) father's use of alcohol;
 - (b) maternal age;
 - (c) violence in the home;
 - (d) socio-economic status;
 - (e) all of above;
 - (f) A and B only;
 - (g) D only.
- (3) Hearing impairments seen in children with FAS are:
 - (a) always related to cleft palate;
 - (b) associated with cranio-facial abnormalities;
 - (c) primarily sensori-neural;
 - (d) of moderate-severe degree.
- (4) Children with prenatal cocaine-exposure:
 - (a) demonstrate cognitive disabilities like those observed in FAS;
 - (b) have a high rate of sensorineural hearing impairment;
 - (c) have subtle cognitive and language deficits when measured at 4–7 years of age;
 - (d) are likely to exhibit physical growth delays;
 - (e) have significant cognitive and language deficits when measured at 4–7 years of age.
- (5) Children with the highest exposures to cocaine:

- (a) have a high rate of central auditory-processing disorders;
- (b) may be placed in adoptive/foster homes with stimulating, language enriched environments and thus show little effect of cocaine on cognitive/language outcomes;
- (c) have cranio-facial anomalies;
- (d) will always need placement in special education programs;
- (e) all of the above.

Key: 1-d; 2-e; 3-b; 4-c; 5-b.

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