SYMPOSIUM

Fetal Alcohol Spectrum Disorders: An Overview with Emphasis on Changes in Brain and Behavior

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Fetal alcohol spectrum disorders constitute a major public health problem. This article presents an overview of important issues that surround these disorders and emphasizes the structural and neurobehavioral consequences associated with prenatal exposure to alcohol. Diagnostic criteria are discussed, and possible moderating factors for the range of outcomes are mentioned. In addition, the prevalence of fetal alcohol spectrum disorders is described, and estimates of the financial impact of these disorders are given. Heavy prenatal alcohol exposure can severely affect the physical and neurobehavioral development of a child. Autopsy and brain imaging studies indicate reductions and abnormalities in overall brain size and shape, specifically in structures such as the cerebellum, basal ganglia, and corpus callosum. A wide range of neuropsychological deficits have been found in children prenatally exposed to alcohol, including deficits in visuospatial functioning, verbal and nonverbal learning, attention, and executive functioning. These children also exhibit a variety of behavioral problems that can further affect their daily functioning. Children exposed to alcohol prenatally, with and without the physical features of fetal alcohol syndrome, display qualitatively similar deficits. Determining the behavioral phenotypes that result from heavy prenatal alcohol exposure is critical, because the identification of these children is crucial for early interventions. In addition, knowing which brain areas are involved might enable the development of better intervention strategies. However, intervention needs to go beyond the affected individual to prevent future cases. As evidenced by the staggering financial impact these disorders have on society, prevention efforts need to be aimed at high-risk groups, and this issue needs to be made a high priority in terms of public health. Exp Biol Med 230:357–365, 2005

Key words: fetal alcohol syndrome; prenatal alcohol; brain imaging; neuropsychological assessment

Introduction

Since the early 1970s the scientific literature on the effects of prenatal alcohol exposure on the developing embryo and fetus has been rapidly expanding. A simple search of the PubMed database using the descriptor *fetal alcohol syndrome* provides 2639 listings as of January 1, 2005. Although the detrimental effects of prenatal alcohol exposure have been alluded to for centuries (1), it was not until 1973, when Jones and Smith (2) and Jones *et al.* (3) described in the *Lancet* 11 children born to alcohol-abusing women, that the long-term consequences of prenatal alcohol exposure attracted the attention of the public and the scientific communities. Shortly thereafter, animal models were developed, which clearly demonstrated the potential teratogenic effects (e.g., growth retardation and physical abnormalities) of alcohol at blood alcohol levels similar to those achieved in humans who abuse alcohol (4, 5).

Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Spectrum Disorders (FASDs)

Fetal Alcohol Syndrome. Perhaps the most widely recognized consequence of prenatal alcohol exposure is FAS (2). Historically, for an individual to be diagnosed as having FAS, anomalies in three distinct areas were required.

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There had to be (i) prenatal and/or postnatal growth retardation, (ii) a distinct facial appearance, and (iii) some evidence of a central nervous system (CNS) dysfunction. Although various diagnostic criteria for FAS have been recently proposed (6, 7), essentially these have been refinements and attempts to better quantify the degree or number of anomalies required for a diagnosis. No attempts have been made to deal with the issue of maternal alcohol use, since in many instances detailed maternal histories are absent or suspect. For the most part, however, the diagnostic criteria remain similar to those initially put forth in the early 1970s: growth retardation, facial appearance, and CNS problems.

Both the Centers for Disease Control and Prevention (CDC) (7) and the revised Institute of Medicine (IOM) (6) guidelines currently recommend that evidence for growth retardation be at or below the 10th percentile for either height or weight, with appropriate corrections for race, sex, gestational age, and other relevant variables. Regarding the facial phenotype, the CDC guidelines recommend that the individual have all three typical facial characteristics—smooth philtrum, thin vermilion, and short palpebral fissures ($\leq$10%)—whereas the revised IOM guidelines only require two of the three facial characteristics. Both guidelines recommend using the appropriate, racially normed lip/philtrum guide developed at the University of Washington, with a score of 4 or 5 being consistent with a diagnosis of FAS (8). The facial phenotype of FAS is presented in Figure 1. Other facial characteristics (e.g., epicanthal folds, strabismus, ptosis, low nasal bridge, ear anomalies) are also common in FAS, but these are not required for the diagnosis. The two guidelines differ more substantially on the deficits required for CNS dysfunction. The revised IOM guidelines list evidence of structural brain abnormalities or a head circumference at or below the 10th percentile. The CDC recommends a more elaborate set of criteria. It includes the two criteria mentioned herein for the revised IOM guidelines, but it also includes neurologic problems or soft signs, as well as a number of functional deficits (e.g., global cognitive or intellectual deficits or functional deficits 1 SD below the mean in at least three domains of functioning). Both sets of guidelines have a mechanism or category for dealing with the issue of unknown maternal alcohol exposure histories. The revised IOM criteria also include a diagnosis of partial FAS, which includes a confirmed history of maternal alcohol exposure, two of the facial characteristics, and one other characteristic such as growth retardation, evidence of deficit brain growth, or a pattern of behavioral or cognitive abnormalities. The behavioral or cognitive abnormalities include deficits in problem solving, planning, arithmetic, language, motor functioning, or social behaviors not explained by other factors.

Fetal Alcohol Spectrum Disorders. It is clear from the scientific and clinical literature that FAS is not the only outcome that results from prenatal alcohol exposure. Rather, it has been suggested that the effects from gestational alcohol exposure lie on a continuum or present a spectrum of disorders. There have been a variety of terms, including *fetal alcohol effects*, *alcohol-related neurodevelopmental disorders*, and *alcohol-related birth defects*, used to address this issue. The term *FASD* was recently adopted at a meeting convened by National Organization on Fetal Alcohol Syndrome (NOFAS), a nonprofit advocacy group that included representatives from families, researchers, and several governmental agencies. The term *FASD* is NOT a diagnostic term but rather an umbrella term that describes the range of effects that can occur in an individual whose mother drank alcohol during pregnancy. These effects can be physical, mental, or behavioral, with possible lifelong implications.

Variations in the FAS and FASD Conditions. The reasons for this range of outcomes are varied but similar to those that provide a range of phenotypes for most other teratogens. Undoubtedly, one of the major factors that influences outcomes is the amount of alcohol that reaches the developing embryo or fetus (Table 1). This, in part, is determined by the dose and pattern of alcohol exposure. Similarly, genetic factors undoubtedly play a role, since these factors affect the metabolism of or functional sensitivity to alcohol. Nutritional factors could influence blood alcohol levels or operate through other means to determine the results. In addition, the timing of exposure will determine which developing structures are affected and how severely they might be affected. Age of the mother is another factor that has been identified as a risk factor for FAS. Thus, it is not surprising that not all individuals exposed to similar amounts of alcohol during gestation have the same outcomes. Some might be severely affected in multiple systems, whereas others may have no apparent effects.

One example of how the phenotype can differ as a function of exposure involves critical periods of exposure. Prenatal alcohol exposure during the first trimester interferes with the migration, proliferation, and organization of brain cells (9–11). Exposure in mice during a period of brain growth development equivalent to the first trimester in humans resulted in severe malformations of the face and brain (12). The degree of craniofacial malformations ranged from bilateral and unilateral cleft lip to small nose and maxillary region to exencephaly with median facial cleft or absent nostrils. These patterns of malformation were highly correlated with areas of cellular death in the anterior neural plate. During the third trimester, alcohol consumption is highly related to damage to the cerebellum, hippocampus, and prefrontal cortex (13–16). Thus, the pattern of structural and functional abnormalities will vary, depending on how the exposure coincides with critical periods of development.

Given this range of outcomes, it is becoming increasingly clear that FAS is a diagnosis of exclusion, particularly when a history of maternal alcohol use is not available (7). Although one frequently hears of the characteristic facial

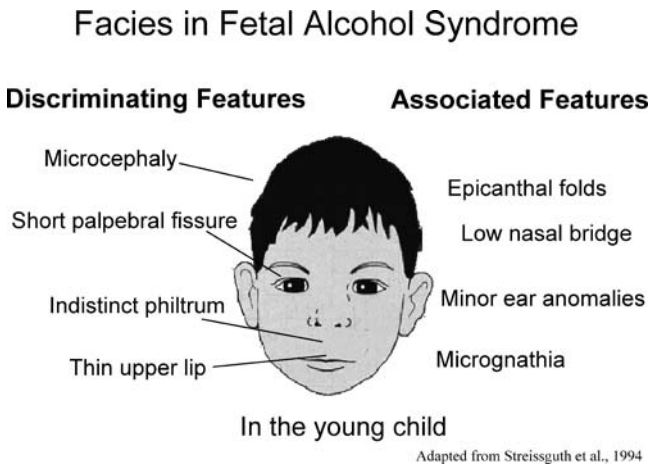

Figure 1. The facial phenotype of FAS in a young child. A smooth philtrum, thin vermillion or upper lip, and short palpebral fissures are typically used in the diagnosis of FAS, although the other features listed are common. Adapted from Streissguth AP. A long-term perspective of FAS. Alcohol Health Res World 18:74-81, 1994.

appearance seen in FAS, other disorders share these characteristics (phenocopies) and therefore have to be excluded before an individual receives a diagnosis of FAS. Some examples of disorders that can be mistaken for FAS include Williams, DeLange, velocardiofacial, fetal hydantoin, and Dubowitz syndromes.

Incidence of FAS and FASDs and Economic Ramifications. The effects of prenatal alcohol exposure are undoubtedly major public health problems wherever women drink during pregnancy. However, the prevalence of FASDs is not well understood, because a number of factors influence the epidemiologic research in this area, including the population under study, the method of ascertainment, and the diagnostic criteria being used (17). Studies on the birth prevalence of FAS generally report a range of 0.2–2.0 per 1000 live births, depending on the ascertainment methods across a variety of populations. In their review, May and Gossage (17) state that "FAS prevalence in the general population of the U. S. can now be estimated to be between 0.5 and 2 per 1,000 births." This would translate to between 2000 and 8000 cases of FAS among the 4,019,280 births that occurred in the United States in 2002. However, in certain groups the prevalence is much higher. For example, studies from a wine-making region in South Africa suggest that the rates of FAS may be more than 50 per 1000 live births (18). This estimate is from a population with generally low socioeconomic status, a long history of wine production, and a high prevalence of binge drinking. However, active case ascertainment in one county in Washington State found a rate of FAS of 3.1 per 1000 (19), and similar methods among certain groups of Native Americans (Plains and Plateau culture tribes) have found an average FAS rate of 9 per 1000 (20). Perhaps one of the most important prevalence rates that needs to be addressed is the prevalence of FAS in families who already have a child with FAS. Although these data have not been independently confirmed, the rate of FAS in the offspring of a woman who already has given birth to a child with FAS is 771 per 1000 (21), making this an extremely high-risk group. Women who have already had a child with FAS are at an especially high risk of having another child if they continue their abuse of alcohol, and in fact it is not uncommon to see the older children in a family less affected than their younger siblings.

As we have already stated, FAS is only one of the possible outcomes that result from exposure to large amounts of alcohol prenatally. When one tries to estimate the prevalence of all FASDs, the situation becomes even less exact. However, estimates of 1 per 100 (1% of live births) being affected by prenatal alcohol exposure have been cited (22). Furthermore, despite the massive educational campaigns about alcohol consumption during pregnancy, the CDC reports that more than half of the women in the United States of childbearing age consumed alcohol in the month before their survey and that approximately 15% of these could be considered moderate or heavy drinkers. Approximately 13% of women continue to use alcohol during their pregnancy and 3% of pregnant women report binge or frequent drinking (7). These numbers are much too high to deny the public health concerns related to prenatal alcohol exposure.

The economic costs of FASDs have also received attention. In the most recent and thorough review of this topic, Lupton *et al.* (23) review the available data and estimate that the adjusted 2002 cost is $2.0 million for each individual with FAS. This comprises $1.6 million for medical treatment, special education, and residential care for persons with mental retardation and $0.4 million for lost productivity. In 1989, the Senate Advisory Council of the Alaska State Legislature estimated the 1988 lifetime cost of each infant born with FAS at $1.4 million (24). This estimate, which adapted the approach used by Harwood and Napolitano (25), is considered conservative because of excluded costs. In terms of the annual cost of FAS to the United States, the estimates vary considerably, but one of the most recent reviews estimates that it cost more than $5 billion in 2003 to care for individuals with FAS (26). Despite the varying opinions, which depend on differing estimates of FAS, varying costs per condition, and other factors, the costs regardless of how they are computed are staggering.

Changes in Brain Structure

Although the facial characteristics seen in patients with FAS are certainly the most obvious signs of heavy gestational alcohol exposure, the most devastating consequences are the ones related to changes in the brain and the behavioral sequelae. The remainder of this overview will concentrate on these changes, which have the greatest impact on the lives affected by prenatal alcohol exposure.

Table 1. Risk Factors Associated with FASDs

Dose of alcohol
Pattern of exposure (binge vs. chronic)
Developmental timing of exposure
Genetic variation
Maternal characteristics
Socioeconomic status
Synergistic reactions with other drugs
Interaction with nutritional variables

Beginning with an early report on FAS in the United States (2), the effects of prenatal alcohol exposure on the brain were evident. In that report, the autopsy of an infant with FAS revealed widespread damage throughout much of the brain. In addition to microcephaly, there were errors in migration, agenesis of the corpus callosum and anterior commissure, and cerebellar and brainstem anomalies. Subsequent autopsy confirmed this widespread CNS disorganization, including microcephaly, neuroglial heterotopias, and ventricle, corpus callosum, basal ganglia, and cerebellar anomalies (27, 28). However, one difficulty with these findings is that the cases that typically come to autopsy are the most severe. Thus, these findings may not be typical of the brain changes that occur in most individuals with FAS.

A growing body of research using magnetic resonance imaging (MRI) has indicated specific alterations in brains of living individuals exposed prenatally to high doses of alcohol with and without a diagnosis of FAS. Since 1992, our laboratory in San Diego has conducted a series of studies using MRI of children with FASDs, both with and without FAS. In early studies, quantitative structural analyses were performed to determine the size and/or volume of particular brain structures. Recent advancements in novel computational image analysis techniques have allowed reassessment of the valuable brain image data and have provided new insight into the damage caused by heavy prenatal alcohol exposure.

Brain Size and Shape. One of the most consistent findings of MRI studies with alcohol-exposed individuals is the overall reduction of the cranial vault and the concomitant reduction in brain size (28–35). A recent series of studies using novel image analytic techniques has demonstrated that all areas of the cortex are not equally affected. With a volumetric approach (29), only the parietal lobe was found to be disproportionately reduced when overall brain size was taken into account. In another study (36), tissue abnormalities on the surface of the whole brain were analyzed on a voxel-by-voxel basis. Results from this study complemented the earlier volumetric findings (29), indicating prominent abnormalities in the perisylvian cortices in the parietal and temporal lobes. Both of these studies also indicated the differential effect of alcohol on white matter compared with gray matter tissue. Compared with controls, alcohol-exposed patients had relative increases in gray matter and decreases in white matter in the perisylvian cortices of the temporal and parietal lobes (36), and white matter hypoplasia was found to be more significant than gray matter hypoplasia (29).

In addition to regional reductions in volume and tissue density, shape abnormalities have also been found in brains of alcohol-exposed patients compared with controls (37). As predicted, shape abnormalities were present in the perisylvian and parietal regions; specifically, a narrowing of the brain occurred in similar regions to where increased gray matter density was seen in the early report (36). Results also indicated highly significant reduced brain growth in the ventral portions of the frontal lobes, which was most prominent in the left hemisphere. Although frontal lobe anomalies were not found in earlier studies (29, 36), these results are consistent with the cognitive and behavioral literature that suggests that children with prenatal alcohol exposure have difficulties with response inhibition, behavioral control, and executive functions (38, 39), which are all known to be related to frontal lobe functioning. Additionally, control brains showed cortical surface gray matter asymmetry that was more prominent in the temporal lobe (right hemisphere greater than left), whereas alcohol-exposed individuals showed a significant reduction in this asymmetry (40). These results imply that brain growth continues to be adversely affected long after the prenatal insult of alcohol on the developing brain, and the brain regions most implicated, the frontal and inferior parietal and perisylvian areas, are consistent with the neurocognitive findings in individuals prenatally exposed to alcohol.

Cerebellum. Reductions in cerebellar volume in FASDs have been reported (28, 29, 31, 32). The reduction in the FAS cases was more than 15%, whereas in the nondysmorphic FASD cases the effect was not as large, although still significant. The changes in the cerebellum were also not uniform, since a regional analysis indicated that the anterior vermis was reduced in size relative to controls, whereas the posterior vermis was unaffected (41).

Corpus Callosum. One of the most significant changes is the alteration reported in the corpus callosum, the fiber tract that connects the two hemispheres. In our first structural imaging study, one child with FAS had agenesis of the corpus callosum and another had a particularly thin corpus callosum (31). Subsequent studies have documented other cases of agenesis (33, 35, 42, 43), and it has been suggested that FAS might be one of the leading causes of this condition (44). However, most individuals with FASDs do not have such severe alterations, and more in-depth evaluation has indicated significant changes in the size and shape of this structure. In one study, the midsagittal section of the corpus callosum was assessed, and the most anterior and posterior regions were shown to be smaller in the FASD group than in controls (43). In a more recent study (45), the corpus callosum was again found to be smaller in individuals with FASDs and significantly displaced in

three-dimensional space. Relative to controls, this structure was displaced more anteriorly and inferiorly in posterior regions. Importantly, this displacement was highly correlated with alcohol-exposed individuals' performance on a verbal learning task. In other words, children with greater callosal displacement exhibited more substantial performance impairments.

Basal Ganglia. The basal ganglia, a group of subcortical nuclei that includes the caudate, appears to be especially sensitive to the effects of prenatal alcohol exposure. Even after overall brain size was controlled for, basal ganglia volume has been found to be reduced in children with FASDs compared with controls (31). A more recent study (29) differentiated the caudate from the lenticular nucleus, and although both were reduced in size compared with controls, after controlling for brain size, only the caudate remained significantly smaller.

Neuropsychological and Behavioral Changes

Heavy prenatal alcohol exposure is associated with a wide range of neuropsychological deficits, including impairments in overall IQ, memory, language, attention, reaction time (RT), visuospatial abilities, executive functioning, fine and gross motor skills, and social and adaptive functioning. Children with and without the physical features of FAS demonstrate qualitatively similar deficits in these areas of neurobehavioral functioning (46). Because of the focus of this article, discussion of neuropsychological and behavioral deficits will be largely limited to findings from our laboratory.

Overall Intellectual Performance. The effect of prenatal alcohol exposure on IQ has received considerable attention, perhaps because FAS is cited as the most frequent, preventable cause of mental retardation (47). However, most individuals with FAS are not mentally retarded, with only approximately 25% having IQ scores <70 (48). IQ scores also vary widely, for example, from a low of 20 (49) to a high of at least 120 (50). The mean IQ is estimated to be between 65 and 72, and children with more dysmorphic features tend to have lower IQ scores than those with fewer features (51).

Learning and Memory. Both verbal and nonverbal learning and memory have been assessed in children with FAS and appear to be impaired, although deficits in memory may not be as global as was once thought. For example, one study that investigated verbal learning and memory (52) found that although the FAS group demonstrated deficits in memorizing verbal information, these deficits resulted from difficulties with the acquisition of the information rather than with the ability to remember the information. Furthermore, studies of implicit memory function indicated no differences between alcohol-exposed and control children (53).

Language. Because children with FAS are often sociable, friendly, and outgoing and appear younger than their chronologic age, their language abilities may seem unimpaired. However, compared with chronologic age-matched controls, children with FASDs show marked deficits. Recent findings from our laboratory found that children exposed prenatally to alcohol performed significantly poorer than controls on measures of word comprehension and naming ability as measured by the Peabody Picture Vocabulary Test–Revised and the Boston Naming Test, respectively (46).

Attention. Activity and attention have also received considerable focus, and children with FAS are frequently compared with those with attention-deficit/hyperactivity disorder (ADHD). In fact, a large number of children with FAS would qualify for a diagnosis of ADHD. In a recent study (54), children with FASDs were compared with nonexposed children with ADHD on the Test of Variables of Attention (TOVA), a computerized test of attention, to determine whether the groups could be distinguished based on their performance. Results suggest that although inattention is representative of children with ADHD with or without heavy prenatal alcohol exposure, impulsivity is more specific to nonexposed children with ADHD. In another study (55), children with heavy prenatal alcohol exposure and nonexposed controls were evaluated using a paradigm developed to test visual and auditory focused attention. Data suggest that children with heavy prenatal alcohol exposure have deficits in attention that are not global in nature. Rather, deficits in visual attention were pervasive, whereas auditory attention deficits occurred only when intertarget intervals were long.

Reaction Time. RT is an indicator of cognitive processing speed. In a recent study (56), RTs were evaluated in children prenatally exposed to alcohol using a paradigm that fractionated RT into premotor and motor components. Fractioning RTs into premotor and motor RTs can help determine whether observed delays are predominantly related to central processing of stimulus information or peripheral motor unit recruitment, respectively. Additionally, two levels of tasks were used: simple RT (SRT), which involves the use of only the dominant hand, and choice RT (CRT), which uses both hands, resulting in a higher cognitive demand. Alcohol-exposed children demonstrated slower overall CRTs compared with control children, as was expected because both central and peripheral mechanisms are believed to be affected. Additionally, alcohol-exposed children exhibited significantly slower premotor RTs during the CRT task and slower motor RTs during both the SRT and CRT tasks.

Visuospatial Abilities. Children with histories of heavy prenatal alcohol exposure have been shown to have deficits in visuospatial processing and memory. Using the global-local test, which presents hierarchical stimuli that consist of a large "global" symbol made up of smaller "local" symbols, Mattson *et al.* (57) found that children with prenatal alcohol exposure are more impaired in local than global analysis of hierarchical visual stimuli, and this

deficit is independent of memory deficits typically associated with such exposure. Additionally, these deficits were not related to the smaller size of the local stimuli. The authors postulate several explanations for this deficit in visuospatial processing. One explanation is that these deficits may be related to the alcohol-exposed children's difficulty in shifting attention. Reductions in the cerebellar vermis have been implicated in attention shifting (58), and as mentioned herein, this area has been shown to be reduced in children with FASDs (41). In addition, the perseveration seen in the drawing of local features may be related to dysfunction of the frontal-subcortical brain systems, of which several components, such as the basal ganglia and frontal lobes, have been shown to be reduced in size in individuals exposed to alcohol (37, 59, 60).

Executive Functioning. Much research has recently focused on executive functioning, a complex construct that has been broadly defined as "the ability to maintain an appropriate problem solving set for the attainment of a goal" (61). A variety of cognitive domains are subsumed under this general definition, including inhibition, set shifting and set maintenance, planning, working memory, and the ability to integrate information across time and space (62). We have recently used the Delis-Kaplan Executive Functioning System (D-KEFS) battery (63) to examine executive functioning in children with FASD (38). Four domains of executive functioning were evaluated: cognitive flexibility, response inhibition, planning, and concept formation and reasoning. Group differences emerged across all four domains even when accounting for deficits in concomitant more basic skills. In another study, both verbal and nonverbal fluency were examined using two additional measures from the D-KEFS in children with FASDs and nonexposed controls (64). When compared with nonexposed controls, children with FASDs displayed deficits in both fluency domains, demonstrating impaired verbal and nonverbal fluency. These deficits in executive functioning may be related to the reduction and thinning of the frontal lobes and reduction in the basal ganglia, which are connected through the frontal-subcortical circuit. These deficits may also be related to deficits in spatial memory, perseverative tendencies, and attentional problems.

Fine and Gross Motor Skills. Early descriptions of children with FAS reported delayed motor development and fine-motor dysfunction, including tremors, weak grasp, and poor hand-eye coordination (3). In a study that compared the neuropsychological functioning of children with FAS and nondysmorphic FASDs, both groups exhibited impaired performance compared with controls on the Grooved Pegboard Test, which measures fine motor speed and coordination (65). Additional evidence from both human and animal studies suggests that balance is particularly affected as a result of prenatal alcohol exposure (66–71). In rats, impairments in balance have been associated with damage to the cerebellum (68, 70, 71). More recently, postural balance was assessed in a group of alcohol-exposed children compared with matched nonexposed controls under conditions of systematic variations of visual and somatosensory information (72). Results suggested that alcohol-exposed children are more reliant on somatosensory input, and when this input is atypical, these children display significant anterior-posterior body sway and are unable to compensate using available visual or vestibular information. These deficits may be related to the cerebellar anomalies reported in children with heavy prenatal alcohol exposure. In a follow-up study (73), corrective postural reactions in response to rapid toe-up movements of the support surface were examined in alcohol-exposed children to understand the nature of balance deficits. Although analyses revealed no group differences on short- and medium-latency electromyographic responses, compared with controls, alcohol-exposed children exhibited increased long-latency responses, which are thought to involve a transcortical pathway. These results suggest that balance deficits seen in these children are, at least in part, central in nature.

Adaptive and Social Skills. Studies that involve parent reports have suggested that alcohol-exposed children are at high risk for problem behaviors that can interfere with their participation in home, school, and social environments. For example, these children are more likely than nonexposed children to be rated as hyperactive, disruptive, impulsive, or delinquent (74, 75). Furthermore, based on parent ratings of their child's behavior, children with histories of prenatal alcohol exposure had significant and profound impairment, with particular difficulties in social, attention, and aggressive domains (74). In a recent study (76), the relationship between social skills and verbal IQ score in children with FAS and controls was assessed. Results from this study suggest that social deficits in children with FAS are beyond what can be explained by low IQ scores and indicate that they may be arrested, and not simply delayed.

Conclusions

Prenatal exposure to alcohol, at least high doses of alcohol, can cause permanent changes in the brain, and these brain changes affect behavior. Brain alterations seen in these individuals include reduced brain size; alterations in shape, tissue density, and symmetry; and volumetric reductions and abnormalities in the cerebellum, basal ganglia, and corpus callosum. These shape and tissue abnormalities highlight the regional nature of brain morphologic differences and suggest that assessment of brain-behavior relationships may be regionally specific and that brain functional abnormalities may not be global in nature. Besides alterations in brain structure, individuals with histories of heavy prenatal alcohol exposure face long-lasting deficits that affect many aspects of cognitive and behavioral functioning. Although a substantial amount of research has been performed on the neuropsychological deficits found in children prenatally exposed to alcohol, researchers

hope to determine a specific pattern of strengths and weaknesses. With this knowledge, it may be possible to characterize the core deficits found in this population, which would allow researchers and practitioners to develop scientifically based interventions. Additionally, knowing which brain areas are involved might enable improved intervention strategies. Research has shown that early identification leads to interventions, services, and improved outcomes (48). Therefore, identification of children with heavy prenatal alcohol exposure is critical for both advancing research and ensuring that children receive appropriate services.

Fetal alcohol spectrum disorders constitute a major public health problem. These effects have an impact on the individual, the family, the communities where these individuals live, and society in general. The economic impact of FASDs is staggering. Fetal alcohol spectrum disorders are also of international concern, since these problems occur wherever women consume alcohol. It is not only a problem of a particular ethnicity or social group but rather one that affects us all. Much would be gained in patient quality of life and economic status if these problems could be prevented. Fetal alcohol spectrum disorders can be prevented with the elimination of alcohol consumption during pregnancy. We need to provide education, target high-risk groups, and make this issue a high priority in terms of public health.

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