ALCOHOL- INDUCED BEHAVIOURAL PROBLEMS IN FETAL ALCOHOL SPECTRUM DISORDER VERSUS CONFOUNDING BEHAVIOURAL PROBLEMS

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ABSTRACT

Prenatal alcohol exposure is strongly associated with disruptive behaviour in childhood and antisocial behaviour later in life. There are numerous confounding risk factors in the lives of alcohol-abusing mothers that may contribute to the behaviour problems seen in their children, rather than direct brain injury by alcohol. In fact, many of these additional environmental and genetic risk factors for childhood behaviour problems co-occur with prenatal alcohol exposure and affect the same child, creating a confluence of risk. As a result, one cannot with any certainty attribute behaviour problems in an individual child to prenatal alcohol exposure. This has important clinical and legal implications.

Key Words: *Alcohol, pregnancy, ARND, Alcohol related neurodevelopmental disorder, conduct problems, externalizing behaviour, problem behaviour, maladaptive behaviour, antisocial behaviour, disruptive behaviour, delinquency*

Clinical Case

The following demonstration case highlights a typical presentation.

Grayson, age 8 years, is brought to the clinic by his adoptive parents. They are worried about a growing pattern of aggressive, impulsive behaviour. Grayson's school has complained several times that he is bullying other children and starting fights at recess. He frequently "acts out" during class time, is rude to his teachers, and does not follow the classroom rules. Last week he was sent to the office because he has been repeatedly cheating on math tests by looking at another student's paper.

At home, his parents have difficulty getting him to complete his homework. They frequently catch him lying, particularly when it helps him to avoid doing homework. Last month, his mother discovered that he had stolen money from her purse to buy a new video game. He had previously asked his parents to buy the game for him but they had refused to buy it until he started behaving better at school and completing his homework regularly. They have been punishing him with increasing severity but are troubled by Grayson's lack of guilt after misbehaving.

When Grayson was 2 years old, Children's Aid Society removed him from his family of origin due to neglect. His biological mother had a history of alcohol abuse and drank heavily while pregnant with him. At the time that Grayson was removed from the home, his father was in prison for assault and drug-related charges. Grayson was in foster care for one year until his current family adopted him.

Grayson had a series of ear infections as a toddler but has otherwise been in good health with normal physical development. Grayson's adoptive parents have no other children.

Grayson's parents believe that his behaviour problems are a result of prenatal alcohol exposure. They hope if he is given an alcohol-related diagnosis that the school will be more understanding and perhaps give him special help.

Introduction

Diagnosing fetal alcohol spectrum disorder (FASD) can be difficult, especially in individuals who lack the physical features of the disorder.[1-3] These individuals with only the cognitive and behavioural features of FASD fall under the sub-category of alcohol-related neurodevelopmental disorder (ARND) (see Table 1).

TABLE 1

Institute of Medicine Criteria[1]

Presence of A and/or B with a history of maternal alcohol exposure[a]***:***

A. Evidence of CNS neurodevelopmental abnormalities, as in any one of the following:

- decreased cranial size at birth
- structural brain abnormalities (e.g., microcephaly, partial or complete agenesis of the corpus callosum, cerebellar hypoplasia)
- neurological hard or soft signs (as age appropriate), such as impaired fine motor skills, neurosensory hearing loss, poor tandem gait, poor eye-hand coordination.

B. Evidence of a complex pattern of behavior or cognitive abnormalities that are inconsistent with developmental level and cannot be explained by familial background or environment alone, such as learning difficulties; deficits in school performance; poor impulse control; problems in social perception; deficits in higher level receptive and expressive language; poor capacity for abstraction or metacognition; specific deficits in mathematical skills; or problems in memory, attention, or judgment

a. A pattern of excessive intake characterized by substantial, regular intake or heavy episodic drinking. Evidence of this pattern may include frequent episodes of intoxication, development of tolerance or withdrawal, social problems related to drinking, legal problems related to drinking, engaging in physically hazardous behavior while drinking, or alcohol-related medical problems such as hepatic disease.

Modification of the Institute of Medicine Criteria[2]

Presence of both A and B:

A. Confirmed maternal alcohol exposure

B. At least 1 of the following:

1. Evidence of deficient brain growth or abnormal morphogenesis, including ≥1 of the following:
- **a**. Structural brain abnormalities
- **b**. Head circumference ≤10th percentile

2. Evidence of a complex pattern of behavioral or cognitive abnormalities inconsistent with developmental level that cannot be explained by genetic predisposition, family background, or environment alone.

a. This pattern includes marked impairment in the performance of complex tasks (complex problem solving, planning, judgment, abstraction, metacognition, and arithmetic tasks); higher-level receptive and expressive language deficits; and disordered behavior (difficulties in personal manner, emotional lability, motor dysfunction, poor academic performance, and deficient social interaction).

Harmonization of the Institute of Medicine and 4-Digit Diagnostic Code Approaches[3]**:**

The diagnostic criteria for alcohol-related neurodevelopmental disorder, after excluding other diagnoses, are:

A. Evidence of impairment in 3 or more of the following central nervous system domains: hard and soft neurologic signs; brain structure; cognition; communication; academic achievement; memory; executive functioning and abstract reasoning; attention deficit/hyperactivity; adaptive behaviour, social skills, social communication.

B. Confirmed maternal alcohol exposure.

The behavioural features of ARND, however, are not specific to this disorder. This makes diagnosing ARND more challenging because most children who have been heavily exposed to alcohol *in utero* also have other environmental and genetic risk factors for these behaviour problems.[4-7] Together, this confluence of risk factors combined with the non-specific etiology of behaviour problems used in ARND diagnosis, make it hard for a clinician to be sure that prenatal alcohol exposure, and not a different variable, is causing the child's behaviour problems.

Behaviour Problems in FASD

A constellation of behaviour problems has been associated with prenatal alcohol exposure. These behaviour problems include: physical aggression, stealing, lying, cruelty, cheating, bullying, emotional lability, impulsivity, hyperactivity, lack of guilt after misbehaving, deficient social skills and communication, self-injury, alcohol and drug use, avoiding school or work, and disobedience at home.[1,3,8-11] These behaviours are variously referred to as conduct problems, externalizing behaviour, problem behaviour, maladaptive behaviour, antisocial behaviour, disruptive behaviour, and delinquency. In this review, we will simply use the term behaviour problems to refer to the set of behaviours associated with FASD.

Childhood behaviour problems form part of the "primary disabilities" defined by Streissguth et al. and frequently lead to poor outcomes later in life, known as "secondary disabilities".[12] Among adolescents and adults with a diagnosis of fetal alcohol syndrome or fetal alcohol effects, Streissguth et al. found a lifetime prevalence of 60% for trouble with the law, 50% for confinement, 49% for inappropriate sexual behaviours on repeated occasions, and 35% for alcohol or drug problems.[12] MacPherson and Chudley found that 10% of inmates had confirmed FASD and another 18% had possible FASD but maternal alcohol use could not be confirmed.[13]

Estimates of the prevalence of behaviour problems and criminality in FASD should, however, be viewed with caution. Most estimates are from clinical or forensic samples as opposed to community samples, leading to the possibility of a referral bias. This can skew both the frequency and type of problems seen in the FASD population, as children with disruptive behaviours are more likely to come to clinical or legal attention.[14] Nevertheless, it is generally accepted that FASD and behaviour problems are strongly associated, even if the exact prevalence remains unclear. While these behaviour problems are not pathognomonic of FASD, they do contribute to FASD diagnosis and, in some children with ARND, may form the principal basis for a diagnosis (see Table 1).

Other Environmental Risk Factors for Behaviour Problems

Despite the strong association, prenatal alcohol exposure is not the only risk factor for behaviour problems. Postnatal environmental factors also play an important role. These postnatal risk factors include: low socioeconomic status[15-17]; adoption[18]; family stress[19]; marital discord[17,20,21]; witnessing parental violence[22,23]; childhood physical abuse[24,25]; childhood sexual abuse[26-28]; a convicted parent, fewer years of parental education[15]; coercive, hostile and inconsistent parenting[19,20,29]; and parental abuse of alcohol or other substances.[30,31] While the evidence suggests that these are independent risk factors for behaviour problems, disentangling the influence of one environmental factor from another can be challenging because many of these factors co-occur and influence each other.[32]

Genetic Predisposition to Behaviour Problems

While the environment has long been known to influence behaviour problems, there is increasing evidence that children can also inherit a genetic predisposition to a set of behaviour problems from their parents.[33-36] A quantitative review of 51 twin and adoption studies of antisocial behaviour found that 41% of the variation in risk for antisocial behaviour was due to genetic factors, 43% was due to experiences specific to the individual (i.e. non-shared environment), and the remaining 16% was due to shared family experiences (i.e. shared environment).[37] Similarly, studies of externalizing behaviour and conduct problems have found that these behaviours are substantially heritable.[38-42] Heritability estimates for conduct problems have

varied between 20% and 80% with the majority between 40% and 70%.[43]

Genetic transmission does not imply a one-to-one relationship between parent and child behaviours. Rather, Waldron et al. found that parents who abuse alcohol tend to transmit to their children a genetic predisposition to behaviour problems such as rule-breaking and aggression.[44] This inherited predisposition appears to be a general tendency toward behavioural disinhibition and undercontrol that in turn leads to specific behaviour problems and personality traits.[45-47]

While genetic and environmental factors are important independent risk factors, some of these factors can also interact with each to further increase an individual's risk of behaviour problems.[48,49] For instance, Jaffee et al. found that, while genetic risk and physical maltreatment both independently predicted conduct problems, these two factors also had a significant interaction effect: physical maltreatment was associated with a 2% increase in risk of conduct problems in children considered to have a low genetic risk, but, in children with a high genetic risk, physical maltreatment was associated with a 24% increase.[49]

Children with Prenatal Alcohol Exposure: A Confluence of Risk Factors

Children who are exposed to alcohol in utero frequently have many of the other risk factors for behaviour problems as well. All children with FASD have mothers who abused alcohol to some extent. This alcohol abuse itself is evidence of a potential genetic predisposition to behaviour problems in the mother that may be passed down to her children. Furthermore, the majority of women who abuse substances during pregnancy also have one or more comorbid mental disorders.[4] Depending on the mother's specific mental disorder, this may increase her child's genetic risk for behaviour problems. Mothers who abuse alcohol are also more likely to choose mates with who abuse alcohol, further increasing their children's genetic loading for behaviour problems.[50,51] The clinician, however, may not be aware of parental psychopathology when assessing a child with prenatal alcohol exposure. The parent may have never received a diagnosis, or the biological parents may no longer be involved in the care of the child, a common scenario. In a study of Finnish children and adolescents with FASD, 64% lived with a foster family or had been adopted, and 16% lived in a children's home.[7] As a result, it is often impossible for the clinician to rule out parental psychopathology as a genetic risk factor for a particular child.

In addition to this genetic risk, children with heavy prenatal alcohol exposure also tend to face environmental risks for behaviour problems. Streissguth et al. found that 61.1% of children aged 6-12 with fetal alcohol syndrome and fetal alcohol effects had experienced physical or sexual abuse.[5] Those children who continue to live with alcohol-abusing parents are more likely to have high levels of intra-family stress, intra-family conflict, family economic difficulties, and impaired mother-child attachment.[6] Furthermore, women who abuse substances during pregnancy are more likely to be victims of domestic violence, increasing the chances that children with prenatal alcohol exposure witness domestic violence.[4] Unfortunately, these various risk factors exert more than a summative effect; as discussed above, they interact with each other, multiplying the risk of behaviour problems in these children.

Does Prenatal Alcohol Exposure Truly Cause Behaviour Problems?

Given this confluence of risk factors, it is possible that the behaviour problems seen in FASD are not due to teratogenic effects from alcohol but instead may be due to the associated genetic and environmental confounders described. This basic problem, however, has received surprisingly little attention both in research and clinical work related to FASD.[14]

A few authors have tried to clarify the causes of behaviour problems in children with prenatal alcohol exposure. They have produced conflicting results. Some evidence supports the hypothesis that the behaviour problems are caused by the confounding risk factors associated with prenatal alcohol exposure, rather than the exposure itself. Lynch et al. found that adolescents with prenatal alcohol exposure were no more likely to be delinquent than unexposed adolescents, as long as other social risk factors were carefully controlled for.[52] Other authors have found that, while prenatal alcohol exposure does cause conduct

problems even when controlling for other risk factors[10,53-56], prenatal alcohol exposure appears to have a smaller effect on behaviour problems and other mental health outcomes than many of the other environmental and genetic risk factors.[11,57,58] Thus, the evidence remains unclear on whether prenatal alcohol exposure is a direct cause of behaviour problems, but, if it is a direct cause, then it is a minor one.

Can We Differentiate between Behaviour Problems Caused by Prenatal Alcohol Exposure and Those Caused by Other Factors in an Individual?

The causality between prenatal alcohol exposure and behaviour problems is unclear at a population level, but it becomes even murkier when assessing an individual. Moreover, in children like "Grayson" in the clinical case above, diagnosing ARND is more difficult because they have no physical features of FASD and we have not determined a precise cognitive and behavioural phenotype for ARND.[1-3] In addition, when children's behaviour problems are the main presenting feature, diagnosis becomes more challenging because these children already have at least one risk factor for behaviour problems: a mother who abused alcohol. As a result, clinicians cannot accurately diagnose these children with ARND. In other words, we should not assign a diagnosis that implies causation when that relationship cannot be proven. Aase et al. made the same argument regarding the term "fetal alcohol effects" when it was still in use.[59] We have since replaced this term with the diagnostic categories ARND and alcohol-related birth defects, but similar problems remain. Given the long and intertwined list of "causes" and risk factors that lead to behaviour problems, we cannot confidently say that one of these risk factors is the true "cause" in an individual child.

This issue goes beyond the difficulty of initial diagnosis. Even in a child presenting with the full physical and neurocognitive features of fetal alcohol syndrome and, thus, a clear diagnosis, the clinician may be asked whether behaviour problems are a result of prenatal alcohol exposure. Once again, in an individual with heavy prenatal alcohol exposure, it is impossible to know whether their behaviour problems are due to this exposure, to the other risk factors typically associated with this exposure, or, most likely, to a combination of all these factors.

DISCUSSION

Does it Matter?

We cannot currently determine the cause of behaviour problems in a child with prenatal alcohol exposure. This matters for several reasons. It has implications for ongoing attempts to accurately characterize the behavioural phenotype of FASD and to delineate useful diagnostic criteria for ARND. More importantly, however, the uncertain etiology of these children's behaviour problems matters for clinical and legal reasons.

The category of FASD diagnoses differs from many of the other common developmental diagnoses in that it is not only descriptive but also ascribes an etiology. This sets FASD apart from purely descriptive diagnoses such as attention-deficit hyperactivity disorder, oppositional-defiant disorder, conduct disorder, learning disability, and mental retardation. While there are etiological theories for all these disorders, the etiology is not an inherent part of the diagnosis, as it is in FASD. Since the etiology of a particular behaviour problem in a particular child is impossible to ascertain, we should be careful not to create abstract and impractical diagnostic criteria for FASD and particularly ARND.

The logic applied here to behaviour problems can also be applied to many of the other neurodevelopmental features of ARND: difficulties with attention, memory, learning, communication, and executive functioning (see Table 1). Although a full discussion of each deficit's risk factors is beyond the scope of this review, these features may also be influenced less by prenatal alcohol exposure than by confounding environmental and genetic factors. If this is the case, then diagnostic category of ARND in its current form is almost useless clinically and needs to be radically reworked. This is not to minimize the real and devastating effect that prenatal alcohol exposure can have on development. But when assessing behaviour problems in an individual, we must remember that prenatal

alcohol exposure is not the only risk factor, nor is it the most potent.

Currently, clinicians face a dilemma when assessing children like Grayson. Diagnosing him with ARND is problematic when the cause of his behavioural problems remains uncertain. A diagnosis of ARND is far from trivial, carrying both positive and negative implications for the child and the family. A more cautious course of action would be to simply document the known prenatal alcohol exposure and assess the child's specific deficits without making conclusions about their root causes. However, clinicians often feel pressured by parents, social workers, or schools to assign an FASD diagnosis so that the child may have better access to services and accommodation.[59] Even in the absence of this overt pressure, clinicians may err on the side of giving a diagnosis of FASD because early diagnosis has been associated with improved outcomes.[12] Children with an early diagnosis of FASD may do better because they receive early intervention and support as a result; a diagnosis of FASD improves access to appropriate school programs, counseling for the child and parents, and other specialized services.[60,61] However, children with behaviour problems benefit from early intervention regardless of whether the behaviour problems are caused by prenatal alcohol exposure or not.[62,63] There is currently no clear evidence that a diagnosis of FASD should, of its own accord, change the treatment plan.[14,64] Rather, treatment should target the specific needs of each child. The FASD population is heterogeneous and requires individualized assessment and treatment like all other children with developmental disabilities.

There have been calls to strengthen services for children and youth with FASD.[60,64,68] This is necessary. However, it is equally necessary for us to strengthen services for all children and youth with behaviour problems. These problems are just as real and pressing whether they are caused by exposure to a substance or not. Funding and developing better services and treatment programs for all children with behaviour problems and developmental disabilities will in turn benefit children with FASD without penalizing other children in need of services.[14] The argument for integrated services is further supported by the fact that we cannot accurately differentiate between behaviour problems caused by prenatal alcohol exposure or by other factors. Nevertheless, more research is needed to clarify whether children with FASD respond differently to specific pharmacological or behavioural interventions compared with children who have similar deficits but no prenatal alcohol exposure.

Although the impact on treatment remains unclear, a diagnosis of FASD can have benefits such as improved access to services, as mentioned above. Adoptive or foster parents may feel validated that their child's problems are "real" and not the result of their parenting. However, a diagnosis can have negative consequences as well. Settling on a diagnosis of FASD too quickly can mean abandoning the search for other causes such as a genetic syndrome or abuse. Children with FASD may also be stigmatized or perceived by schools as incapable of achievement.[59,67]

The legal implications of a diagnosis of FASD vary from case to case. Fast and Conry describe that the courts have sometimes relates to FASD as a mitigating factor, rendering an individual less responsible for their actions due to underlying brain damage, but in other cases FASD was seen to make an individual more dangerous to society and harder to rehabilitate.[69] People with FASD may also be sentenced differently, given conditional sentences, for instance, that allow them to serve their sentence in an alternative venue such as their parents' house under supervision.[69]

A diagnosis of FASD affects the ways in which an individual's behaviours are viewed and treated. This is a problem. Because we cannot determine whether behaviour problems in an individual are caused by prenatal alcohol exposure or by other associated factors, we should not be treating these behaviour problems any differently based on such questionable etiology.

Acknowledgements

Supported in part by the Public Health Agency of Canada, Canadian Institutes for Health Research, The Research Leadership for Better Pharmacotherapy During Pregnancy and Lactation, and the Ivey Chair in Molecular Toxicology.

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