Fetal Alcohol Syndrome Disorders: Comments on Astley, O'Brien and Mattson, and O'Connor

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Introduction

Jones and Smith[1] coined the term fetal alcohol syndrome (FAS) to label a pattern of altered growth and morphogenesis observed in a group of children born to alcoholic mothers. This pattern of dysmorphia included a cluster of facial anomalies (e.g., short *palpebral fissures*), growth retardation, and evidence of central nervous system (CNS) involvement (e.g., *microcephaly* and developmental delays). In the years following the publication of the Jones et al. paper, it became evident that the expression of this syndrome varied considerably as a function of differences in exposure (e.g., quantity, frequency, timing) and genetic factors. Since clinicians were reluctant to diagnose those individuals with partial expression of the syndrome, Clarren and Smith[2] introduced the term "suspected fetal alcohol effects (FAE)" to refer to such individuals. Although this term was meant to serve as a "bookmark" to facilitate further studies, service providers and teachers began to misuse it as a diagnostic term for labeling developmental issues in children with known or suspected histories of prenatal alcohol exposure. Since clinicians did not have a firm basis for linking developmental problems in these children to prenatal alcohol exposure, Aase et al.[3] recommended that the term FAE be abandoned. This presented the clinician with a challenging problem: Given that the majority of children with prenatal alcohol exposure do not exhibit clinically discernable dysmorphia, what labels should be used to denote their neurocognitive difficulties? The Institute of Medicine (IOM) report[4] sought to address the issues related to diagnosis by replacing the term FAE with two new diagnostic categories: alcohol related birth defects and alcohol related neurodevelopmental disorders. The replacement of the old term with two new ones did not, however, solve the primary diagnostic issue of linking prenatal alcohol exposure to cognitive-behavioural problems in a child. Astley and Clarren[5,6] developed the 4-Digit Code diagnostic system to tackle this issue.

Another approach to identifying alcohol-affected children without dysmorphia has involved a search for a

syndrome-specific neurocognitive profile. It is now known that prenatal exposure to alcohol produces a wide range of morphological and functional outcomes in the offspring, which are collectively called fetal alcohol spectrum disorders (FASDs). While alcohol-induced dysmorphia have been observed only in a minority of alcohol-exposed children,[7] cognitive behavioural problems have been found to be pervasive across the spectrum. However, the delineation of neurocognitive profile in alcohol-affected children has proven to be methodologically challenging because a wide range of factors interactively contribute to cognitive behavioural functioning. Therefore, the cognitive-behavioural phenotype in FASDs has been dubbed a moving target.[8] The focus of the paper by O'Brien and Mattson is to assess the progress that has been made in identifying a syndrome specific neurocognitive profile in children with FASDs.

An important question related to the functional outcomes of prenatal alcohol exposure concerns whether different levels of cognitive-behavioural problems in individuals with FASDs can be delineated. Streissguth et al.[9] reported a range of adverse life outcomes in adolescents and adults with FASDs, including mental health problems, disrupted school experience, trouble with the law, confinement, inappropriate sexual behaviour, alcohol/drug problems, dependent living and problem with employment. These adverse outcomes were labeled secondary disabilities since primary disabilities directly resulting from alcohol-induced brain damage, such as diminished IQ and memory problems, were considered to underlie them. Given that social-emotional problems cut across most of these secondary disabilities (e.g., trouble with the law, inappropriate sexual behaviour, problem with employment), some researchers have sought to understand the mechanisms underlying socio-emotional functioning of alcohol-affected individuals. O'Connor presents an overview of the findings from this line of research.

Research and Conclusions

The 4-Digit Code system[5,10] offers a non-medical, pragmatic approach to diagnosing the full spectrum children with FASDs. In this system, a diagnostic category is formed by combining the ratings of four variables relevant for diagnosing FASDs: growth, facial phenotype, CNS abnormalities, and prenatal alcohol exposure. Because this diagnostic system does not make biological assumptions, each variable is treated independent of others. Therefore, the question of whether CNS damage observed in a child resulted from prenatal alcohol exposure does not arise.

The 4-Digit method has made two important contributions to diagnosing fetal alcohol spectrum disorders. First, it has considerably improved the reliability of diagnosis through the development of tools to measure facial features, standardization of measurements, and manualization of the diagnostic procedures. Second, since the 4-Digit Code System employs a standardized procedure of classification, it can be used by a clinical team without specialized training in dysmorphology. This has allowed identification of children with prenatal alcohol exposure in clinics where dysmorphology services are not available.

Despite these merits, the 4-Digit Code system has some shortcomings, which, in my view, result from using a non-biological approach to classifying and understanding a biological phenomenon. From a statistical point of view, improved reliability of measurements does not ensure greater validity. Classification of a diagnostic feature using conventions such as "two standard deviations below the mean" will result in arbitrary groups which may not correspond to real divisions (taxa) in the phenotype. As Meehl[11] reminds us, classification is an "enterprise that aims to carve nature at its joints (plato), identifying categories of entities that are in some sense

(not metaphysical essentialist) non-arbitrary, not man-made" (pp 268).

O'Brien and Mattson summarize the key findings from the studies of neurocognitive functioning of children with FASDs and suggest that this clinical group exhibits a specific profile in comparison to IQ-matched controls and those with ADHD. For example, group comparisons between FASD and ADHD revealed that both groups showed impaired performance on a sorting task, but only the FASD group displayed deficits in letter fluency and letter-number switching. Compared to IQ-matched controls, the FASD group had more externalizing problems, impaired adaptive skills, and verbal learning difficulties. While these findings are interesting, a question can be raised about their generalizability. Particularly, parent-rated behaviours such as externalizing problems and adaptive skills are substantially influenced by socio-cultural experiences and the quality of parenting. A wide range of variables including language, cultural experiences, and genetic/epigenetic factors, are also known to moderate performances of complex tasks.[12] As the authors point out, contributions from different variables to the aforementioned group differences should be addressed in future research.

O'Connor underscores the importance of considering the interactive effects of multiple variables on socio-emotional functioning in individuals with FASDs. Particularly, psychiatric difficulties in this population develop within the matrix of a multitude of factors including maternal nutrition, socio-economic status, genetic loading for psychiatric illness, problems in parenting, and adverse life experiences. Therefore, O'Connor and others[13,14] have used a transactional model in the study of emotional difficulties in children with prenatal alcohol exposure. Research conducted within the transactional model has demonstrated that neurobehavioural effects of prenatal alcohol exposure in infants such as jitteriness and irritability have a negative impact on early mother-child interactions, which, in turn, lead to long-term adverse emotional outcomes in the child. Consistent with these findings, research in social neuroscience has revealed that the quality of mother-child interactions influence the child's stress responses, which is mediated through the *hypothalamus-pituitary-adrenal (HPA) axis*.[15]

Implications for Services and Policy

I agree that the 4-Digit Code system has had a significant impact on diagnosis of fetal alcohol spectrum disorders, particularly in the U.S. and Canada. The Canadian Diagnostic guidelines[16] have incorporated the 4-Digit Code and the diagnostic categories proposed by the IOM report. The Canadian investigators found the 4-Digit method appealing mainly because its use of quantitative, objective measurement scales and specific case definitions. According to Astley et al.[17] parents and service providers have expressed satisfaction with the diagnostic reports which provide the information necessary for qualifying children for services.

Despite these advances, I believe that diagnosis of the full spectrum of fetal alcohol effects can be improved by incorporating the findings from cognitive and behavioural neurosciences. Meehl[11] compellingly argued that a solution to the question, "how shall we classify?" should be sought through applied mathematics. Taxometric analyses of morphological, neuroanatomical, cognitive and behavioural measures from children with FASDs may reveal whether the underlying (latent) patterns of data reflect non-arbitrary categories or dimensional distributions. Identification of natural categories or dimensions will lead to the development of appropriate interventions.

As O'Brien and Mattson point out, the identification of syndrome-specific profiles would allow diagnosing alcohol-exposed children without discernable dysmorphia. The delineation of a neurocognitive profile will also

inform the development appropriate therapies. We have recently proposed that children with FASDs have a deficit in the integration of multiple elements or relations in working memory due to slow processing of information.[18] This proposal has specific implications for the development of interventions for alcohol exposed children. O'Connor has presented evidence that psychiatric problems are highly prevalent among individuals with prenatal alcohol exposure.[19] This finding highlights the importance of early screening for socio-emotional problems in this population. The finding that positive mother-child interactions and the stability of home environment support emotional development in children has implications for the development of policies pertaining to placement of alcohol-affected children in foster care and parent training.

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