Assessing Diagnostic Classification Accuracy of Neurobehavioral Disorder associated with Prenatal Alcohol Exposure (ND-PAE)

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Abstract

Background: Diagnostic criteria have recently been introduced in the Diagnostic and Statistical Manual for Mental Disorders – 5th Edition (DSM-5) for Neurobehavioral Disorder associated with Prenatal Alcohol Exposure (ND-PAE) as a condition requiring further study. The purpose of this study is to assess the classification accuracy of the DSM-5 criteria, using multidisciplinary clinical assessment as the "gold standard" of comparison.

Methods: Eighty-two patients underwent multidisciplinary clinical assessments in rural Alberta between 2011 and 2015. A database was developed to include diagnostic and outcome data retrieved from patient files. Two clinicians independently reviewed client files for evidence of meeting the diagnostic criteria for ND-PAE. Good inter-rater reliability was established between clinicians based on 90% agreement (Kappa = .79).

Results: Classifications from the clinical assessments and DSM-5 criteria were moderately correlated (Cramer's V (82) = .44, $p<.01$). Total classification accuracy of the DSM-5 guidelines was 61%. All classification errors were false negative (n = 32). For this reason, the DSM-5 possessed high specificity (100%, 95% CI [87.7%, 100.0%]) but low sensitivity (47%, 95% CI [33.7%, 60.0%]) in identification of a disorder associated with PAE.

Interpretation: Despite largely assessing the same neurobehavioural domains, the DSM-5 criteria for ND-PAE was far less likely to identify prenatal alcohol disorder. Although the neurobehavioural domains assessed by ND-PAE are supported in the research, there are limitations with its diagnostic structure that restrict the identification of a prenatal alcohol disorder.

Keywords

Fetal Alcohol Spectrum Disorder (FASD); Diagnostic and Statistical Manual of Mental Disorders (DSM); Neurobehavioral Disorder associated with Prenatal Alcohol Exposure (ND-PAE); diagnosis; assessment.

Introduction

The adverse effects of prenatal alcohol exposure (PAE) on the developing fetus have been recognized for over 40 years [1–3]. The effects of PAE on the developing central nervous system (CNS) are widespread, cutting across domains of intelligence, executive functioning, learning and memory, academic achievement, communication, visual-spatial ability, motor skills, attention and hyperactivity, externalizing behaviours, and adaptive functioning [4]. Early diagnosis is associated with improved long-term outcomes for patients and their families [5–7].

Given the impacts of PAE, there have been efforts to accurately identify and classify the symptom presentations of exposed individuals. Diagnostic criteria for fetal alcohol syndrome (FAS), including growth restriction, characteristic facial features, and CNS dysfunction were identified in early years of fetal alcohol research [2]. It was soon apparent, however, that the CNS could be impacted by PAE in the absence of growth and facial features [8]. In subsequent years, diagnostic guidelines for Fetal Alcohol Spectrum Disorder (FASD) were developed to identify patients affected by PAE [9–12]. However, the diagnosis of FASD is not ubiquitous, with varying systems that can be contradictory [13]. Despite calls for consensus in FASD diagnosis [14], different multidisciplinary diagnostic systems continue to emerge [15,16].

Current FASD diagnostic practices are multifaceted and complex, with the use of multidisciplinary clinic teams being considered best practice [4]. While the multidisciplinary team approach results in comprehensive assessment, they are costly and limit clinical capacity [5]. The development of more efficient diagnostic systems are needed in order to identify a wider range of patients impacted by PAE and to improve access to services [17].

With the publication of DSM-5 [18], criteria were developed for a PAE-related diagnosis, Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure (ND-PAE) as a condition requiring further study. The DSM-5 criteria propose symptoms related to impairment in 1) neurocognitive functioning, 2) self-regulation, and 3) adaptive functioning, with confirmation of more than minimal exposure to alcohol in utero. Impairment in neurocognitive functioning may be seen in one or more of the following areas: global intellectual functioning; executive functioning; learning; memory; or visual-spatial reasoning. Impaired self-regulation is manifest in one or more of: impaired mood or behavioural regulation; attention deficit; or impaired impulse control. Impaired adaptive functioning is manifest in two or more of the following symptoms: communication deficit; impairment in social communication and interaction; impairment in daily living; or impaired motor skills. Additionally, a communication deficit or impairment in social communication or interaction must be present to satisfy criteria within the adaptive functioning domain.

The purpose of this study is to assess the classification accuracy of the DSM-5 criteria, using multidisciplinary clinical assessment as the "gold standard" of comparison. While there is considerable overlap between the domains assessed in DSM-5 and those used in the clinical assessment, it is hypothesized that the DSM criteria will have low sensitivity in identifying prenatal alcohol disorder given the requirement for impairment across the three general domains, impairment on two symptoms within the adaptive functioning domain, and the required symptom "hit" on either communication deficit or impaired social communication and interaction.

Methods

Setting

Data was collected through a multidisciplinary FASD diagnostic clinic in Alberta, Canada. The clinic team included physicians, psychologists, speech/language pathologists, and occupational therapists, using the Canadian Guidelines for Diagnosis of FASD [12]. Nine CNS domains were assessed by the multidisciplinary clinic team including: motor skills; intelligence; communication; academic achievement; memory; executive functioning; attention deficit/hyperactivity; brain structure; and adaptive behaviour, social skills, and social communication. Significant deficits (i.e. -2 SD) in at least three domains plus confirmation of alcohol exposure is necessary for a FASD-related diagnosis.[12]

Child/adolescent clinics were held for children ages 7-17, and adult clinics for patients aged 18 and older. Confirmation of alcohol exposure was obtained from direct maternal self-report or professional documentation such as hospital, social work, or police records. Ethical approval for the project was obtained through the University of Lethbridge Human Subject Research Committee. Informed consent was obtained from patients or their legal guardians for the use of the clinical data for research purposes.

Patients

Eighty-two patients (41 male, 41 female) who were assessed between 2011 and 2015 participated in this study. Sixty-three were assessed through the Children and Adolescent (mean age 11.1 years, SD = 3.4) and nineteen were adults (mean age 29.1 years, SD = 9.9). Seventy-nine patients had confirmed PAE. 73% of patients (n = 60) received a diagnosis under the umbrella of FASD, including FAS (n = 1), partial FAS (n = 13), and alcohol related neurodevelopmental disorder (n = 46).

Design

A database was developed to include diagnostic and outcome data retrieved from patient files. These included the identification of significant deficits for each of the nine domains described in the Canadian Guidelines [12], as well as prenatal risk factors, and growth and facial measurements. Two clinicians independently reviewed client files for evidence of meeting the diagnostic criteria for ND-PAE [18]. While the Canadian Guidelines specifies the degree of deficit necessary for a symptom count (typically 2 SD below the mean), the DSM-5 criteria makes no such distinction for the majority of symptoms apart from identification of "impairment". Within the intellectual domain the DSM-5 does specify a score of >2 SD below the mean as necessary for symptom identification, consistent with the 2005 Canadian guidelines. Therefore, "impairment" on other DSM-5 symptoms was classified based on scores >2 SD below the mean where available.

Domains of significant deficit on clinical assessments were identified as impairments on equivalent DSM-5 symptoms in the areas of intelligence, executive functioning, learning, memory, attention deficit, impulse control, communication, motor skills, and adaptive behaviour including daily living skills and social communication and interaction. Impairment in mood or behavioural regulation were assessed by the presence of a diagnosed mood, anxiety, or relevant externalizing behaviour disorder. Impairment in visual-spatial reasoning was assessed by scores at the second percentile or lower on the copy trial of the Rey Complex Figure Test [19] and other clinical information as available. Case files were reviewed for additional information.

Analysis

Classification accuracy, sensitivity and specificity analyses, and positive and negative predictive values of the DSM criteria was assessed against the results of multidisciplinary clinical assessments from 2011-2015. Because diagnoses are dichotomous in nature, crosstabulations was used to describe the data and Cramer's V was used to assess the correlations between the criteria. Percent agreement and Kappa were used to assess inter-rater reliability [20].

Results

Inter-rater reliability

Two clinicians independently reviewed each case file, identifying symptom criteria and diagnoses for ND-PAE. Good inter-rater reliability was established [21] based on 90% agreement on DSM-5 criteria (Kappa = .79).

Classification Accuracy of ND-PAE

Dichotomous classifications of the clinical assessments and DSM-5 criteria were moderately correlated (Cramer's V (82) = .44, $p<.01$). Against multidisciplinary clinic assessments as the "gold standard", total classification accuracy of the DSM-5 guidelines was 61%. Table 1 outlines the crosstabulation of DSM-5 and clinical assessment. Of particular importance, all classification errors were false negative (n = 32), meaning that all errors were the result of non-classification in DSM-5 in the presence of classification on clinical assessment. For this reason, the DSM-5 possessed high specificity (100%, 95% CI [87.7%, 100.0%]) but low sensitivity (47%, 95% CI [33.7%, 60.0%]). Positive predictive value refers to the probability that a diagnosis is present when the test is positive, and negative predictive value refers to the

probability that a diagnosis is absent when a test is negative. Given the absence of false positive classifications, the positive predictive value was identical to specificity (100%, 95% CI [87.7%, 100.0%]) and the negative predictive value was identical to sensitivity (47%, 95% CI [33.7%, 60.0%]).

Interpretation

The DSM-5 criteria for ND-PAE were moderately correlated with multidisciplinary clinical assessment. The presence of some correlation is expected given that both systems assess a relatively consistent range of symptoms across cognitive, regulatory, and adaptive domains. However, compared to multidisciplinary clinical assessment using the Canadian guidelines [12] the DSM-5 criteria were less sensitive in identifying prenatal alcohol disorder despite largely assessing the same domains.

There are three reasons why the DSM-5 criteria are less sensitive in identifying prenatal alcohol disorder. First, the Canadian guidelines [12] as well as other established FASD classification systems [10,11], do not specify in *which* domains patients with FASD will be impaired. In contrast, the DSM-5 guidelines specify that patients with prenatal alcohol disorder will have impairment in neurocognitive functioning, self-regulation, *and* adaptive functioning categories. Second, the adaptive functioning domain is weighted more heavily in the DSM-5 guidelines, whereby ND-PAE patients will present with at least 2 of 4 adaptive functioning symptoms. In established FASD guidelines, no symptom domain is given additional weighting over another. Third, meeting DSM-5 symptom criteria in the adaptive functioning category requires the presence of at least one of a) communication deficit, or b) impairment in social

communication and interaction, whereas no specific impairment domains *must* be present with established diagnostic systems.

The DSM-5 criteria as is implies a shared neurobehavioural profile for patients affected by prenatal alcohol disorder, in terms of defining which impairments are present. Domains of communication deficit and impairment in social communication and interaction are core features of ND-PAE, and other areas of adaptive functioning including impairments in daily living and motor skills are more salient than other important domains including attention, impulse control, executive functioning, learning, memory, and intellect. Additionally, DSM-5 criteria stipulates that all patients with ND-PAE possess a combination of neurocognitive, self-regulatory, *and* adaptive functioning deficits.

The DSM-5 domains are based on evidence of a broad range of neurocognitive, self-regulatory, and adaptive functioning deficits [22,23]. However, research has yet to delineate a specific neurobehavioural profile or core symptoms of FASD [4]. Given the variable effects of dose, timing, and pattern of alcohol use during pregnancy [24] in conjunction with varying stages of central nervous system development, the identification of core symptoms common to *all* patients with prenatal alcohol disorders is formidable.

Strengths and Limitations

A potential limitation is that the "gold standard" of multidisciplinary clinical assessment in this study used the 2005 Canadian guidelines. There are several guidelines in use around the world [10,11,15,16] without an unequivocal gold standard. However, the use of a comprehensive multidisciplinary assessment is important given that this approach considers additional factors such as external, developmental, or familial factors, independent of the

criteria that may result in a diagnosis or non-diagnosis on a case by case basis. These could not be fully accounted for in applying DSM-5 criteria retroactively to case files. In addition, the terms FASD and ND-PAE were used synonymously as disorders caused by prenatal alcohol exposure, given the lack of differentiation between the two terms in DSM-5 criteria. Accuracy of classification based on DSM-5 guidelines in this study is limited by lack of clarity of what constitutes impairment. Finally, while the same guidelines were used with patients of all ages in the multidisciplinary clinical assessments, there may be limitations with classifying patients of all ages in the study.

The timeliness of this study is important given the recent publication of DSM-5 and the stated need to evaluate ND-PAE criteria [17,22]. The multidisciplinary clinical assessments allowed for in-depth evaluation of each patient, accounting for external and developmental factors that affect results. While informed by the 2005 Canadian guidelines [12], clinical assessments were more comprehensive than the cursory classification of patients based on file data. Finally, this study provides an explanation that the low sensitivity of the DSM-5 criteria is rooted in the organizational structure of the diagnostic domains, not the domains themselves.

Conclusion

While the DSM-5 criteria captures many domains in which individuals with prenatal alcohol disorder may experience impairment, the structure of these criteria limits its sensitivity in diagnostic classification. Until common core or central features of FASD are delineated, all potential symptom criteria should be considered important in assessing for prenatal alcohol disorder.

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Table 1

Crosstabulation - Clinical Assessment and ND-PAE Diagnoses

		Diagnosis from Multidisciplinary Clinical Assessment		
		No	Yes	Total
Diagnosis from DSM-5 ND-PAE	No	22	32	54
	Yes	0	28	28
Total		22	60	82