THE IMPACT OF AN ADHD CO-MORBIDITY ON THE DIAGNOSIS OF FASD

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ABSTRACT

Objective
Many children with Fetal Alcohol Spectrum Disorders (FASD) also have co-morbid ADHD. The goal of this study was to examine the impact of having a co-morbid ADHD diagnosis on FASD diagnostic results. We compared children with FASD to those with FASD and co-morbid ADHD across the neurobehavioral domains recommended by the Canadian Guidelines in the diagnosis of FASD.

Methods
We retrospectively analyzed data from 52 children, aged 4 to 17 years, diagnosed with an FASD at a hospital FASD clinic. Thirty-three of these children had a co-morbid diagnosis of ADHD and 19 did not. Children with FASD and those with FASD and co-morbid ADHD were compared on the following neurobehavioral domains: sensory/motor, cognition, communication, academic achievement, memory, executive functioning, attention, and adaptive behavior.

Results
Children with FASD and ADHD performed significantly worse than those without ADHD on attention but better on academic achievement. No other group differences were significant.

Conclusions
Having an ADHD co-morbidity had little effect on the FASD diagnosis. The results of this project will inform the diagnostic process for FASD and have implications for standardizing diagnostic processes across clinics.

Keywords: *Fetal Alcohol Spectrum Disorder (FASD), Prenatal Alcohol Exposure (PAE), ADHD, diagnosis, neurobehavioral*

Fetal Alcohol Spectrum Disorders (FASD) lead to lifelong primary and secondary disabilities in affected individuals[1] and FASD is one of the most common known causes of mental retardation.[2] Obtaining an accurate diagnosis of an FASD can be challenging because it can be difficult to obtain a reliable history of prenatal alcohol exposure (PAE) and a unique profile of neurobehavioral deficits among children with FASD has not been identified.[3] The diagnostic process for alcohol-related disorders has changed a great deal since the term Fetal Alcohol Syndrome (FAS) was coined in 1973.[4] In 1978, Clarren and Smith[5] developed specific diagnostic criteria for FAS and Fetal Alcohol Effects (FAE), which were typically differentiated by the presence or absence of facial dysmorphology. In 1996, the Institute of Medicine (IOM)[6] distinguished five different types of FAE using a gestalt approach. Then in 1997 (and revised in 1999 and 2004), the Fetal Alcohol Syndrome Diagnostic and Prevention Network (FAS DPN) 4-Digit Diagnostic Code was developed, creating a more standardized and objective method of diagnosis looking at growth factors, facial dysmorphology, and most importantly, brain

dysfunction.[7-9] Prenatal exposure to alcohol, other prenatal factors and postnatal factors were also considered in this approach.

Finally, in 2005, Chudley et al.[10] published the Canadian Guidelines for Diagnosis of FASD which recommends using a multidisciplinary approach to diagnosis, while harmonizing the IOM classifications and the 4-Digit Diagnostic Code approach. The Canadian Guidelines focus more on the neurobehavioral assessment over growth deficiencies and facial dysmorphology, which we now know do not occur in all children prenatally exposed to alcohol.[11,12] Chudley et al.[10] recommend an extensive assessment of 9 neurobehavioral domains (hard and soft neurological signs – including sensory/motor, brain structure, cognition, communication, academic achievement, memory, executive functioning, attention, and adaptive behaviour). According to the Canadian Guidelines, a neurobehavioral domain is considered to be impaired if scores are at least 2 standard deviations below the mean and/or if a discrepancy of at least 1 standard deviation between sub-domains is documented. A minimum of 3 neurobehavioral domains must be impaired for an FASD diagnosis.

Although both the Canadian Guidelines and 4-Digit Diagnostic Code approach are widely used, few researchers have examined how having a co-morbid ADHD diagnosis impacts the FASD diagnostic process. Numerous studies have reported significant attention problems among children and adolescents with FASD.[13-15] Streissguth, Barr, Kogan, et al.[16] found that 60% of fetal alcohol affected individuals aged 6 to 20 experienced attention related problems, as reported by caretakers. Although there are no national statistics on the concordance rate between FASD and ADHD, Clark et al.[17] found that 65% of their sample of adults with FASD had a co-morbid ADHD diagnosis. Fryer et al.[18] found that 95% of their alcohol-exposed group had ADHD as compared to 30% in their control group. Furthermore, children with ADHD are 2.5 times more likely to have mothers who drank during pregnancy than children without ADHD.[19] Bhatara et al.[20] have reported that rates of ADHD increase according to increased risk of PAE. Theories on the link between PAE/FASD and ADHD include speculations that women with ADHD are at an increased risk for drinking during pregnancy,[21] and that postnatal impairments in bonding and providing adequate care due to maternal substance abuse may be responsible for the link.[20] In addition, the attention impairments in FASD may share a common physiological etiology with ADHD, or ADHD among those with PAE may be due to effects of alcohol on the developing dopaminergic neurotransmitter system.[21] Whatever the cause, the high rates of co-morbidity between FASD and ADHD carry many clinical implications and pose numerous challenges to the accurate diagnosis of both. Children with both FASD and ADHD may be more difficult to treat and may possess a distinctive clinical quality consisting of an earlier onset, inattention subtype with greater psychiatric and medical co-morbidities.[21]

Given the high co-morbidity of ADHD and FASD it is important to understand how having a concurrent diagnosis of ADHD affects the FASD diagnostic process, particularly the pattern of impairment across neurobehavioral domains. In addition to attention problems, children with ADHD also have deficits in many of the neurobehavioral areas that are assessed during an FASD diagnosis including: executive functioning,[22] academic achievement,[23] memory,[24] adaptive behavior,[25] and communication.[26] Thus, in children with FASD and co-morbid ADHD it can be difficult for clinicians to determine whether observed deficits are due to ADHD or FASD. In this study we compared children with FASD with and without a co-morbid ADHD diagnosis to determine the impact of having a co-morbid ADHD diagnosis on the FASD diagnostic results.

METHODS

Participants

Data from 52 children (28 males) who were diagnosed with an FASD through the Glenrose Rehabilitation Hospital FASD Clinical Services using the Canadian Guidelines as a model were reviewed for the study. The mean age was 8.8 years (range 4-17 years). Among these participants with FASD: one child was diagnosed with FAS, 6 with partial FAS, 13 with Neurobehavioral Disorder, and 32 with Static Encephalopathy (according to the 4-Digit Diagnostic Code). Thirty-three of these children

had a co-morbid diagnosis of ADHD and 19 did not. There was no difference in mean age between the children with FASD and ADHD (8.3 years) and those with only FASD (9.6 years), $F(1, 51) = 1.91$, $p > .05$. All children were required to be taking their current medication at the time of the assessment.

Referrals to the clinic must come from the child's managing physician and there must be a history of confirmed prenatal alcohol exposure and reports of dysfunction. We analyzed data for all children diagnosed with an FASD from 2005 to 2008. It was not possible to include a control group of non-exposed children in this study because this was a clinical study on children who had gone through an extensive 1.5 day assessment at a specialized FASD clinic. Thus, we would not be able to include non-exposed control children and put them through the same 1.5 day clinical assessment for many reasons (feasibility, funding, time constraints, availability of the clinic staff, etc.). Also, we were interested in within group analyses among the FASD groups and how an ADHD co-morbidity impacted the FASD diagnosis. All data collected for this manuscript were obtained in compliance with regulations of a University Ethics Review Board.

FASD Diagnosis

The diagnostic process involved assessments conducted by a multidisciplinary team (Psychologist, Speech-Language Pathologist, Occupational Therapist, Social Worker, and Developmental Pediatrician) using a combination of approaches including formal standardized and non-standardized measures, rating scales, interviews, clinical observations, photographic analysis, and information from families, caregivers, preschools, schools, community clinicians, and Child and Youth Services. As recommended by the Canadian Guidelines, the FAS DPN 4-Digit Diagnostic Code was the objective tool used to rank diagnostic categories. The FAS DPN 4-Digit Diagnostic Code consists of a 4-point Likert scale in the areas of growth deficiency, facial features, brain dysfunction, and alcohol-use, along with prenatal (e.g. genetic conditions, exposure to other known teratogens) and postnatal (e.g. abuse, multiple placements) factors which could have impacted outcome.[7] For growth and facial features a code of 1 indicates normal, 2 mild, 3 moderate, and 4 severe. For brain dysfunction a code 1 indicates unlikely, 2 possible, 3 probable, and 4 definite. For alcohol a 1 indicates no risk, 2 unknown, 3 some risk, and 4 high risk. For all participants prenatal exposure to alcohol was confirmed, with alcohol-use scores of 3 (some risk) or 4 (high risk). The clinic coordinator confirmed alcohol exposure prior to acceptance into the clinic. Information pertaining to alcohol was obtained from birth records, Child and Youth Services documentation, from the birth mother directly, or other reliable sources. Except for birth mother report, corroborative evidence of prenatal alcohol exposure was required. Only alcohol scores of 3 and 4 were seen as significant enough to lead to potential brain damage and thus were acceptable for admission into the clinic. Prenatal and postnatal factors were assessed and ranked by the Social Worker and Developmental Pediatrician after an extensive review of prenatal history, birth documents, health records, Child and Youth Services documentation, school records, and caregiver psychosocial interviews on clinic day. This information was then shared with all team members in a team conference format so that all test scores could be interpreted within the context of the child's life and environment. Other differential diagnoses were also carefully considered. For prenatal and postnatal risks, a rank of 1 was equivalent to no risk, 2 to unknown risk, 3 to some risk, and 4 to high risk. Rankings of growth deficiency and facial phenotype were made by a Developmental Pediatrician with training in dysmorphology. Co-morbidities (including ADHD) were diagnosed by a community clinician prior to the child being assessed in the clinic or by the clinical team during the assessment. During the FASD assessment, children are tested on both rating scales and computerized tests of attention to confirm any previous ADHD diagnosis and other mental health problems such as ODD, CD, Anxiety, Depression, or RAD.

Brain rankings were determined by a multidisciplinary assessment across the 9 neurobehavioral domains outlined in the Canadian Guidelines: sensory-motor signs (which may include hard and soft neurological signs), brain structure, communication, attention, cognition, academic achievement, memory, executive functioning, and adaptive behaviour. For a list of tests used in each neurobehavioral domain, see Appendix A. Each neurobehavioral domain was assessed and ranked by the testing clinician during a team conference using a 3-point scale with the following values: 1 = within

normal limits, 2 = mild to moderate impairments, and 3 = significant impairments (a code of 0 was given if it was not assessed or unknown). To be considered significantly impaired on a neurobehavioral domain and receive a score of 3, test results had to fall 2 or more standard deviations below the mean or exhibit a difference of at least 1 standard deviation between sub-domains. Each clinician interpreted their results within the context of other clinician's findings. Care was given to ensure that the impairment in each domain was unique and there was no overlap across domains. Once all domains had been ranked, an overall brain score was assigned based on the level of impairment noted. A functional brain code of 1 indicated no evidence of brain damage, a code of 2 indicated mild to moderate delay of dysfunction, and a brain code of 3 indicated significant dysfunction. A structural brain code of 4 was given to those with definite brain damage as determined by structural evidence, including microcephaly, structural abnormalities on MRI, and/or other hard neurological findings. Criteria for a brain code of 3 (indicative of probable brain damage) required significant impairment across 3 or more of the neurobehavioral domains listed above, while a brain code of 2 (suggesting possible brain dysfunction) was assigned when current data did not support a ranking of 3 or 4, despite strong histories of behavioral and/or cognitive problems. Functional and structural brain codes were separated because, for example, a child could have a structural brain code of 4 and still have a functional brain code of 2. Thus, the team felt it was necessary to separate the structure from function, as they do not measure the same type of dysfunction. Due to young age or other confounding factors, not all children could be assessed across the full range of domains. In these cases, data was not included for these specific areas. The Canadian Guidelines specify that an FASD diagnosis can only be made with a brain code of 3 or 4, unless the child is less than 6 years of age, in which case a brain ranking of 2 can qualify for an FASD diagnosis. However, the 4-Digit Diagnostic Code[7] does include brain rankings of 2 under FASD. Using the Canadian Guidelines as only a model, the Glenrose Rehabilitation Hospital FASD Clinic, using clinical judgment (and according to the DPN 4-digit code), diagnosed an FASD in 10 children with a brain code of 2 who were nevertheless over the age of 6.

RESULTS

Participant demographics are presented in Table 1. Table 2 presents the distribution of scores across the 4-Digit Coding system. The vast majority of children scored a 1 or 2 for growth (93%) and face (87%), but most children scored 4s for prenatal and postnatal factors. Two children (due to etiology other than prenatal alcohol exposure) had brain structural codes of 4; both children also had a functional brain code of 3. Figure 1 shows the mean performance of all children with FASD across the various neurobehavioral domains. We conducted a repeated measures ANOVA across the 8 neurobehavioral domains to determine whether there was a profile among the FASD group. There was a significant effect $F(7, 224) = 6.68$, $p < .001$, in that performance was poorest on communication, attention, and adaptive and executive functioning and best on academic achievement and intellect. Ninety percent of children with FASD had at least one of the co-morbidities listed in Figure 2. The most common co-morbidities were ADHD, Mental Retardation, and sleep abnormalities. Next, we examined how an ADHD co-morbidity impacted performance on the neurobehavioral domains. We compared children with and without an ADHD co-morbidity on each neurobehavioral domain using separate univariate ANOVAs (*see* Figure 3).

TABLE 1 Summary of Participant Demographic Characteristics

Ethnicity	
Aboriginal[a]	35 (67%)
Caucasian	12 (23%)
Other	5 (10%)
Current Placement	
Foster Care	19 (37%)
Birth Parent(s)	13 (25%)
Adopted	11 (21%)
Kinship	9 (17%)
Number of Placements in Lifetime	
1	8 (15%)
2-5	36 (69%)
6 -9	6 (12%)
10 or more	2 (4%)
Foster Placement Ever in Lifetime	
Yes	29 (56%)

[a]Aboriginal included those of Indian, Inuit, or Metis descent. The definition of Metis used for this study was anyone of mixed heritage (i.e. half Aboriginal).

TABLE 2 Percentage of Children with FASD who received each score for the 4-Digit Code

Code	Growth	Face	Brain	Alcohol	Prenatal	Postnatal
4	6%	4%	0	25%	69%	65%
3	2%	10%	73%	75%	31%	19%
2	14%	23%	27%	0	0	2%
1	79%	64%	0	0	0	14%

Note: 1 reflected complete absence of the FASD feature and 4 reflected a strong "classic" presence of the FASD feature. The brain domain contained only brain function scores; there were only 2 children with brain structure codes (all 4s).

FIG. 1 Performance of all Children with FASD across Neurobehavioral Domain

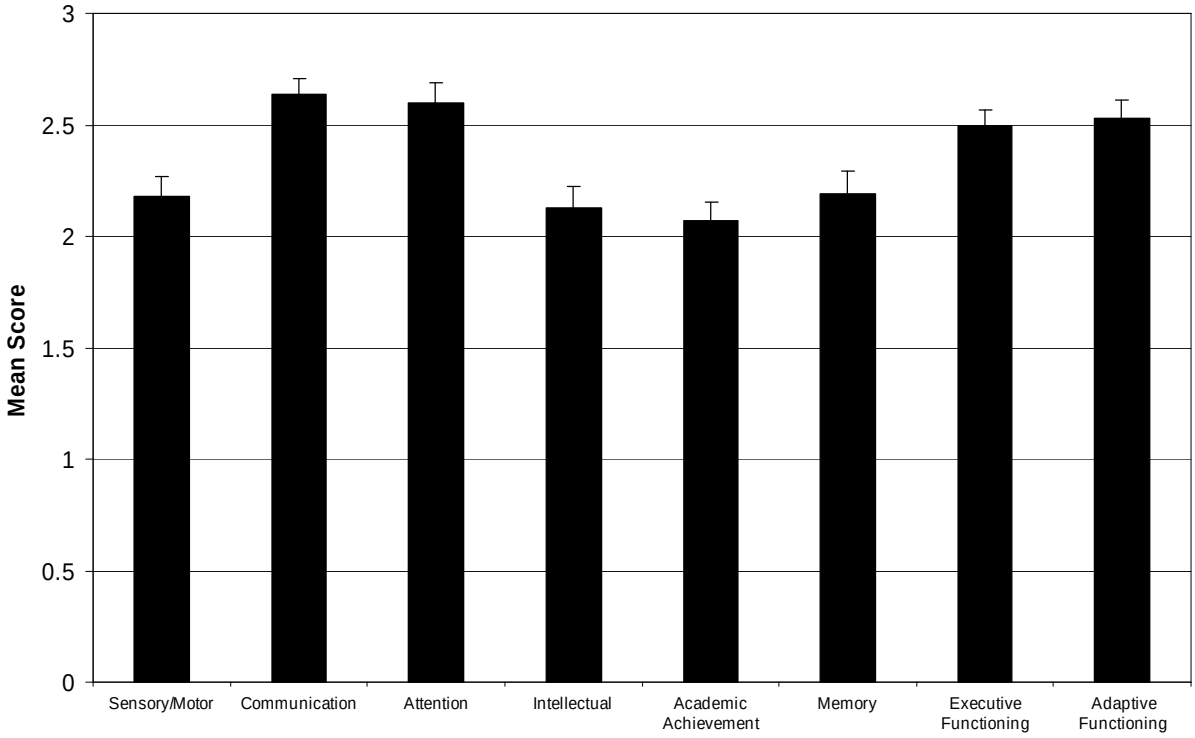


FIG. 2 Percentage of Children with FASD with Different Co-morbidities

Organic brain damage refers to impairments unrelated to PAE, such as cerebral palsy along with multiple and unknown etiologies. Other medical issues included (n): hearing loss/ear dysfunction (6), enuresis (4), atopy (4), premature birth (3), congenital heart defect/heart murmur (3), possible seizures (2), significant dental problems (2), cleft palate, early surgery for misshapen skull, strabismus, myopia, tumour, generalized hyptonia, Steven-Johnson Syndrome, gastroesophageal reflux, encopresis.

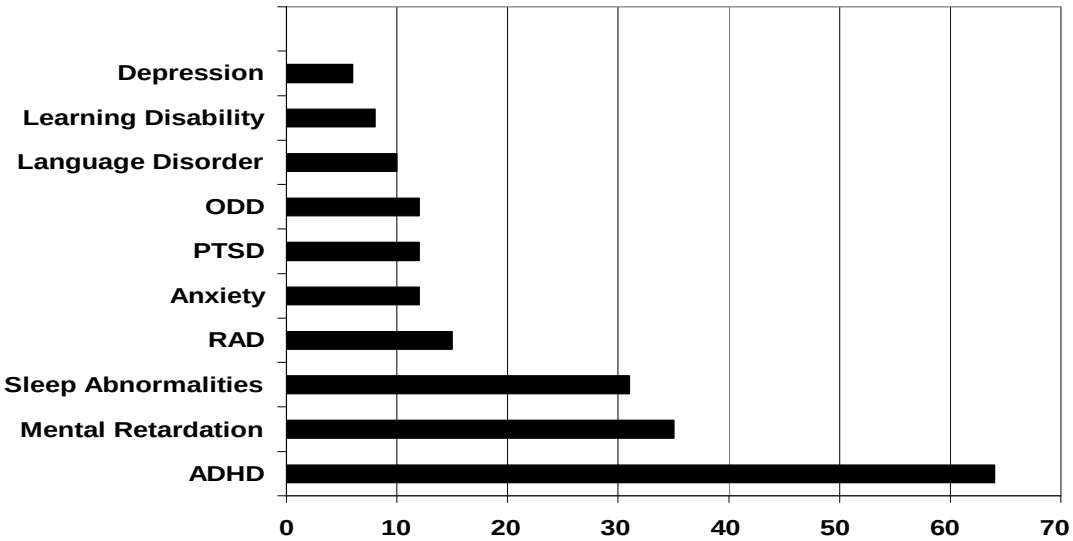
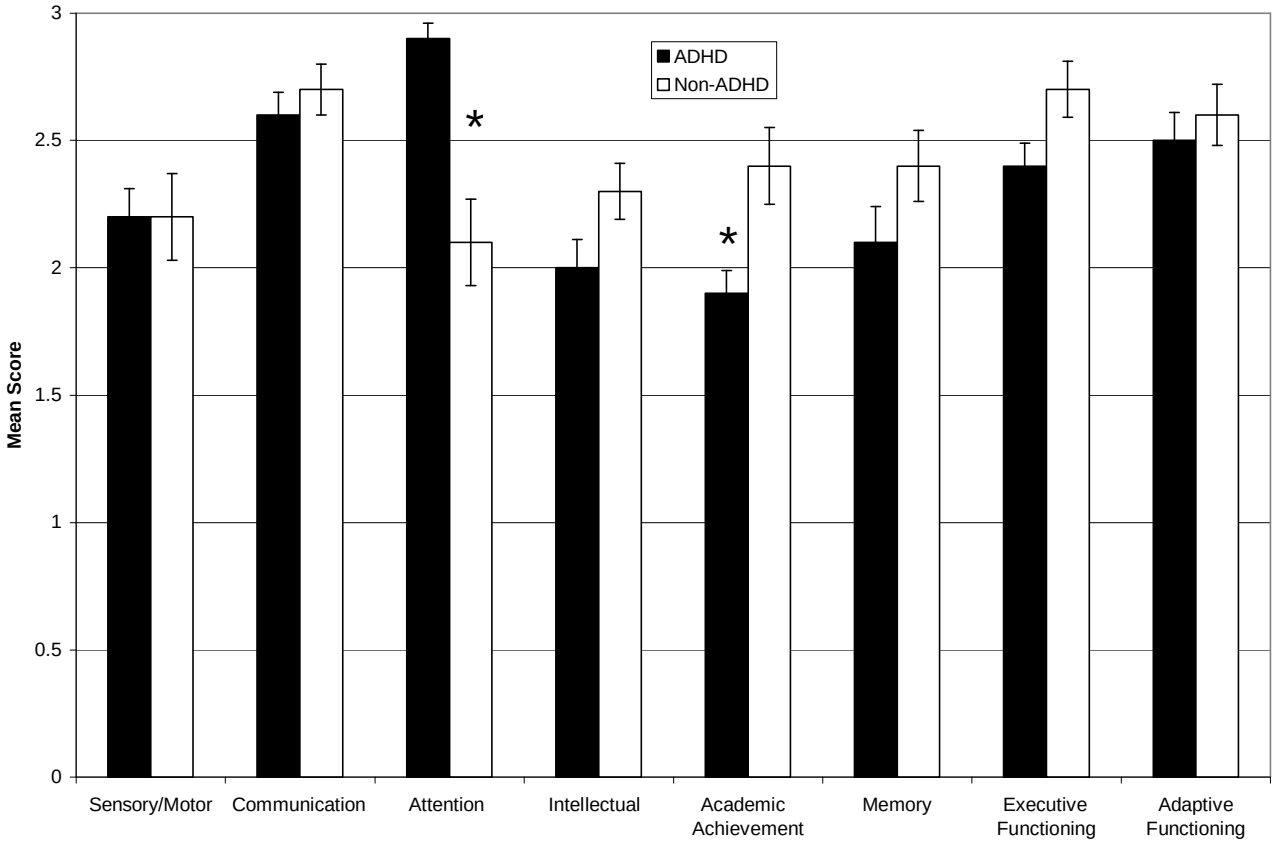


FIG. 3 Mean score on each neurobehavioral domain for children with FASD with and without an ADHD co-morbidity.



Note: Bars represent standard errors. Higher scores indicate more impairment. *$p < .05$.

Children with FASD and ADHD performed significantly worse than those without ADHD on attention, $F(1, 49) = 28.57$, $p < .01$, $\eta_p^2 = .37$, but better on academic achievement $F(1, 43) = 10.11$, $p < .01$, $\eta_p^2 = .19$. No other group differences were significant (all *p*s > .05). As would be expected, significantly more children with FASD and co-morbid ADHD (42%) were currently taking ADHD medication as compared to those with only FASD (5%), χ^2 (1) = 8.11, p < .01. The most common ADHD medication was Dexedrine but others included Ritalin, Strattera, Chlonidine, and Concerta.

DISCUSSION

The goal of this study was to examine the impact of having a co-morbid ADHD diagnosis on FASD diagnostic results. We compared children with FASD to those with FASD and co-morbid ADHD across the neurobehavioral domains recommended by the Canadian Guidelines for the diagnosis of FASD.

Very few of the children diagnosed with FASD exhibited the growth deficiencies and facial anomalies classically associated with FAS, which is consistent with previous research.[11] Streissguth's[27] 25-year longitudinal study found that alcohol's effects on growth parameters were transient and indistinguishable by 18 months of age. In addition, similar neurobehavioral profiles have been delineated across all sub-types of FASD, regardless of facial dysmorphology.[28,29] The majority of children with FASD scored poorly on pre- and postnatal factors, highlighting the significant pre- and postnatal factors that may impact a diagnosis.

Overall, among all children with FASD, there was a significant difference across the neurobehavioral domains. Children with FASD were most likely to be impaired on communication, attention, adaptive functioning, and executive functioning. These findings are consistent with numerous previous studies indicating that children with PAE and/or FASD have significant deficits in attention,[13-15] communication,[30,31] adaptive functioning,[32] and executive functioning.[33] However, children with FASD were least likely to be impaired on academic achievement and intellect, indicating that these may be relative strengths for these children and therefore may be of less importance in the assessment as compared to more affected domains.

An alarming 90% of children with FASD had at least one co-morbidity, with ADHD being the most common. The high rates of psychopathology observed in this study are compatible with the numbers reported by several other investigations.[34-36] In particular high rates of behavioural diagnoses such as Conduct Disorder and Oppositional Defiant Disorder have been described for this population, and linked to the over-representation of these individuals in the justice system.[18] Further study into this area could reveal whether these diagnoses are an appropriate representation of those affected by FASD, or instead reflect shared symptomology but lack an appreciation of the underlying brain dysfunction. Consequences of diagnosing behavioural disorders may include stigmatization as intentionally bad children, and also may lead to programming that is geared towards behavioural remediation without appreciation for underlying brain dysfunction. Sleep abnormalities were also very common among children with FASD. Sleep disorders are a common issue for individuals with FASD,[36] and (at least in animals with PAE) may be related to a disrupted circadian rhythm.[37,38] These findings underscore the importance of exploration of these issues within the diagnostic process, looking beyond the FASD diagnosis alone to other factors that might impact functioning and direct interventions.

More than half of the children with FASD (63%) had a co-morbid diagnosis of ADHD. However, there were very few differences on the neurobehavioral domains between children with FASD and those with FASD and ADHD. Not surprisingly, children with FASD and ADHD were more impaired on the attention domain than those with FASD. However, children with ADHD and FASD performed significantly better than those with FASD on academic achievement. Thus, it does not appear that having a co-morbid ADHD diagnosis resulted in more domains being impaired that could be attributed to ADHD and not FASD (other than attention which would be expected). Academic achievement was higher among those with FASD and ADHD perhaps because these children received extra supports in school due to their co-morbid ADHD diagnosis, or possibly because more were taking ADHD medication. The finding that the FASD and ADHD group were more impaired *only* on attention indicates that having a co-morbid ADHD diagnosis may not bias the FASD diagnostic results and that the two disorders are separable. Furthermore, research indicates that the pattern of executive functioning[39] and attention deficits is different among children with ADHD and those with FASD, indicating that the two disorders may result from different neurocognitive deficits.[40] Coles et al.[40] compared children with FAS/FAE and children with ADHD from the similar SES and ethnic backgrounds on a battery of cognitive and behavioral measures of attention. The children with FAS/FAE and ADHD had similar intellectual scores, however, they displayed very different profiles of attentional deficits on Mirsky's model of attention. Moreover, behavioral reports as measured by parent and teacher questionnaires showed that children with FASD were less impulsive and displayed less behavior problems. Thus, although both children with FAS/FAE and ADHD are characterized by having attention deficits, the types of attention deficits the two groups of children display are quite different, and both groups have a unique attention profile. Furthermore, Vaurio et al.[39] found that although both children with PAE and those with ADHD had executive function deficits, the pattern and degree of deficits was quite different between the two groups, which may inform differential diagnosis. These results have implications for the assessment of attention and the use of stimulants within the FASD population. In our study, 29% of the entire sample was currently on ADHD medication. However, there is

some evidence that psychostimulants may actually worsen the clinical situation for children with FASD.[21,40] Differential responses have been observed between different stimulants, and thus some may be more effective within the FASD population than others.[41] Overall, these findings elucidate the importance of accurate diagnosis and differentiation of ADHD and FASD, which in turn will facilitate the appropriate implementation of interventions according to functional needs.

Despite the significance and importance of these findings, some limitations must be noted. This study was a retrospective chart review of clinically-referred children who had gone through an extensive FASD assessment. Thus, referral bias may exist in this sample and our results may not be entirely generalizable to all children with FASD. We were also not able to examine group differences on specific tests and measures within a domain (as the clinic uses a variety of tests in each domain); rather we examined group differences on each neurobehavioral domain. Due to the large age range in our study, different tests may have been used at different ages to measure the same construct within a neurobehavioral domain. Furthermore, the proportion of Aboriginal children in our study may not be generalizable to the entire FASD population. Finally, significantly more children with FASD and co-morbid ADHD were taking ADHD medication than those with only FASD which may affect the pattern of performance on some measures.

The results of this study highlight the importance of considering the impact of attention in ranking the neurobehavioral domains. In assessing for FASD, clinicians cannot assume that a child prenatally exposed to alcohol who has attention difficulties is therefore FASD. The lack of differences between children with FASD and those with FASD and co-morbid ADHD provides evidence that the current model of team-based clinical assessment of FASD is sufficiently sensitive to detect differences between ADHD and FASD in testing, and identify impairment specific to FASD.

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APPENDIX A

Neurobehavioral Domain	Tests Used to Assess
Sensory/Motor	The Sensory Profile Adolescent/Adult Sensory Profile Short Sensory Profile Bruininks-Oseretsky Test of Motor Proficiency – Second Edition Movement Assessment Battery for Children – Second Edition (Movement ABC-2)
Communication	Clinical Evaluation of Language Fundamentals – Fourth Edition (CELF-4) Clinical Evaluation of Language Fundamentals – Preschool, Second Edition (CELF-P:2) Coggins Mental State Reasoning Tasks Comprehensive Assessment of Spoken Language (CASL) Expressive Language Test (ELT) Expressive Vocabulary Test – Second Edition (EVT-2) Mercer Mayer Wordless Story Books (Retell, Generate, Comprehension) Oral and Written Language Scales (OWLS) Peabody Picture Vocabulary Test – Fourth Edition (PPVT-4) Preschool Language Assessment Instrument – Second Edition (PLAI-2) Renfrew Bus Story – American Edition Test of Language Competence – Expanded Edition (TLC-E) Test of Language Development – Primary, Third Edition (TOLD-P:3) Test of Narrative Language (TNL) Test of Problem Solving 2 – Adolescent (TOPS-2 A) Test of Problem Solving – Third Edition (TOPS-3) Test of Word Knowledge (TOWK)
Attention	Behavior Assessment System for Children – Second Edition (BASC-2) Conners Rating Scales – Revised (CRS-R) Continuous Performance Test (CPT)
Intellect	Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV) Test of Nonverbal Intelligence – Third Edition (TONI-3)
Academic Achievement	Wechsler Individual Achievement Test – Second Edition (WIAT-II) or Wide Range Achievement Test – Fourth Edition (WRAT-4)
Memory	Children's Auditory Verbal Learning Test (CAVLT) Rey Complex Figure Test (also in EF) Memory subtests from the NEPSY-II
Executive Function	NEPSY – Second Edition (NEPSY-II) Behavior Rating Inventory of Executive Function (BRIEF)
Adaptive Function	Adaptive Behavior Assessment System – Second Edition (ABAS-II)
Brain Structure	Head circumference for microcephaly, MRI, EEG as indicated clinically

Not all children would receive every test on the list, or each test listed in each domain. Measures used are primarily selected from this list of tools. Not all tests are used in their entirety and measures are selected based on individual needs.
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