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Factors predictive of a fetal alcohol spectrum disorder: Neuropsychological assessment

Leah N. Enns[a,b] and Nicole M. Taylor[a,b]

[a]Department of Clinical Health Psychology, University of Manitoba, Winnipeg, Canada; [b]Manitoba FASD Centre, SSCY Centre, Winnipeg, Canada

ABSTRACT

A variety of neurodevelopmental impairments related to fetal alcohol spectrum disorder (FASD) diagnoses have been consistently documented. However, it is not clear whether such variables are predictive of a diagnosis. The purpose of the present study is to use logistic regressions to identify predictors of FASD in neuropsychological assessment. Charts of 180 children and adolescents with prenatal alcohol exposure (PAE) who underwent psychological and diagnostic assessment for FASD were retrospectively reviewed. A total of 107 received an FASD diagnosis (the PAE-FASD group) and 73 did not (the PAE group). Following preliminary analyses, direct logistic regressions were performed to assess the contribution of different neuropsychological testing measures on the likelihood of a child or adolescent receiving an FASD diagnosis. The results indicate that the classification accuracy of the PAE-FASD and PAE groups is clinically significant across models of intelligence, academic achievement, memory, and executive functioning. Classification rates across the various models range from 67.1% to 75.5%, with models incorporating 10 intelligence subtests or 3 academic subtests emerging as superior to those using broad indices of intelligence and/or individual subtests of memory or executive functioning. A "test battery" model incorporating verbal intelligence, verbal/auditory working memory (digit span), basic reading and spelling skills, math calculations, delayed story recall, and spatial planning and problem-solving yielded a classification rate of 74.7%. These results suggest that neuropsychological testing is a critical component of FASD assessment and help guide decisions to maximize the efficiency and efficacy of the diagnostic process and treatment recommendations.

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Fetal alcohol spectrum disorder (FASD) is a heterogeneous disorder that is the leading cause of preventable developmental disabilities. The term FASD represents a spectrum of disorders, all of which include gestational exposure to alcohol and subsequent central nervous system (CNS) damage or dysfunction (Paley & O'Connor, 2011), but vary according to the presence and degree of physical manifestations of the disorder (Astley,

CONTACT Nicole M. Taylor ntaylor@hsc.mb.ca Manitoba FASD Centre, SSCY Centre, 1155 Notre Dame Avenue, Winnipeg, MB R3E 3G1
The supplemental data for this article can be accessed here.

2004; Astley & Clarren, 2000; Chudley et al., 2005; Cook et al., 2016; Hoyme et al., 2005; Stratton, Howe, & Battaglia, 1996). CNS dysfunction is measured using indicators including—but not limited to—intelligence, mastery of academic skills, memory, and aspects of executive functioning (Chudley et al., 2005; Cook et al., 2016; Senturias & Burns, 2014). It is estimated that approximately 10% of women in Canada and 15% of women in the United States (US) consume alcohol during pregnancy, with 3% across both countries engaging in binge drinking during pregnancy (Popova, Lange, Probst, Parunashvili, & Rehm, 2016). Among the general population, FASD is estimated to affect 1–2% of individuals worldwide (Roozen et al., 2016), and 1–3% of Canadians and Americans (Health Canada, 2006; Popova et al., 2016; Roozen et al., 2016). These rates are higher among suspected high-prevalence subpopulations, such as for children in care (Roozen et al., 2016). While new Canadian diagnostic guidelines were released in 2016 (Cook et al., 2016), the present study is based on the 2005 Canadian guidelines and its classifications (Chudley et al., 2005). In this system, children who meet some or all of the physical indicators of the disorder as well as CNS dysfunction are diagnosed with fetal alcohol syndrome (FAS) or partial fetal alcohol syndrome (pFAS). Children who do not meet the physical criteria but present with CNS dysfunction are diagnosed with alcohol-related neurodevelopment disorder (ARND).

FASD has lasting physical, mental, behavioral, and/or learning ability consequences for affected individuals (Senturias, 2014). Children with FASD have been shown to demonstrate a variety of impairments in the realms of intelligence, language and communication, memory, academic achievement, visual perception and construction, executive functioning, adaptive and social functioning, social cognition, motor skills, and attention and emotional regulation, and to exhibit a range of maladaptive and clinically significant behavior problems (for reviews, see Kodituwakku, 2009; Mattson, Crocker, & Nguyen, 2011; Vaurio, Crocker, & Mattson, 2010). Given that the vast majority of individuals affected by prenatal alcohol exposure (PAE) do not manifest the physical characteristics of the disorder (i.e., FAS or pFAS; Rasmussen, Horne, & Witol, 2006; Sampson, Streissguth, Bookstein, & Barr, 2000), the establishment of a neuropsychological profile of FASD would contribute to more accurate diagnoses and subsequent implementation of individualized treatments and interventions appropriate for each child and his or her family.

Numerous studies have been undertaken to ascertain whether PAE is associated with a particular set of neurodevelopmental or neurobehavioural dysfunctions (Aragón, Coriale, et al., 2008; Aragón, Kalberg, et al., 2008; Mattson et al., 2010, 2013; Nash et al., 2013; Quattlebaum & O'Connor, 2013; Stevens et al., 2013) and whether a particular constellation of impairments is unique to an FASD diagnosis (Glass et al., 2014; Kingdon, Cardoso, & McGrath, 2015; Raldiris, Bowers, & Towsey, 2014; Vaurio et al., 2010). Many of these investigations have employed means-comparison approaches to examine differences among: (1) FASD groups (e.g., FAS, pFAS, ARND), (2) FASD groups and non-alcohol-exposed controls, and (3) PAE groups and non-alcohol-exposed controls (Aragón, Kalberg, et al., 2008; Mattson et al., 2010, 2013; Nash et al., 2013; Quattlebaum & O'Connor, 2013; Rasmussen et al., 2006; Stevens et al., 2013). For instance, Rasmussen et al. (2006) measured cognitive and memory functioning in a sample of 50 Canadian children with PAE. When compared against age-based norms, children with PAE showed weaknesses across many elements of

intelligence, memory, auditory attention and speed of mental processing. Further mean comparisons of the differences between children identified as having "possible" brain dysfunction to those having "probable" brain dysfunction revealed lower scores on tests of overall intelligence, verbal intelligence, auditory attention and visual memory for faces in the latter, more impaired group. Other studies comparing children with FAS and pFAS to non-exposed control children have noted impairments in overall intellectual functioning, nonverbal reasoning, language comprehension, executive functioning (e.g., verbal fluency, planning), and memory functioning (Aragón, Coriale, et al., 2008; Aragón, Kalberg, et al., 2008). Similar results are reported by Quattlebaum and O'Connor (2013), who compared the performance of children with FASD (FAS, pFAS, ARND) against non-exposed control children and found impaired working and visuospatial memory, language abstraction, and social cognition among the children with FASD. These studies provide strong confirmation of the deleterious effects of alcohol on the developing brain in utero and provide some indication of the types of measures that may prove most fruitful in diagnostic assessment.

In another line of research, comparisons were made between children with PAE who received an FASD diagnosis to those who did not (Nash et al., 2013). This type of comparison has several advantages: first, it enables examination of whether and what differences exist amongst a group of children with PAE, only some of whom meet a diagnostic threshold of impairment according to Canadian diagnostic guidelines. Second, by virtue of the fact that both groups under investigation have PAE, there is a greater likelihood that other environmental variables (e.g., prenatal nutrition, pre- and post-natal stressors, etc.) are equalized among the groups. This was indeed the case in the study conducted by Nash et al. (2013) wherein no differences emerged among the groups on a number of such environmental variables (number of placements, socioeconomic status, other prenatal exposures). These findings reveal a profile of weaker overall intelligence, verbal reasoning, memory (general memory and spatial memory following a long delay), language functioning, and math reasoning and calculation in the group diagnosed with FASD. Thus, a pattern of functioning can be seen that distinguishes those who meet criteria for neurodevelopmental impairment associated with PAE (i.e., an FASD diagnosis) versus those who do not, particularly when both groups have had equivalent exposure histories. What is less clear, however, is whether any specific measures are especially helpful for diagnostic formulation—that is, while these and previous studies have shown that a number of neurodevelopmental impairments are *related* to an FASD diagnosis based on mean comparisons, are any of these findings *predictive* of an FASD diagnosis?

The Present Study

The objective of the present study is to use logistic regressions to determine whether any of the variables in an extensive neuropsychological battery are predictive of an FASD diagnosis (FAS/pFAS/ARND vs. no diagnosis) in a group of children and adolescents with PAE. As noted above, previous studies have primarily relied on comparing group means, which limits their ability to make diagnostic predictions. In a different approach, Mattson et al. (2010, 2013) used logistic regressions to show that a model that incorporates a number of tests of executive functioning, attention, spatial

learning and memory, fine motor speed, and visual-motor integration can be used to distinguish (a) children with FAS/pFAS from non-exposed controls and (b) non-dysmorphic children with PAE (ARND or no diagnosis) from non-exposed controls. However, these researchers failed to directly compare PAE groups with and without an FASD diagnosis, which is the aim of the present study (PAE-FASD vs. PAE). Given that in most cases a diagnosis of FASD requires confirmation of PAE, plus the fact that the majority of children do not show the physical manifestations of the disorder, the reliance on careful examination of neurodevelopmental functioning is essential and thus requires further research. As no single indicator or profile has emerged as pathognomonic to FASD, and given the considerable overlap that can be seen behaviorally with other developmental disorders—e.g., attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD; for a review of the difficulties inherent to an FASD diagnosis, see Benz, Rasmussen, & Andrew, 2009)—the objective of the present study is to provide unique information about the neuropsychological measures that contribute most toward diagnosis in FASD. Ultimately, the primary goal of the present study is to inform clinical assessment in efforts to streamline testing and increase diagnostic clarity.

Method

Participants

All participants were clinic-referred children at the Manitoba FASD Centre in Manitoba, Canada, who were required to have a confirmed history of PAE. Confirmation of alcohol exposure was made using the 2005 Canadian guidelines (Chudley et al., 2005), the 4-Digit Diagnostic Code developed at the University of Washington (Astley, 2004, 2006), and the clinical expertise of the Centre's multidisciplinary team members, including a developmental pediatrician, a clinical psychologist, a speech and language pathologist, an occupational therapist, social workers, and FASD coordinators. Factors examined include—but are not limited to—the quantity, timing, frequency, and certainty of exposure, the reliability of the informants, other exposures (e.g., marijuana, cocaine), and whether or not siblings have also been diagnosed. Between 2010 and 2014, 180 children and adolescents aged 5.83–17.83 years attended the clinic. Each of the participants of the present study had psychology involvement (e.g., neuropsychological assessment, interpretation of questionnaires, and/or involvement in the diagnostic clinic). Out of the 180 children and adolescents with PAE assessed, 107 (59.5%) received an FASD diagnosis (PAE-FASD group mean age = 10.10 years, *SD* = 3.23, range = 5.83–17.83, 63% male) and 73 (40.5%) did not receive an FASD diagnosis (PAE group mean age = 9.87 years, *SD* = 2.98, range = 6.25–17.83, 52% male). Of those diagnosed, 97 (90.7%) received a diagnosis of ARND, 10 (9.3%) received a diagnosis of pFAS, and 0 (0%) received a diagnosis of FAS. Of the children who did not receive a diagnosis, 2 were deferred (2.7%). The diagnostic assessments were conducted by a multidisciplinary team consisting of a clinical psychologist, a developmental pediatrician, a geneticist, a speech and language pathologist, an occupational therapist, and a social worker. Data were collected using a combination of standardized and non-standardized measures, including standardized tests, caregiver

and teacher rating scales, interviews, clinical observations, and developmental history. Diagnoses were made using the Canadian Guidelines (Chudley et al., 2005), which follows Astley's 4-Digit Diagnostic Code (Astley, 2004, 2006).

The purpose of the psychology assessment was to evaluate the domains of intellectual functioning, academic achievement, memory, attention, executive functioning, and adaptive functioning. Data on socio-emotional functioning was also gathered at that time. Information was collected through formal neuropsychological testing, as well as caregiver and/or teacher questionnaires. For the purpose of the present study, objective measures of intelligence, academic achievement, memory and executive functioning were analyzed. In line with the Canadian guidelines (Chudley et al., 2005), scores were either 2 *SD*s below the mean or there was a difference of 1 *SD* between indices within a domain (e.g., the verbal comprehension and perceptual reasoning indices as assessed for the intellectual functioning domain) to meet criteria for significant impairment. To receive an FASD diagnosis, children and adolescents were required to meet criteria in at least three of the domains assessed.

Materials and Procedures

Data were gathered retrospectively via chart review. Ethics approval for this retrospective chart review was obtained from the University of Manitoba Bannatyne Campus Human Research Ethics Board (HREB). During the intake and referral process, all caregivers (i.e., parents or legal guardians) provided signed informed consent for all pre-assessments and the final diagnostic assessment. Although all 180 children were administered a number of the same standardized tests, not all completed every test due to age constraints, level of functioning, having completed previous psychology assessments, time, or testing fatigue. Therefore, only subsets of the total number of children were analyzed depending on the number of tests that were completed. For those children who had previous assessments that were recent enough that they did not require reassessment, raw and standard scores were obtained and used in the present analyses.

Demographic Information

Caregivers of the children and adolescents assessed at the Manitoba FASD Centre completed a general information form—a questionnaire created by the Centre to help plan for assessment during the intake process. If child protective services (Manitoba Child and Family Services) were involved, a social history form was also completed. The general information form provides basic demographic information, including child age and sex, family structure, developmental history, exposure to alcohol and other toxins, and stressful or adverse life events the child has experienced or witnessed (e.g., upsetting losses or changes, family conflict and stress, extended separation from primary caregiver). The social history form provides additional details regarding stressful or adverse life events the child has experienced or witnessed (e.g., physical, emotional, and sexual abuse and neglect, family violence, abandonment).

Tests of Intellectual Functioning

The intelligence domain was assessed using the Wechsler intelligence scales, which were administered individually to obtain overall intelligence profiles of 177 children and adolescents assessed at the Centre. Canadian norms were used. Standard scores have a mean of 100 and an *SD* of 15, while subtests have a mean of 10 and an *SD* of 3. Standard scores above 110 are in the above average range, scores of 90–110 are in the average range, scores of 80–89 are in the low average range, scores of 70–79 are in the borderline range, and scores below 70 are in the extremely low range. A total of 167 of the children and adolescents were assessed using the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2003), a standardized measure of general intelligence for children aged 6 to 16 years across four indices: the Verbal Comprehension Index (VCI), the Perceptual Reasoning Index (PRI), the Working Memory Index (WMI), and the Processing Speed Index (PSI). A full-scale IQ (FSIQ) score is also provided. To assess intellectual functioning in the older adolescents, 7 participants were evaluated using the Wechsler Adult Intelligence Scales – Fourth Edition (WAIS-IV; Wechsler, 2008), which provides the same four indices and an FSIQ score. The remaining 3 participants were assessed using the Wechsler Preschool and Primary Scale of Intelligence – Third Edition (WPPSI-III; Wechsler, 2002). Based on the children's ages, they were assessed using the standardized tests for the age range 4 years to 7 years and 3 months. The WPPSI-III provides an FSIQ, a Verbal composite score and a Performance (i.e., nonverbal) composite score. A Processing Speed composite score is also provided, although not included in the FSIQ. Given the small number of participants who completed the WPPSI-III and WAIS-IV, as well as the theoretical and statistical commonalities underlying the indices across tests (Wechsler, 2003), the verbal and performance composite scores from the WPPSI-III were incorporated into the VCI and PRI used in the WISC-IV and WAIS-IV.

Tests of Academic Achievement

The academic achievement domain was assessed using the Wechsler Individual Achievement Test – 2nd Edition (WIAT-II; Wechsler, 2005), the Wechsler Individual Achievement Test – 3rd Edition (WIAT-III; Wechsler, 2009a), or the Wide Range Achievement Test – 4th Edition (WRAT4; Wilkinson & Robertson, 2006). All tests have a mean of 100 and an *SD* of 15. Canadian norms were available and used for the WIAT-II and WIAT-III, which feature subtests that tap into basic academic skills including sight word reading, word decoding, reading comprehension, spelling, math computational skills, and math problem-solving skills. Similarly, the WRAT-4 measures reading skills, math skills, spelling, and comprehension. A total of 170 children and adolescents completed at least one subtest assessing academic achievement: 27 completed subtests from the WIAT-II, 85 from the WIAT-III, and 58 from the WRAT-4. Given the theoretical and statistical support in the literature regarding similarities between the reading, spelling, and math tests on the WIAT (Wechsler, 2009b) and the WRAT (e.g., Smith & Smith, 1998), the scores from the Spelling, Word Reading, and Numerical Operations/Mathematical Composite (referred to as "Math Calculations") subtests from the WIAT-II, the WIAT-III and the WRAT-4 were combined.

Tests of Memory

A total of 170 of the children and adolescents who underwent an FASD assessment completed one or more memory tests. These include the Children's Memory Scale (CMS; Cohen, 1997), the California Verbal Learning Test – Children's Version (CVLT-C; Delis, Kramer, Kaplan, & Ober, 1994), the NEPSY-II (Korkman, Kirk, & Kemp, 2007), and the Wechsler Memory Scales – 4th Edition (WMS-IV; Wechsler, 2009c). Components of the CMS were administered to 160 children and youth. The CMS yields eight index scores: Visual Immediate, Visual Delayed, Verbal Immediate, Verbal Delayed, General Memory, Attention/Concentration, Learning, and Delayed Recognition. Index scores have a mean of 100 and an *SD* of 15, ranging from 50 to 150. Individual subtests examined as part of the present study include scores from Immediate and Delayed Dot Locations and Faces (visual memory), as well as Stories and Word Pairs or Word Lists (verbal memory recall and recognition). Individual subtests have a mean of 10 and an *SD* of 3. The CVLT-C was administered to assess learning, immediate and delayed recall, and delayed recognition of a list of words, with *z*-scores used to evaluate performance. Only 2 participants were assessed using the CVLT-C, while 66 participants completed the Memory for Designs (immediate and delayed) and Memory for Faces (immediate and delayed) subtests from the NEPSY-II. Finally, the WMS-IV was designed to assess various aspects of memory in older adolescents and adults, which are described using standard scores based on indices of Immediate Memory, Delayed Memory, Verbal Memory, and Visual Memory. A total of 6 of the adolescents assessed at the FASD Centre completed the WMS-IV. Memory indices and subtests common between the CMS, the NEPSY-II and the WMS-IV were combined as follows: Faces (CMS and NEPSY-II), spatial memory (CMS Dot Location Total Score and NEPSY-II Spatial Score), Stories (CMS and WMS-IV), and word list learning (CMS Word Pairs, CMS Word List, CVLT-C List A Trial 5 Free Recall, and WMS-IV Verbal Paired Associates).

Tests of Executive Functioning

Aspects of executive functioning were assessed using the Delis–Kaplan Executive Functioning System (D-KEFS; Delis, Kaplan, & Kramer, 2001) and the NEPSY-II (Korkman et al., 2007). Subtests from the D-KEFS (Trail Making Test, Verbal Fluency, Color-Word Interference Test, Tower Test) were administered individually to children and adolescents 8 years of age and older to assess verbal and nonverbal components of executive functioning skills, including inhibition, cognitive flexibility, fluency, and planning and problem-solving. The 6- to 7-year-olds children were administered the Inhibition subtest from the NEPSY-II to assess verbal inhibition and cognitive flexibility. Subtests on both the D-KEFS and the NEPSY-II have a mean scaled score of 10 and an *SD* of 3. Scores from the Color-Word Interference Test from the D-KEFS and the Inhibition subtest from the NEPSY-II were combined.

Data Analysis

The means, *SD*s, and ranges for the demographic information and assessment measures per group (PAE-FASD and PAE) are presented in Table 1. All data are standardized to a common metric and were analyzed using IBM SPSS v22 (IBM

Table 1. Means, *SD*s, and Range or Percentage of Sample within a Demographic Variable for FASD and Non-FASD groups.

	FASD Group			Non-FASD Group		
Domain	*n*	Mean (*SD*)	Range or %	*n*	Mean (SD)	Range or %
Demographic Information						
Age (years)	107	10.10 (3.23)	5.83–17.83	73	9.87 (2.98)	6.25–17.83
Sex	107	0.37 (0.49)	62.6% males	73	0.48 (0.50)	52.1% males
ADHD Diagnosis	107	0.56 (0.50)	56.1%	73	0.70 (0.46)	69.9%
Additional Diagnosis	107	0.72 (0.45)	72.0%	73	0.78 (0.42)	78.1%
Stressors/Adverse Life Events	105	3.16 (2.92)	0–11	73	4.44 (3.22)	0–11
Placement	107	1.69 (1.19)	Foster care (67.3%) Birth family (11.2%) Adoptive family (12.1%) Extended family (6.5%) Group home (2.8%)	73	1.75 (1.21)	Foster care (63.0%) Birth family (15.1%) Adoptive family (11.0%) Extended family (8.2%) Group home (2.7%)
Intelligence						
Indices						
Full-Scale IQ (FSIQ)	103	77.62 (11.75)	41–108	71	88.45 (9.84)	70–116
Verbal Comprehension Index (VCI)	104	75.44 (13.17)	47–104	71	86.90 (10.06)	65–116
Perceptual Reasoning Index (PRI)	103	88.92 (14.17)	52–128	71	97.01 (12.78)	70–126
Working Memory Index (WMI)	101	78.02 (12.29)	52–117	71	87.69 (11.14)	68–117
Processing Speed Index (PSI)	103	85.48 (14.41)	41–115	71	93.11 (13.40)	65–123
Subtests						
Similarities	102	5.78 (2.94)	1–12	70	7.90 (2.50)	2–15
Vocabulary	103	5.60 (2.39)	1–12	70	7.60 (2.10)	4–15
Comprehension	99	5.61 (2.61)	1–12	66	7.53 (2.11)	2–13
Block Design	103	8.22 (2.75)	1–15	70	9.44 (2.84)	4–16
Matrix Reasoning	103	8.27 (2.83)	2–16	70	9.13 (2.83)	4–15
Picture Concepts	101	8.13 (3.16)	1–16	66	9.98 (2.55)	1–15
Digit Span	99	6.33 (2.75)	1–14	70	8.19 (2.46)	3–15
Letter-Number Sequencing	97	6.04 (2.75)	1–13	66	7.74 (2.45)	1–13
Coding	101	7.29 (3.11)	1–15	70	8.36 (2.54)	3–16
Symbol Search	101	7.37 (2.79)	1–13	70	9.19 (2.75)	3–15
Academic Achievement						
Spelling	99	79.44 (15.63)	41–112	68	92.65 (10.93)	53–116
Reading Comprehension	48	74.44 (12.94)	50–113	34	86.26 (9.49)	64–105
Word Reading	94	80.66 (15.58)	40–128	66	92.38 (12.73)	52–121
Pseudoword Decoding	53	79.92 (12.73)	64–117	40	92.35 (14.86)	59–117
Math Problem-Solving	59	78.19 (14.17)	44–115	44	87.50 (12.41)	59–128
Math Calculations	100	75.70 (11.40)	52–106	68	88.04 (11.16)	62–120

(*Continued*)

Table1. (Continued).

	FASD Group			Non-FASD Group		
Domain	*n*	Mean (*SD*)	Range or %	*n*	Mean (SD)	Range or %
Sentence Comprehension	33	85.76 (10.99)	58–109	21	96.33 (10.66)	77–115
Reading Composite	31	85.13 (12.03)	61–108	21	94.38 (11.43)	74–116
Memory						
Indices						
Immediate Visual Index	59	92.76 (13.97)	50–118	33	97.79 (15.69)	69–128
Delayed Visual Index	58	93.50 (14.17)	57–118	33	99.45 (15.32)	57–125
Immediate Verbal Index	88	79.75 (16.06)	50–122	65	94.78 (14.84)	50–134
Delayed Verbal Index	85	80.65 (16.25)	50–118	64	96.59 (15.37)	60–131
Delayed Recognition Index	86	84.07 (20.25)	50–118	63	99.30 (12.07)	69–125
General Memory Index	54	81.11 (17.33)	50–120	32	94.22 (19.51)	66–137
Subtests						
Faces: Immediate	94	8.33 (3.28)	1–17	64	9.23 (2.80)	2–15
Faces: Delayed	92	8.10 (2.99)	1–17	64	9.36 (3.17)	1–17
Spatial Location: Immediate	95	9.28 (3.43)	1–15	69	9.88 (3.12)	3–16
Spatial Location: Delayed	93	9.65 (3.29)	2–15	68	10.47 (2.75)	5–14
Designs Content: Immediate	35	7.60 (3.11)	2–14	36	8.25 (2.98)	2–14
Designs Content: Delayed	35	7.97 (3.37)	2–16	35	8.66 (2.87)	4–14
Designs Total: Immediate	35	7.66 (3.51)	1–14	36	8.53 (2.85)	2–14
Designs Total: Delayed	35	8.06 (3.04)	3–14	35	8.69 (2.48)	4–13
Word List Learning: Immediate	93	6.52 (3.06)	1–14	69	9.12 (3.28)	1–16
Word List Learning: Delayed	91	7.10 (3.36)	1–15	68	9.68 (2.93)	3–18
Word List Learning: Recognition	88	7.27 (4.45)	1–16	66	10.47 (2.46)	2–13
Stories: Immediate	96	6.96 (3.04)	1–16	69	9.04 (2.83)	2–16
Stories: Delayed	91	6.44 (3.30)	1–15	69	9.14 (3.05)	2–17
Stories: Delayed Recognition	91	7.52 (3.61)	1–16	66	9.27 (2.89)	2–15
Executive Functioning						
Verbal Tasks						
Inhibition:						
Response Time	49	7.16 (3.40)	1–13	46	7.72 (3.07)	1–13
Total Accuracy	49	7.33 (3.81)	1–14	45	7.91 (3.87)	1–14
Self-Corrected Errors	49	7.65 (3.21)	3–14	45	7.62 (3.03)	1–14
Uncorrected Errors	49	9.65 (3.56)	3–14	45	10.82 (3.61)	3–14
Inhibition and Switching:						
Response Time	47	7.28 (3.38)	1–14	43	8.86 (3.08)	3–14
Total Accuracy	47	6.30 (3.61)	1–13	42	7.76 (4.24)	1–14
Self-Corrected Errors	47	7.23 (3.20)	3–14	42	8.43 (3.56)	1–14

(*Continued*)

Table1. (Continued).

	FASD Group			Non-FASD Group		
Domain	*n*	Mean (*SD*)	Range or %	*n*	Mean (SD)	Range or %
Uncorrected Errors	47	9.09 (3.46)	3–14	42	9.40 (3.26)	3–14
Verbal Fluency:						
Letter Total Correct	54	7.33 (2.56)	2–14	41	8.98 (2.39)	5–14
Category Total Correct	54	8.43 (2.90)	2–15	41	10.02 (2.36)	4–15
Category Switching:						
Total Correct	54	7.63 (3.48)	1–17	42	10.10 (2.46)	4–14
Set-Loss Errors	53	7.51 (4.77)	1–14	41	9.41 (4.15)	1–14
Repetition Errors	52	7.77 (4.48)	1–14	41	8.59 (3.85)	1–13
Total Accuracy	53	8.04 (3.99)	1–12	42	9.12 (3.56)	1–14
Nonverbal Tasks						
Trail Making Test:						
Visual Scanning	53	8.77 (3.06)	1–13	45	10.24 (3.14)	2–15
Number Sequencing	56	9.45 (3.16)	1–15	46	11.20 (2.26)	6–15
Letter Sequencing	56	7.91 (3.79)	1–14	46	9.76 (3.52)	1–15
Letter-Number Sequencing	56	6.84 (3.74)	1–16	46	7.57 (3.21)	1–14
Motor Speed	54	9.78 (3.64)	1–14	46	11.50 (1.86)	8–16
Total Errors Condition 4	51	9.16 (3.08)	1–12	46	8.59 (3.10)	1–16
Design Fluency:						
Condition 1	35	9.43 (2.55)	4–17	21	9.71 (2.69)	5–15
Condition 2	35	9.71 (2.81)	4–18	20	10.65 (2.87)	5–18
Condition 3	35	8.86 (2.40)	3–15	20	11.05 (2.69)	7–16
Set-Loss Errors	34	10.76 (3.47)	1–14	20	9.95 (3.32)	4–14
Repetition Errors	34	11.18 (2.29)	3–13	20	11.05 (1.67)	8–13
Total Attempted	34	10.29 (3.65)	3–19	20	11.80 (2.59)	6–16
Total Accuracy	35	8.29 (3.48)	1–14	20	8.30 (3.34)	2–13
Tower Test:						
Total Achievement	44	9.41 (2.09)	5–15	40	10.35 (1.72)	7–14
Mean First Move Time	38	10.11 (3.10)	1–15	38	11.13 (2.03)	5–14
Rule Violations	42	8.76 (3.78)	2–14	39	9.92 (3.86)	1–14
Time per Move Ratio	43	9.72 (2.59)	1–14	38	10.47 (2.25)	1–14
Move Accuracy Ratio	43	7.14 (2.87)	2–12	38	8.05 (2.91)	2–14
Rule Violations per Item	42	8.52 (2.76)	1–11	39	9.28 (2.88)	1–12

Corp, 2013). For each set of analyses, bivariate correlations were initially reviewed to examine the relationship between an FASD diagnosis and the predictor variables (see supplemental data). Next, the relationship between predictor variables that are significantly related to an FASD diagnosis ($p < .05$) or that tend toward significance ($p < .10$) were assessed for multicollinearity, which is when two predictor variables are highly correlated with each other ($p > .70$; Tabachnick & Fidell, 2001). In order to account for multicollinearity, predictor variables with the largest sample size and/or a stronger correlation with receiving an FASD diagnosis were subsequently chosen for logistic regression analyses.

Direct logistic regressions were performed to assess the impact of neuropsychological testing measures, as well as several control variables, on the likelihood of a child or youth receiving an FASD diagnosis (see Table 2 for a summary of each regression). All continuous variables were standardized to a common metric. For each logistic regression model, a significant full model calculated using a chi-square (χ^2) test indicated that the model was able to distinguish between those who were diagnosed with an FASD and those who were not. The odds ratios described in the text that are less than 1 are inversed for ease of interpretation. The explained variance of the model is indicated in Table 2 using Cox and Snell R^2 and Nagelkerke R^2, the former being a more conservative estimate of the explained variance. The Wald statistic was used to test the significance of the individual coefficients in the model. As in Aragón, Coriale, et al. (2008), variables were tested at $\alpha = .0025$ to reduce the likelihood of Type 1 errors that can occur when running multiple analyses.

Results

A number of control variables are significantly correlated with whether or not the child received an FASD diagnosis, including child age and sex, legal guardian, whether or not the child had an ADHD diagnosis or other co-morbid diagnosis (e.g., ODD, depression), and number of adverse and/or stressful life events experienced by the child. Multicollinearity was found between an ADHD diagnosis and other diagnoses. ADHD was used in subsequent analyses as 73% of children and adolescents in the present sample had this diagnosis. After assessing for multicollinearity, the control variables influencing whether a child or adolescent receives an FASD diagnosis were sex, ADHD diagnosis, and number of psychosocial stressors and adverse life events. That is, children who receive an FASD diagnosis are more likely to be male, less likely to have an ADHD diagnosis, and likely to have experienced fewer psychosocial stressors.

The logistic regression model contains all three demographic variables that are significantly related to an FASD diagnosis (child sex, ADHD diagnosis, and number of adverse and/or stressful life events experienced by the child). The full model containing all predictors is statistically significant, $\chi^2(3, n = 178) = 17.59$, $p = .001$, and correctly classifies 64.6% of cases. As shown in Table 2, sex, ADHD diagnosis, and number of psychosocial stressors make unique statistically significant contributions to the model. The strongest predictor of an FASD diagnosis is not having or receiving an ADHD diagnosis. The odds ratio indicates that children with ADHD are 2.33 times less likely to receive an FASD diagnosis, controlling for all other factors in the model. Boys were over 2 times more likely to receive an FASD diagnosis. Finally, those who experienced

Table 2. Logistic Regressions Predicting the Likelihood of Receiving an FASD Diagnosis: Demographic Variables, Intellectual Functioning, Academic Achievement, Memory, and Executive Functioning.

Domain	Cox & Snell R^2	Nagelkerke R^2					
Predictor Variables			*B* (*SE*)	Wald	*p*	Odds Ratio	CI (95%)
Demographic Information	9.4%	12.7%					
Age (years)			0.04 (0.05)	0.46	.50	1.04	0.93–1.15
Sex			0.74 (0.34)	4.73	.03**	2.09	1.08–4.05
ADHD Diagnosis			0.85 (0.35)	5.73	.02**	2.33	1.17–4.67
Psychosocial Stressors			−0.18 (0.06)	10.87	.00***	0.83	0.75–0.93
Intelligence							
Full-Scale IQ (FSIQ)	19.6%	26.5%	−1.17 (0.23)	26.65	.00***	0.31	0.20–0.48
Indices	22.9%	30.9%					
Verbal Comprehension Index (VCI)			−0.75 (0.25)	8.83	.00***	0.47	0.29–0.77
Perceptual Reasoning Index (PRI)			−0.11 (0.22)	0.23	.63	0.90	0.58–1.39
Working Memory Index (WMI)			−0.54 (0.23)	5.72	.02**	0.58	0.37–0.91
Processing Speed Index (PSI)			−0.24 (0.21)	1.28	.26	0.79	0.52–1.19
Subtests	28.4%	38.2%					
Similarities			−0.33 (0.26)	1.57	.21	0.72	0.43–1.20
Vocabulary			−0.48 (0.32)	2.36	.13	0.62	0.33–1.14
Comprehension			−0.10 (0.30)	0.12	.73	0.90	0.51–1.61
Block Design			−0.16 (0.23)	0.45	.50	0.86	0.54–1.35
Matrix Reasoning			0.23 (0.25)	0.84	.36	1.26	0.77–2.05
Picture Conception			−0.32 (0.25)	1.64	.20	0.73	0.45–1.18
Digit Span			−0.50 (0.23)	4.87	.03**	0.60	0.39–0.95
Letter-Number Sequencing			−0.38 (0.25)	2.41	.12	0.68	0.42–1.11
Coding			0.04 (0.26)	0.02	.89	1.04	0.63–1.72
Symbol Search			−0.29 (0.30)	0.95	.33	0.75	0.42–1.34
Academic Achievement	34.1%	46.0%					
Spelling			−1.10 (0.51)	4.63	.03**	0.33	0.12–0.91
Reading Comprehension			−0.12 (0.44)	0.08	.78	0.89	0.38–2.09
Math Calculations			−0.78 (0.35)	4.97	.03**	0.46	0.23–0.91
Memory							
Indices	19.1%	26.1%					
Delayed Visual Index			−0.05 (0.29)	0.03	.87	0.95	0.54–1.67
Delayed Verbal Index			−0.62 (0.35)	3.09	.08*	0.54	0.27–1.07
Delayed Recognition Index			−0.63 (0.35)	3.27	.07*	0.53	0.27–1.05
Subtests	20.1%	27.9%					
Faces: Delayed			−0.05 (0.21)	0.05	.83	0.96	0.64–1.43
Spatial Location: Delayed			−0.11 (0.21)	0.26	.61	0.90	0.60–1.35
Word List Learning: Immediate			−0.46 (0.25)	3.30	.07*	0.63	0.39–1.04
Word List Learning: Delayed			−0.40 (0.25)	2.53	.11	0.67	0.41–1.10
Stories: Delayed			−0.53 (0.23)	5.57	.02**	0.59	0.38–0.91
Executive Functioning							
Verbal Tasks	19.3%	25.7%					
Inhibition:							
Response Time			−0.15 (0.31)	0.25	.62	0.86	0.47–1.57
Total Accuracy			−0.23 (0.36)	0.40	.53	0.80	0.40–1.60
Self-Corrected Errors			0.11 (0.37)	0.10	.76	1.12	0.54–2.32
Verbal Fluency:							
Letter Total Correct			−0.57 (0.30)	3.64	.06*	0.56	0.31–1.02
Category Total Correct			−0.33 (0.35)	0.93	.34	0.72	0.36–1.41
Category Switching:							
Total Correct			−0.43 (0.33)	1.65	.20	0.65	0.34–1.25
Set-Loss Errors			−0.37 (0.31)	1.49	.22	0.69	0.38–1.25
Nonverbal Tasks	13.9%	18.6%					
Trail Making Test:							
Visual Scanning			−0.31 (0.35)	0.78	.38	0.74	0.38–1.45
Number Sequencing			−0.14 (0.34)	0.18	.68	0.87	0.45–1.69
Letter Sequencing			−0.09 (0.31)	0.08	.78	0.92	0.50–1.69

(*Continued*)

Table2. (Continued).

Domain Predictor Variables	Cox & Snell R^2	Nagelkerke R^2	*B* (*SE*)	Wald	*p*	Odds Ratio	CI (95%)
Tower Test:							
Total Achievement			−0.57 (0.28)	4.17	.04**	0.56	0.32–0.98
Mean First-Move Time			−0.19 (0.32)	0.34	.56	0.83	0.44–1.56
Test Battery	35.1%	46.8%					
Verbal Comprehension Index (VCI)			−1.07 (0.42)	6.64	.01**	0.34	0.15–0.77
Working Memory Index (WMI)			−0.05 (0.37)	0.02	.90	0.95	0.46–1.98
Spelling			0.11 (0.42)	0.07	.80	1.12	0.49–2.53
Math Calculations			−1.08 (0.42)	6.55	.01**	0.34	0.15–0.78
Stories: Delayed			−0.43 (0.35)	1.51	.22	0.65	0.33–1.29
Tower: Total Achievement			−0.43 (0.31)	1.91	.17	0.65	0.35–1.20

Note. *$p < .10$; **$p < .05$; ***$p < .01$.

fewer psychosocial stressors were just under 1.25 times more likely to receive an FASD diagnosis.

Following examination of the demographic information and its relationship to an FASD diagnosis, direct logistic regressions were performed to assess the impact of the predictor variables on the likelihood of a child or youth receiving an FASD diagnosis. Hierarchical logistic regressions were run with sex, ADHD diagnosis, and number of psychosocial stressors and adverse life events as step 1 followed by the predictor variables in step 2. Since the relationship between the predictor variables and an FASD diagnosis did not change when controlling for the demographic variables, the logistic regression results subsequently reported were run in a single step.

Neuropsychological Tests

Intellectual Functioning

Bivariate correlations between index scores on the Wechsler scales and an FASD diagnosis were examined. Given the multicollinearity found between the FSIQ and the four individual indices (VCI, PRI, WMI, and PSI), the FSIQ was analyzed in a separate regression from the indices.

The logistic regression model containing the FSIQ is statistically significant, $\chi^2(1, n = 174) = 38.02$, $p < .001$, and correctly classifies 69.0% of cases. As shown in Table 2, those who have a lower FSIQ are almost 3.25times more likely to receive a diagnosis.

The logistic regression model containing measures of verbal comprehension, perceptual reasoning, working memory, and processing speed is also statistically significant, $\chi^2(4, n = 171) = 44.54$, $p < .001$, and correctly classifies 69.0% of cases as well. Both verbal comprehension and working memory make unique statistically significant contributions to the model (Table 2). Those who score lower on verbal comprehension tests are over 2 times more likely to receive a diagnosis. Similarly, those who score lower on tasks assessing working memory are just under 1.75 times more likely to receive an FASD diagnosis.

An additional logistic regression was performed to assess the impact of individual factors measuring intellectual functioning on the likelihood of a child or adolescent receiving an FASD diagnosis. The model contains 10 subtests common to the WISC-IV,

the WAIS-IV, and to a lesser extent the WPPSI-III: Similarities, Vocabulary, Comprehension, Block Design, Matrix Reasoning, Picture Concepts, Digit Span, Letter-Number Sequencing, Coding, and Symbol Search. The full model containing all predictors is statistically significant, $\chi^2(10, n = 159) = 53.02$, $p < .001$, and correctly classifies 75.5% of cases. Only the Digit Span subtest makes a unique statistically-significant contribution to the model (Table 2). Those who score lower on the Digit Span subtest are almost 1.67 times more likely to receive a diagnosis.

Academic Achievement

Bivariate correlations between subtest scores and an FASD diagnosis were examined next. Multicollinearity between the Spelling, Word Reading, Pseudoword Decoding, Sentence Comprehension, and Reading Composite variables was found and the Spelling test was subsequently chosen as a representative variable of basic reading and writing skills for the logistic regression. Furthermore, multicollinearity was also found between the Math Problem-Solving subtest and the Math Calculations variable. The latter was chosen for subsequent analyses.

The logistic regression model contains three independent variables: Spelling, Reading Comprehension, and Math Calculations. The full model is statistically significant, $\chi^2(3, n = 81) = 33.81$, $p < .001$, and correctly classifies 75.3% of cases. As shown in Table 2, both the Spelling and Math Calculations variables make unique statistically-significant contributions to the model. Children and youth who score lower on tests of Spelling and Math Calculations are 3 times and over 2 times more likely to receive a diagnosis, respectively.

Memory

Bivariate correlations were examined between the memory subtests and indices and an FASD diagnosis. Multicollinearity was common among variables, therefore two logistic regressions were conducted: one including only indices and one including only subtests that are significantly correlated to an FASD diagnosis.

The logistic regression model examining indices contains three predictor variables: the Visual Delayed composite, the Verbal Delayed composite, and the Delayed Recognition composite. The full model containing all predictors is statistically significant, $\chi^2(3, n = 85) = 18.01$, $p < .001$, and correctly classifies 67.1% of cases. However, as shown in Table 2, none of the variables make unique statistically-significant contributions to the model.

The direct logistic regression model examining individual subtests contains the following five independent variables: Stories Delayed, Word List Learning Immediate, Word List Learning Delayed, Memory for Faces Delayed, and Spatial Memory Delayed. The full model containing all predictors is statistically significant, $\chi^2(5, n = 145) = 33.80$, $p < .001$, and correctly classifies 68.3% of cases. Only the Stories Delayed subtest makes a unique statistically-significant contribution to the model. Children and youth who score lower on the Stories Delayed subtest are over 1.67 times more likely to receive a diagnosis.

Executive Functioning

Bivariate correlations between the executive functioning subtests and an FASD diagnosis were examined. Multicollinearity between the Verbal Fluency Category Switching

Responses score (number of correct switches) and the Category Switching Accuracy score (number of correct responses) was found. The Category Switching Responses score was used in the logistic regression. Verbal and nonverbal tasks were analyzed in separate regressions.

The logistic regression model contained seven independent verbal variables: Inhibition/Switching completion time, Letter Fluency, Category Fluency, Category Switching Responses, Verbal Fluency set-loss, Inhibition/Switching total errors, and Inhibition/Switching self-corrected errors. The full model containing all predictors is statistically significant, $\chi^2(7, n = 75) = 16.04$, $p < .05$, and correctly classifies 66.7% of cases. However, as shown in Table 2, none of the variables make unique statistically-significant contributions to the model. The direct logistic regression model contains five nonverbal variables: Trail Making conditions 1, 2, and 3, the Tower Test achievement score, and the Tower Test mean first-move time. The full model containing all predictors tends toward significance, $\chi^2(5, n = 73) = 10.96$, $p = .052$, and correctly classifies 67.1% of cases; however, only the Tower Test achievement score makes a unique statistical contribution to the model. Children and youth who score lower on the Tower Test are about 1.75times more likely to receive a diagnosis.

Test Battery

For the final set of analyses, the correlations between all significant predictors in the abovementioned logistic regressions with an FASD diagnosis were examined. Multicollinearity between the WMI and Digit Span subtest was found, therefore the WMI was used in the logistic regression.

The full logistic regression model containing the seven predictor variables is statistically significant, $\chi^2(6, n = 75) = 32.44$, $p < .001$, and correctly classifies 74.7% of cases. As shown in the Table 2 below, only the VCI and Math Calculations variables make unique statistically-significant contributions to the model. Those who have poorer VCI and Math Calculations scores are almost 3 times more likely to receive a diagnosis.

Discussion

The present study seeks to identify a number of neuropsychological variables that contribute significantly toward an accurate diagnosis of FASD among a group of children and youth with PAE. Consistent with previous studies, a large number of neuropsychological outcomes that are *significantly related* to an FASD diagnosis have been identified, including almost all indicators of intelligence, many elements of memory (i.e., delayed memory for faces, immediate and delayed verbal memory, recognition memory), executive functioning (i.e., set-shifting, inhibition, verbal fluency, visual sequencing, visual fluency, visual spatial planning), and all academic functions.

However, the present findings also point to a more circumscribed set of outcome variables that are *predictive* of a diagnosis, namely verbal intelligence, auditory working memory (especially digit span), delayed story recall, spelling (as a variable representing basic reading and spelling skills), mathematical calculations, and spatial planning. Children with PAE who have poorer functioning on these variables are 1.67 to 3 times more likely to receive an FASD diagnosis. Additionally, a number of trends were observed between performance on several measures (letter fluency, delayed verbal

memory, recognition memory, and immediate list learning) and likelihood of an FASD diagnosis. Conversely, overall intelligence, nonverbal intelligence, processing speed, reading comprehension, delayed visual memory (including spatial memory and memory for faces), and a number of executive functioning indicators (verbal inhibition, set-shifting, visual sequencing) do not contribute significantly toward the prediction of an FASD diagnosis.

On the surface, these results are both consistent and inconsistent with previous findings. For example, variables such as intelligence, executive functioning (e.g., set-shifting, inhibition, working memory), visual and verbal memory, mathematics ability, and spatial reasoning are frequently cited as being related to FASD (Aragón, Kalberg, et al., 2008; Kodituwakku, 2009; Mattson et al., 2011; Rasmussen et al., 2006). While group differences were found in the majority of these variables, only some of the variables remained when considering their predictive value in FASD. In addition, other variables that are cited with less regularity (e.g., basic reading and spelling ability) emerged as predictive of a diagnosis in this study. One key reason for this differential finding relates to the different methodology employed to ascertain which variables are predictive of FASD (i.e., logistic regressions in this study versus mean-comparison approaches in others). Some of the differential findings could also pertain to differences in the nature of the groups under investigation. As noted earlier, the majority of previous studies compare individuals with and without alcohol exposure. In the present study, both groups consisted of children and adolescents who were prenatally exposed to alcohol. As such, this study captures the variables that might be of most interest when attempting to differentiate diagnostically within a PAE group.

While previous studies have shown general intelligence (FSIQ) to be related to an FASD diagnosis (Nash et al., 2013; Rasmussen et al., 2006), this study found that it is also predictive of an FASD diagnosis in a group of children and adolescents with PAE. When examined separately, the verbal comprehension and verbal/auditory working memory indices appear to be the predictive factors behind the full-scale score. Indeed, difficulties with verbal intelligence and reasoning have been shown previously to distinguish between groups of alcohol-exposed children (Nash et al., 2013; Rasmussen et al., 2006), with poorer outcomes found for those (a) having evidence of greater CNS dysfunction or (b) meeting diagnostic thresholds for FASD. In the present study, not only was verbal intelligence found to be associated with FASD, but it was also found to be predictive of such a diagnosis.

Similarly, while numerous memory functions were found to be associated with an FASD diagnosis, only a few play a predictive role (i.e., delayed story recall and, to a lesser degree, overall delayed verbal memory, immediate list learning and overall delayed recognition memory). How do these compare to other studies of individuals with PAE? Nash et al. (2013) found FASD diagnosis to be associated with poorer delayed spatial memory and general memory, as well as trends toward immediate spatial memory and delayed verbal memory. Rasmussen et al. (2006) noted weaknesses across a large number of verbal and visual memory tests, but the only indicators that distinguish PAE groups based on severity of CNS dysfunction are measures of immediate facial memory and delayed facial memory (with the latter being represented as a trend). A significant point of divergence between the present study and these others is

that it appears that indicators of verbal memory emerge more consistently in the present results compared to indicators of visual memory in the others. Associations and trends for the same elements of visual memory are observed, but the strongest associations and predictors in the data for the present study are related to verbal memory. One potential explanation may lie in the work of Rasmussen et al., who showed a distinct memory profile for Caucasian (stronger verbal than visual memory) and Aboriginal (stronger visual than verbal memory) children. Given that Manitoba shares similar demographic characteristics to Saskatchewan, it is possible that ethnic variables may have come into play in this finding. This will need to be a point of future study, as information regarding ethnicity for the participants in the present study is not available.

A number of additional outcomes deserve specific attention, including mathematical ability and executive functioning. First, the present study adds to an ever-growing body of literature documenting specific difficulties in mathematical ability in FASD (Goldschmidt, Richardson, Stoffer, Geva, & Day, 1996; Howell, Lynch, Platzman, Smith, & Coles, 2006; Kopera-Frye, Dehaene, & Streissguth, 1996; Nash et al., 2013; Rasmussen & Bisanz, 2009; Streissguth et al., 1994). In addition, associations have been made between poor mathematics skills and reduced processing speed, working memory and visuospatial abilities in FASD (Burden, Jacobson, Sokol, & Jacobson, 2005; Crocker, Riley, & Mattson, 2015; McLean & Hitch, 1999; Rasmussen & Bisanz, 2011). While a predictive role for processing speed in FASD has not been identified in the present findings, the remaining areas of functioning that have been identified (mathematical ability, spatial reasoning, and working memory) represent a constellation of findings that are indeed predictive of a diagnosis. Structural and functional neuroimaging studies have implicated alterations in parietal regions in FASD that are related to poor mathematical ability (Crocker et al., 2015). Parietal regions are also implicated in a number of other functions, including visuospatial abilities (for a review, see Teixeira et al., 2014), which are predictive of an FASD diagnosis in the present study.

As noted, auditory working memory, spatial planning (and to a smaller degree letter fluency) are predictive of an FASD diagnosis in the present sample, whereas other executive functions (i.e., set-shifting, inhibition, and visual sequencing) do not play a predictive role. These findings are in keeping with the evidence for a robust *but differential* association between executive dysfunction and PAE (Khoury, Milligan, & Girard, 2015). In particular, Khoury et al. (2015) conducted a meta-analytic review of three constellations of executive functioning (i.e., inhibition, set-shifting and working memory). A differential effect magnitude was noted dependent on a variety of factors, including the measure(s) utilized and the nature of the groups being compared. Effect sizes were found to be largest for set-shifting tasks (unlike the present findings), while working memory was most robust to smaller differences between groups (as in the present findings). In other work, Mattson et al., (2010, 2013) have shown that measures of executive functioning and spatial processing are most sensitive to PAE and thus most effective at distinguishing PAE groups (with or without FASD) from non-exposed controls. One of the reasons why many of the executive functioning indicators analyzed in this study were not found to be predictive of a diagnosis is that both PAE groups had difficulty with these functions. Indeed, an examination of Table 1 suggests that both

groups exhibited weak executive functioning relative to normative data (e.g., measures of verbal inhibition, as well as verbal and nonverbal set-shifting), and the PAE-FASD group was no worse than the PAE group. Thus, while a number of objective measures of executive functioning may be sensitive to PAE, they may not necessarily be predictive of an FASD diagnosis. Rather, it is possible that subjective indicators of executive functioning (i.e., parent and/or teacher ratings) may be more predictive of an FASD diagnosis. Indeed, clinical and research data suggest a divergence between objective and subjective measures of a number of factors of executive functioning (Glass et al., 2014; Gross, Deling, Wozniak, & Boys, 2015), with more pronounced difficulties often evident on subjective measures. Caregiver and teacher ratings of executive functioning have been shown to distinguish between diagnosed and non-diagnosed children with PAE (Stevens et al., 2013), but it remains to be seen whether any of those indicators accurately predict diagnosis. This is a focus of other work in our lab.

The classification accuracy of PAE-FASD and PAE groups is clinically significant across models of intelligence, academic achievement, memory, and executive functioning. The classification rates across the various models range from 67.1% to 75.5%, with models which incorporate ten intelligence subtests or three academic subtests emerging as superior to those using broad indices of intelligence and/or individual subtests of memory or executive functioning. A "test battery" model incorporating verbal intelligence, verbal working memory (digit span), spelling, math calculations, delayed story recall, and spatial planning yielded a classification rate of 74.7%. These rates suggest that neuropsychological testing is a critical component of an FASD assessment. While these classification rates are consistent with or lower than those reported by Mattson et al., (2010, 2013), they are not directly comparable due to differing methodologies and sample properties. Importantly, the comparisons being made by Mattson et al., (2010, 2013) were between dysmorphic FASD children (FAS/pFAS) and non-exposed controls, and between non-dysmorphic children with PAE (ARND or no diagnosis) and non-exposed controls. Generally, the rates were found to be higher among the former more disparate groups (88%, 77%) than in the latter groups (68%, 70%). The children in the present study cut across both clinical groups used in the Mattson et al., (2010, 2013) studies (indeed, the authors note that 70% of their non-dysmorphic sample would likely have met criteria for ARND), thus 100% of their FAS/pFAS sample and 70% of their non-dysmorphic sample would have comprised the present PAE-FASD group and 30% of their non-dysmorphic sample would have comprised the present PAE group. Presumably, the present study is looking at smaller group differences than those being examined by Mattson et al., (2010, 2013) in that they are making comparisons with non-exposed controls.

Several limitations in this study should be acknowledged. First, data were collected retrospectively through a chart review of a clinic-referred sample. As such, not all children underwent identical test batteries (i.e., due to factors such as testing fatigue, time limitations, varying age groups, and other clinical factors). An attempt was made to manage this by collapsing across measures that are clinically and statistically related, but future studies verifying the predictive power of these models are warranted. Another limitation connected to the retrospective nature of this study is that certain background information is not available or was not gathered in a way that permits careful analysis. For example, only limited information about trauma history is

available, and there is no information about factors related to socioeconomic status and ethnicity—factors that have known associations with neuropsychological outcomes (Fry, Langley, & Shelton, 2016; Rasmussen et al., 2006). Furthermore, while the combined sample size is fairly large (n = 180), the number of children and youth assessed using each measure is significantly more variable and often resulted in a smaller subset of samples used in the analyses.

Despite these limitations, the theoretical and practical implications of the present study are hard to ignore. First, the findings of the present study can inform the development of step-wise or weighted models that could be utilized in clinical assessments. In other words, the present findings suggest that relative weightings applied to different outcome measures or planning for a more restricted or reduced testing battery that is expanded only when necessary could be implemented when planning assessments. Specifically, these results suggest that a battery which includes a complete intellectual assessment (with relative emphasis on verbal and working memory skills), a screen of academic achievement (with relative emphasis on basic reading and spelling skills and math skills), and a sampling of memory and/or executive functioning skills (with emphasis on spatial planning and delayed story recall) may provide a suitable initial framework for the assessment of children with PAE. This may lead to improved screening and increased efficiency in assessment, reduced time commitments for children and families, shortened waitlists, and better allocation of resources without sacrificing diagnostic clarity. The present findings also contribute to knowledge regarding the nature of impairments in FASD in order to identify appropriate targets for intervention. For example, these results add to converging evidence of deficits in mathematics, spatial reasoning, and working memory in children and adolescents with an FASD diagnosis, and this understanding can help to inform the types of accommodations that should be considered both at home and in academic environments, as well as the types of interventions that should be considered for development and further study.

This study is one of the first to provide information on how several demographic factors may impact on whether or not a child seen for an FASD assessment will receive a diagnosis in Manitoba. For instance, in this study, individuals who were diagnosed with FASD are more likely to be male, less likely to have a comorbid diagnosis of ADHD, and less likely to have a history of psychosocial stressors. Given that the indicator of psychosocial stressors is based on a retrospective demographic questionnaire that includes limited information on past or recent traumas, only a broad sense of the association of these factors is provided. Therefore, the psychosocial stressor indicator used in this study may not be sensitive to the real impact of past trauma on present functioning. Furthermore, if children or adolescents present with an extensive past or current history of trauma (physical, emotional or sexual abuse, neglect, frequent changes in caregivers) and appear to show signs of trauma-related disturbance (e.g., attachment issues, post-traumatic stress disorder, etc.), diagnosticians are less likely to confirm a diagnosis of FASD given that it is difficult to declare that PAE is the primary cause of the child's impairments. As such, some children in the non-diagnosed group may be overlooked due to challenges in attributing deficits to alcohol over other relevant genetic and environmental factors. More research is needed to understand

the relationship between FASD, psychosocial stressors and past trauma in order to disambiguate such influences from the effects of PAE.

Finally, while the current study highlights the relative predictive value of a variety of formal assessment measures, it also points to the need for additional research in a number of areas. For example, the predictive value of indirect measures such as parent and teacher ratings (e.g., the BRIEF versus the D-KEFS for executive functions) in disambiguating FASD from PAE has not yet been described. As noted above, these indicators can be quite discrepant and further research is currently underway to determine the role that parent and teacher ratings of daily functioning can play in making an FASD diagnosis. Another line of research may include examining whether the current predictions are maintained when using the criteria outlined in the updated Canadian diagnostic guidelines (Cook et al., 2016), or in other diagnostic systems (e.g., Astley, 2004, 2006; Hoyme et al., 2005). In addition, critical assessment tools have been recently updated (e.g., the WISC-IV to the WISC-V); thus, investigations are needed to examine whether new or updated measures alter these predictive outcomes. Finally, it remains important to examine how specific the models described in the present study are to FASD and whether they can distinguish FASD from other clinical groups, such as ADHD, ODD, and intellectual disability.

Ultimately, understanding the nuances that help to differentiate PAE from PAE-FASD is critical to the assessment process. Further research is needed to develop and test the predictive value of all factors considered in FASD assessment in the quest for greater diagnostic efficiency and accuracy in PAE-affected children and adolescents.

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No potential conflict of interest was reported by the authors.

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