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Mechanisms of Mathematics Deficits in Fetal Alcohol Spectrum Disorders

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Mechanisms of Mathematics Deficits in Fetal Alcohol Spectrum Disorders

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy

in

Clinical Psychology

by

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The Dissertation of Nicole Crocker is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Chair

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Chapters 1, 2, 3 and 4, in part, are currently being prepared for submission for publication of the material. Crocker, Nicole; Mattson, Sarah N. The dissertation author was the primary investigator and author of this material.

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ABSTRACT OF THE DISSERTATION

Mechanisms of Mathematics Deficits in Fetal Alcohol Spectrum Disorders

by

Nicole Crocker

Doctor of Philosophy in Clinical Psychology

University of California, San Diego, 2014
San Diego State University, 2014

Professor Sarah N. Mattson, Chair

Fetal Alcohol Spectrum Disorders (FASD) are associated with a broad range of neuropsychological and behavioral impairments, from diminished general intelligence to subtle attention and motor deficits. The extant literature suggests that children with prenatal alcohol exposure have mathematics difficulties, however the nature and specificity of these deficits have not been thoroughly examined. The current study sought to evaluate mechanisms of mathematics abilities in children with prenatal alcohol exposure by testing their core capacity to represent and process numerical information. Mathematics achievement and numerical processing skills in children with prenatal alcohol exposure (n = 27) and typically developing controls (n = 32) ages 8:0 to 16:11 were evaluated using the Calculation, Math Fluency, Applied Problems, and Quantitative Concepts subscales of the Woodcock Johnson III Tests of Achievement (WJ-III) and three experimental tasks designed to measure different aspects of numerical processing: approximate number sense (ANS), symbolic and nonsymbolic magnitude judgment (MJ), and automaticity of numerical magnitude processing (numerical stroop). Analysis of variance (ANOVA) techniques were utilized to examine between group differences on mathematics achievement measures and numerical processing skills. To evaluate whether performance on number processing tasks was related to global mathematics achievement in the sample, linear regression analyses were conducted with WJ-III standard scores as the dependent variable and reaction time and accuracy data from experimental tasks and group as independent variables. Group differences were observed on all four WJ-III measures of mathematics achievement, with alcohol-exposed children performing more poorly than their typically developing peers. In addition, children with prenatal alcohol exposure showed deficits on all indices of numerical processing, with the exception of MJ accuracy and numerical stroop accuracy. Overall, numerical processing abilities were positively related to children's mathematics achievement across groups, however, numerical processing abilities were also related to measures of reading and spelling. Finally, when IQ was considered in the model, differential relationships between group and IQ emerged and the relations between measures of numerical processing and mathematics achievement were attenuated, suggesting that numerical processing abilities may not represent a specific pathway underlying mathematics deficits in children with histories of heavy prenatal alcohol exposure. This investigation aids in the characterization of mathematics deficits in alcohol-exposed children. Greater understanding of the mechanisms underlying neuropsychological impairments in children with prenatal alcohol exposure will lead to more informed interventions and ultimately better outcomes for affected individuals.

I. Introduction

Specific Aims of the Current Project

Fetal alcohol spectrum disorders (FASD) are associated with a wide range of deleterious neurobehavioral consequences including academic difficulties. In particular, mathematics has emerged as a specific area of weakness (Howell, Lynch, Platzman, Smith, & Coles, 2006; Streissguth et al., 1994; Streissguth, Barr, Sampson, & Bookstein, 1994), though little is known about the nature of these deficits. The clinical utility of studying this domain is clear, as early mathematics competence is important for future academic and vocational success (Barnes et al., 2002; Rivera-Batiz, 1992). Interventions focused on remediation of math skills in children with FASD appear promising (Coles, Kable, & Taddeo, 2009; Kable, Coles, & Taddeo, 2007) but could be greatly improved if more was understood about the underlying mechanisms of math difficulties in this population. The overarching goal of this study was to evaluate the nature of mathematics difficulties in children with heavy prenatal alcohol exposure. The methods used to study this domain allow for assessment of specific processes underlying math deficits observed in alcohol-exposed children and findings may contribute to more informed interventions tailored specifically for affected individuals.

Recent theories suggest that math difficulties arise as a result of deficits in basic numerical processing skills, such as magnitude comparison and implicit processing of quantity (Butterworth, 2005; Landerl, Bevan, & Butterworth, 2004); yet numerical processing in children with FASD has received little attention. Limited evidence suggests that prenatal alcohol exposure may be associated with deficits in some aspects of basic number processing (Jacobson, Dodge, Burden, Klorman, & Jacobson, 2011; Kopera-Frye, Dehaene, & Streissguth, 1996), however the relationship between these skills and mathematics achievement in FASD has not been fully assessed. Prenatal alcohol exposure also is related to brain abnormalities in areas known to be associated with mathematics abilities and numerical processing, particularly the parietal lobe (Archibald et al., 2001).

Traditional assessment of mathematics abilities is via tests of global mathematics achievement. A goal of current research is to incorporate alternative assessment methods to increase understanding of the range of processes associated with mathematics abilities. Therefore, the current study utilized three experimental tasks to evaluate the extent to which basic numerical processing skills are associated with mathematics performance in children with prenatal alcohol exposure.

Children with heavy prenatal alcohol exposure and typically developing controls ages 8:00 to 16:11 were tested with both standardized and experimental measures in order to meet the following study aims:

Aim 1: To evaluate mathematics achievement in children with histories of prenatal alcohol exposure and typically developing controls.

Mathematics achievement was evaluated using the Calculation, Math Fluency, Applied Problems, and Quantitative Concepts tests of the Woodcock Johnson III Tests of Achievement (WJ-III; Woodcock, Schenk, McGrew, & Mather, 2007).

Hypothesis 1. Because children with prenatal alcohol exposure consistently demonstrate impaired performance on measures of academic achievement, it was hypothesized that they will perform more poorly than controls on all mathematics tests of the WJ-III.

Aim 2: To investigate fundamental numerical processing abilities and the extent to which they are associated with mathematics achievement in children with histories of prenatal alcohol exposure and typically developing controls.

Children were assessed with three tasks designed to measure different aspects of numerical processing: approximate number sense, symbolic and nonsymbolic magnitude judgment, and automaticity of numerical magnitude processing (numerical stroop). While some of these tasks had never been tested in FASD, hypotheses were based on limited evidence suggesting that prenatal alcohol exposure is related to deficits in numerical processing and on studies using similar tasks in children with mathematics learning disorders.

Hypothesis 2a: Approximate Number Sense (ANS). Children with prenatal alcohol exposure will demonstrate slower reaction time and poorer accuracy relative to controls on the ANS task.

Hypothesis 2b: Symbolic and Nonsymbolic Magnitude Judgment (MJ). Children with prenatal alcohol exposure will demonstrate slower reaction time and poorer accuracy than controls on both conditions of the MJ task. In addition, alcohol-exposed children will show a relative weakness in symbolic MJ vs. nonsymbolic MJ.

Hypothesis 2c: Numerical Stroop. On the physical size condition of the numerical stroop task, controls will demonstrate a size congruency effect (SCE; i.e., differential reaction times based on whether stimuli presented are neutral, congruent, or incongruent). However, children with prenatal alcohol exposure will not produce a SCE and will demonstrate similar reaction times across all conditions of the task.

Hypothesis 2d. Performance on these three numerical processing tasks will be positively associated with WJ-III performance in both groups.

Introduction to the Current Project

Fetal Alcohol Spectrum Disorders (FASD) represent a major public health concern, with prevalence estimates as high as 1 in every 100 live births (Sampson et al., 1997). This spectrum of disorders is associated with a broad range of neuropsychological and behavioral impairments, including diminished general intelligence and deficits in learning, memory, language, executive and motor function, visual-spatial ability, adaptive behavior, attention, and academic achievement (for review see, Mattson, Crocker, & Nguyen, 2011). Neurobehavioral difficulties persist into adulthood and result in adverse life outcomes such as disrupted school experiences, trouble with the law, and substance abuse (Streissguth et al., 2004).

Early identification of affected individuals can lead to better outcomes (Streissguth et al., 2004), however intervention research in this population remains limited. One promising rehabilitation effort has focused on improving behavior and math functioning in children with FASD. This intervention, which utilized an interactive math-tutoring program, demonstrated greater improvement in children following the math intervention than a control intervention (Kable et al., 2007). In addition, gains were maintained at 6-month follow up (Coles et al., 2009). Intervention focused on improving mathematics ability in children with FASD is crucial given the importance of math skills for academic and vocational success (Barnes et al., 2002; Rivera-Batiz, 1992). However, current interventions could be greatly improved if more was understood about the underlying processes related to math difficulty in children with FASD. The current study sought to evaluate mechanisms of mathematics abilities in children with heavy prenatal alcohol exposure by testing their core capacity to represent and process numerical information.

Mathematics Learning Disorder. The essential feature of mathematics learning disorder (MLD) is difficulty mastering number sense, number facts, or calculation. These affected skills must be substantially and *quantifiably* below those expected for the individual's chronological age and cause significant interference with academic or occupational performance, or with activities of daily living, as confirmed by individually administered standardized achievement measures and comprehensive clinical assessment (American Psychiatric Association, 2013). It is estimated that 5 to 8% of school-aged children are diagnosed with MLD (Geary, 2004) and preliminary evidence suggests that children with FASD meet criteria for MLD at a higher rate than their non-exposed peers (Infante et al., 2011). Literature indicates that the frequently utilized IQ-achievement discrepancy may not be an adequate marker of learning disorders and highlights the importance of using alternative models and methodologies for the assessment of mathematics difficulties (Fletcher, Denton, & Francis, 2005). As such, the proposed study will evaluate fundamental numerical processing and its relationship to mathematics difficulty in children with histories of prenatal alcohol exposure.

Numerical Processing. Although competing theories have been proposed, recent studies suggest that MLD is related to abnormalities in fundamental numerical processing (sometimes referred to as the *domain specific* model; Butterworth, 2005; Landerl et al., 2004). This fundamental processing refers to one's implicit and automatic understanding of *exact* quantities of small collections of objects and of the *approximate* magnitude of larger sets of objects (Feigenson, Dehaene, & Spelke, 2004; Geary, 2010). This ability to understand and manipulate numerosity (i.e., the number of objects in a set) seems to be an innate capacity as it is manifested in infants (Xu & Spelke, 2000; Xu, Spelke, & Goddard, 2005) and children without formal mathematical instruction (Gilmore, McCarthy, & Spelke, 2007) as well as nonhuman primates (Cantlon & Brannon, 2007). These early abilities are associated with later mathematics achievement (Halberda, Mazzocco, & Feigenson, 2008; Holloway & Ansari, 2009; Siegler & Booth, 2004) and serve as the foundation on which higher-level mathematics processing, such as complex calculations, are built (Butterworth, 2005). Studies of number processing in children with MLD suggest that they have deficits in a range of skills, including numerical estimation and depicting numerical magnitude information (Butterworth, 2005; Landerl et al., 2004; Rubinsten & Henik, 2005; von Aster & Shalev, 2007).

Accurate mapping of numerical magnitudes on to symbols (i.e., Arabic numerals) is an additional ability important in the development of adequate mathematical skills (Holloway & Ansari, 2009; Mundy & Gilmore, 2009). When children begin formal schooling, they learn a new symbolic system with which to represent numbers that involves precise representations of quantity. This new technique for manipulating numerosity does not replace the preexisting nonsymbolic system; rather the two are mapped on to one another. Evaluation of both symbolic and nonsymbolic number processing is important to determine whether mathematical deficits result from impaired numerical magnitude processing or from an inability to access numerical magnitude from abstract symbols (Holloway & Ansari, 2009). Some investigations report that children with MLD are only impaired when evaluating magnitude of Arabic digits and not when evaluating collections of objects, suggesting that deficits may be related to inefficiency in mapping between number representations, rather than in processing basic numerosity, per se (Rousselle & Noel, 2007).

Several studies of typically developing individuals also have suggested that accessing magnitude representation from symbols occurs automatically, even in instances where magnitude information is irrelevant to the task (Ashkenazi, Rubinsten, & Henik, 2009; Girelli, Lucangeli, & Butterworth, 2000; Zhou et al., 2007). For example, numerical stroop paradigms have demonstrated that the *numerical value* of Arabic digits interferes with speed and accuracy of determining which of two numbers is larger in *physical size* (Ashkenazi et al., 2009; Girelli et al., 2000; Zhou et al., 2007). However in studies of MLD, children fail to demonstrate this effect (Ashkenazi et al., 2009; Rubinsten & Henik, 2005), suggesting that they are deficient in the automaticity of numerical processing and that these skills may be important for proficient mathematics functioning.

Neuroanatomical aspects of numerical processing. The entire parietal area appears to be important for arithmetic abilities and numerical processing; however, the most robust finding is the involvement of the intraparietal sulcus located within the posterior parietal lobe (Dehaene, Molko, Cohen, & Wilson, 2004; Dehaene, Piazza, Pinel, & Cohen, 2003). This region is thought to be specifically involved in the processing of both symbolic and nonsymbolic numerical magnitude (Dehaene et al., 2004). Other studies suggest that mathematical processing might involve a more diffuse network of regions that includes areas in the inferior temporal cortex and inferior frontal lobe (Rykhlevskaia, Uddin, Kondos, & Menon, 2009). Relative to adults, children rely more heavily on prefrontal regions (precentral gyrus and inferior frontal gyrus) when performing numerical tasks. This recruitment from frontal networks decreases throughout development and shifts to increasing engagement of parietal areas (Ansari & Dhital, 2006; Ansari, Garcia, Lucas, Hamon, & Dhital, 2005; Kucian et al., 2006). In studies of children with MLD, reduced grey matter volume in the superior parietal lobe and right anterior temporal cortex and reduced white matter in the left frontal lobe and right parahippocampal gyrus have been reported (Rotzer et al., 2008; Rykhlevskaia et al., 2009). In addition, compromised white matter integrity in the right temporal-parietal cortex has been correlated with tests of numerical operations in children diagnosed with developmental dyscalculia (Rykhlevskaia et al., 2009).

Mathematics in FASD. The extant literature suggests that children with prenatal alcohol exposure have math difficulties (Coles et al., 1991; Goldschmidt, Richardson, Stoffer, Geva, & Day, 1996; Howell et al., 2006; Jacobson et al., 2011; Streissguth et al., 1994; Streissguth et al., 1994), however the nature and specificity of these deficits has not been thoroughly examined. Alcohol-exposed children consistently perform lower than controls on measures of global mathematics achievement (Mattson, Riley, Gramling, Delis, & Jones, 1998; Streissguth et al., 1994) even after controlling for IQ (Goldschmidt et al., 1996), but only two investigations have evaluated processes underlying mathematical difficulties. These studies suggest that individuals with histories of prenatal alcohol exposure may have particular deficits in basic numerical processing skills (Jacobson et al., 2011; Kopera-Frye et al., 1996). Kopera-Frye, Dehaene, and Streissguth (1996) administered a numerical processing battery to adolescents and adults with prenatal alcohol exposure and controls. While alcohol-exposed subjects performed worse than controls on almost all tasks, they were most impaired on those tapping cognitive estimation. Similarly, Jacobson and colleagues (2011) demonstrated that children with prenatal alcohol exposure were impaired on both exact and approximate calculation skills, number comparison, and proximity judgment. They also demonstrated that the effect of prenatal alcohol exposure on simple calculation was entirely mediated by magnitude comparison ability, suggesting that for children with prenatal alcohol exposure, basic numerical processing skills are important for later mathematical problem solving, as has been demonstrated in other developmental populations (Halberda et al., 2008; Holloway & Ansari, 2009; Siegler & Booth, 2004). However, the extent to which numerical processing skills in alcohol-exposed children might relate to other aspects of mathematics achievement (e.g. more complex calculations and word problems) is still unknown and the more fine-grained mechanisms of these abilities (e.g., symbolic vs. nonsymbolic aspects and automaticity of processing) remain unclear.

Neuroanatomical Findings in FASD. Evidence suggests that parietofrontal brain regions thought to support mathematics abilities are abnormal in children with FASD. Reports indicate that parietal lobe volume is disproportionately reduced (Archibald et al., 2001) and compromised white matter integrity has been reported in the temporal lobes and in tracts connecting the occipital lobe with inferior frontal and parietal lobes (Fryer et al., 2009; Lebel et al., 2008; Sowell et al., 2008). In a study that specifically evaluated the relationship between mathematical skill and brain white matter structure using diffusion tensor imaging (DTI) in children with prenatal alcohol exposure, authors identified four key regions related to mathematical ability (Lebel, Rasmussen, Wyper, Andrew, & Beaulieu, 2010). These regions were located in the left parietal areas, left cerebellum and bilateral brainstem, highlighting the importance of parietal regions for mathematics functioning and suggest the possibility that other areas may be specific to mathematics in children with FASD.

In addition to structural differences, alterations in brain function related to prenatal alcohol exposure have been noted. One investigation utilized functional magnetic resonance imaging (fMRI) to examine the effects of alcohol exposure on brain activation during a subtraction task (Santhanam, Li, Hu, Lynch, & Coles, 2009). Authors noted decreased neuronal activation in children with histories of prenatal alcohol exposure in left superior parietal regions, right inferior parietal regions, and medial frontal gyrus. Another fMRI study (Meintjes et al., 2010) demonstrated that while control children activated expected frontal and parietal regions to perform exact addition and number processing tasks, alcohol-exposed children recruited a broader range of parietal regions to complete the same tasks. These effects persisted even after statistically controlling for IQ and further confirm that the parietal lobe is particularly affected by alcohol exposure and may be subsequently related to deficits in mathematical function in children with FASD.

Summary. A focus of recent research has been better identification of the MLD phenotype by increasing understanding of the range of deficits associated with poor mathematics (Dennis, Berch, & Mazzocco, 2009). However, because assessment of mathematics abilities is typically via global tests of achievement collapsed across a wide range of skills, understanding key deficits and mechanisms of MLD is sometimes difficult. Further research on mathematics is particularly relevant for children with FASD given their specific weakness in this domain, the importance of math skills in several aspects of daily living, and the promising efficacy of improving mathematics abilities in affected individuals. Thus, utilizing the *domain specific* model of mathematical functioning, the current study seeks to evaluate specific aspects of numerical processing that may be affected in children with FASD in order to broaden the understanding of mathematics difficulty in this population and to inform intervention strategies for remediation of deficits.

Chapter 1, in part, is currently being prepared for submission for publication of the material. Crocker, Nicole; Mattson, Sarah N. The dissertation author was the primary investigator and author of this material.

II. Methods

Subjects

Two groups of children were assessed: children with heavy prenatal alcohol exposure (the AE group; n = 27) and non-exposed typically developing controls (the CON group; n = 32). Descriptions of the groups are below. Recruitment for this project was concurrent with recruitment at the Center for Behavioral Teratology (CBT) at San Diego State University.

General Recruitment Procedure. Children in both groups were recruited through various sources: referrals from Dr. Kenneth Lyons Jones, a pediatric dysmorphologist, or other professionals; CBT community outreach; and other forms of publicity, including the internet.

Inclusion Criteria. The following criteria were required for inclusion in the proposed project: (1) aged 8:0 to 16:11; (2) English as their primary language; (3) met requirements for one of the groups detailed below.

Exclusion Criteria. The following criteria were used for exclusion from the proposed project: (1) significant head injury with loss of consciousness for > 30 minutes; (2) significant physical (e.g., uncorrected visual impairment, hemiparesis) or psychiatric (e.g., active psychosis) disability that would preclude participation; (3) other *known* causes of mental deficiency (e.g., congenital hypothyroidism, neurofibromatosis, chromosomal abnormalities); (4) parent report of either mathematics learning disorder (dyscalculia) or reading disorder (dyslexia) diagnosis; (5) children were excluded from the CON group if they met criteria for

ADHD based on the NIMH Diagnostic Interview Schedule for Children Version IV (C-DISC-4.0; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000) or (6) if greater than minimal prenatal alcohol exposure (>1 drink per week on average or >2 two drinks on any one occasion during pregnancy) was known or suspected or if information was unavailable. Because attention deficits are a hallmark feature of children with prenatal alcohol exposure and rates of ADHD diagnosis in these individuals are high (up to 95% in some samples; (Fryer, McGee, Matt, Riley, & Mattson, 2007), children were not excluded from the AE group if they met criteria for ADHD based on the C-DISC-4.0.

AE Group. Children in the AE group may or may not meet criteria for a diagnosis of fetal alcohol syndrome (FAS). As part of our larger research projects, all children received a dysmophology exam from Dr. Jones who determined all alcohol-related diagnoses, using standard criteria (Mattson et al., 2010). FAS is defined as the presence of two of three key facial features (short palpebral fissures, smooth philtrum, thin vermillion) and either microcephaly or growth deficiency or both. All children were identified retrospectively, thus precise levels and timing of exposure generally were unavailable. In all cases, positive exposure histories were confirmed via review of medical, legal, or social service records or maternal report, if it was available. Hearsay or supposition was not accepted as documentation.

Control Group. Children in the control group were recruited using similar methods but do not have histories of prenatal alcohol exposure.

Procedure

General Testing Procedures. In addition to the study tasks outlined below, children received a general neuropsychological test battery as part of regular participation within the CBT. These data include an estimate of IQ – either the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2004) or the Differential Abilities Scale (DAS; Elliott, 2007) – that was utilized in the current study. IQ scores were missing for one subject in the CON group. Children were screened for presence of psychopathology using the C-DISC-4.0. In addition, parents of children completed assessments to measure demographic and pregnancy variables, family history of substance use disorders, current caregiver psychiatric status, children's medical history, children's school and educational status, and behavioral problems in the child. Neuropsychological testing was conducted in a quiet, distraction-free room. Frequent breaks during testing were employed to minimize fatigue and maintain motivation to participate. Testing for the study was approximately 90 minutes, including breaks, and was completed in one session. Following completion of testing, subjects and their parents were provided with a financial incentive for participation ($10/hour of testing).

Measures. See Table 1. To address Specific Aim 1, four tests of the Woodcock Johnson III Tests of Achievement (WJ-III; Woodcock et al., 2007) were administered to children with prenatal alcohol exposure and controls. The *Calculation* test was used to evaluate children's ability to perform mathematical computations.

Table 1. All measures administered for the current study
Mathematics Achievement Measures
Woodcock Johnson III Tests of Achievement Calculation test Woodcock Johnson III Tests of Achievement Math Fluency test Woodcock Johnson III Tests of Achievement Applied Problems test Woodcock Johnson III Tests of Achievement Quantitative Concepts test
Reading and Spelling Achievement Measures
Woodcock Johnson III Tests of Achievement Letter-Word Identification test Woodcock Johnson III Tests of Achievement Word Attack test Woodcock Johnson III Tests of Achievement Spelling test
Numerical Processing Measures
Approximate Number Sense (ANS) Symbolic and Nonsymbolic Magnitude Judgment (MJ) Numerical Stroop
Reaction Time Measure
Choice Reaction Time (CRT) Test from the CANTAB

Items include addition, subtraction, multiplication, division, and combinations of these basic operations, as well as some geometric, trigonometric, logarithmic, and calculus operations, if age appropriate. The *Math Fluency* test was used to evaluate children's ability to perform simple addition, subtraction, and multiplication quickly. Children are given a three-minute time limit and a series of math facts to complete using paper and pencil. The *Applied Problems* test was used to evaluate children's ability to analyze and solve math problems. To solve the problems, the subject must listen to the problem, recognize the procedure to be followed, and then perform relatively simple calculations. Because many of the problems include extraneous information, each child must decide not only the appropriate mathematical operations to use but also which numbers to include in the calculation. The *Quantitative Concepts* test was used to measure children's knowledge of mathematical concepts, symbols, and vocabulary.

This test consists of two subtests: Concepts and Number Series. In the Concepts subtest, the initial items require counting and identifying numbers, shapes, and sequences. The remaining items require knowledge of mathematical terms and formulas. The subject does not perform any paper-and-pencil calculations. In the second subtest, the task requires the child to look at a series of numbers, figure out the pattern, and then provide the missing number in the series. Dependent variables are standard scores for each subtest.

In order to test the specificity of the relationships between numerical processing variables and mathematics achievement, three additional tests from the WJ-III, measuring reading and spelling, also were administered. The *Letter-Word Identification* test was used to measure children's single word reading skills. The *Word Attack* test was used to assess children's skill in applying phonic and structural analysis skills to the pronunciation of nonsense words. The *Spelling* test was used to measure children's ability to write orally presented words correctly. Early items measure prewriting skills such as drawing and tracing letters and writing upper and lower-case letters while the majority of items require subjects to spell dictated words of increasing difficulty. Dependent variables are standard scores for each subtest.

To address Specific Aim 2, three experimental tasks were administered to children with prenatal alcohol exposure and controls. These tasks have been used successfully with both typically developing (Gebuis, Cohen Kadosh, de Haan, & Henik, 2009; Halberda et al., 2008; Siegler & Booth, 2004; Zhou et al., 2007) and MLD (Ashkenazi et al., 2009; Rousselle & Noel, 2007) children ages 5 (Gebuis et al.,

2009) to 14 (Halberda et al., 2008) and adults (Halberda & Feigenson, 2008) and evaluate three related but distinct aspects of numerical processing: approximate number sense, symbolic and nonsymbolic magnitude judgment, and automaticity of numerical processing. Examples of task stimuli are included in Figures 1-4.

Approximate Number Sense (ANS). ANS refers to an individual's ability to estimate numerosity. To measure this ability, subjects performed a more/less judgment task (Halberda & Feigenson, 2008; Halberda et al., 2008). Children were presented with sets of blue and yellow dots on a computer screen (see Figure 1). These dots appear too quickly (200 ms) to be serially counted. Children were asked to indicate which dot color was more numerous by pressing a key corresponding to each color. There were 5-16 dots in each set and the ratio of blue to yellow dots (1.17, 1.28, 1.45, 2.45) was varied randomly, as was the color of each set (i.e., the larger set will not always be the same color). In addition, two perceptual controls were employed. On half of all trials, the area coverage of the dots was controlled by manipulating the size of the dots so that each set, while differing in numerosity, covered the same area. On the other half of trials, the size of the dots was controlled and all dots presented were the same size. These controls ensure that responses are made on the basis of number of dots and not total area covered by dots. Subjects participated in one session of 160 trials. Testing time was approximately 8 minutes. In typically developing children, numerical discrimination improves as the ratio between presented numerosities increases, a phenomenon known as the numerical distance effect (NDE; Halberda & Feigenson, 2008; Halberda et al., 2008). For example, subjects are generally faster and

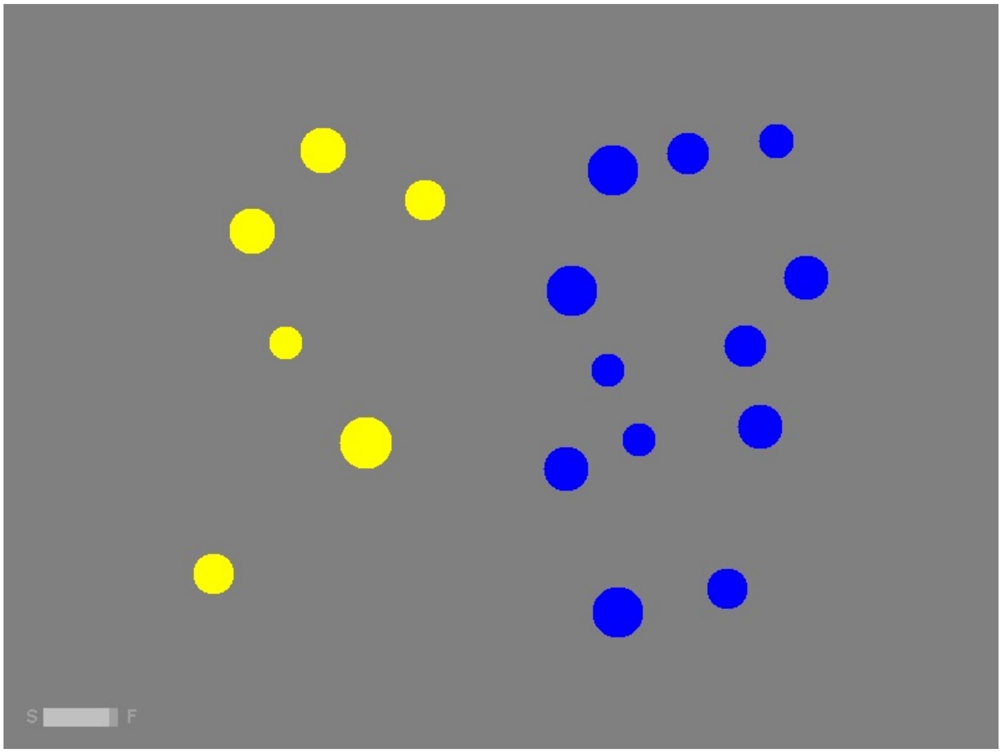


Figure 1. Example of Approximate Number Sense (ANS) task stimuli (Halberda, et al., 2008).

more accurate when the blue:yellow dot ratio is 2.45 than when it is 1.17. ANS acuity is positively correlated with mathematics achievement (Halberda et al., 2008) and children with MLD have shown deficits on similar tasks (Landerl et al., 2004). Dependent variables are mean reaction time (RT) of correct trials and accuracy (percent correct) at each level of task difficulty (i.e., at each ratio).

Symbolic and Nonsymbolic Magnitude Judgment (MJ). To evaluate whether children with prenatal alcohol exposure have difficulty accessing meaning from Arabic numerical symbols, subjects performed a symbolic and nonsymbolic MJ task. This task, adapted from Holloway and Ansari (2009), builds on the ANS task and also includes a symbolic number comparison condition in which children are presented with two Arabic digits from 1 to 9 and are asked to select the larger of the two digits. The numerical distance between stimuli ranged from 1-6 with 12 comparison trials per distance (see Figure 2). The side of the correct response was counterbalanced and reaction times were removed for trials in which a subject makes an erroneous response. Similar to findings of nonsymbolic numerical discrimination, in symbolic MJ tasks, typically developing children are faster and more accurate at making responses when the numerical distance separating two numbers is relatively large than when it is small (Holloway & Ansari, 2009). The nonsymbolic condition is similar in principle to the ANS measure, however, stimuli in this task are arrays of squares (see Figure 3). This condition provides a nonsymbolic analog to the Arabic number condition. As in the ANS task, perceptual controls were employed by varying the individual area, total area, and density of the squares across trials. Specifically, in 4 of each of the 12 distance pairings, the smaller numerosity was presented with the larger overall area. In another 4 exemplars of a particular distance, the smaller numerosity was presented with the smaller overall area. In the final 4 pairings, both the small and large numerosities had equal areas. In addition, within each group of 4 pairs, 2 of the small numerosity stimuli had larger density and 2 had smaller density compared with the large numerosity with which each was paired. Finally, individual square sizes were varied over all stimuli. Conditions (symbolic and nonsymbolic) were completed in 2 blocks of 72 presentation pairs each. Breaks between blocks were allowed. Total testing time was approximately 15 minutes for each subject. This task assesses children’s ability to map nonsymbolic magnitude information onto Arabic symbols.

Greater discrepancy between a child's symbolic and nonsymbolic magnitude judgment indicates less efficient ability to map nonsymbolic magnitude information onto Arabic numbers. In typically developing children, efficiency of symbol-to-referent connections is positively correlated with mathematics achievement (Holloway & Ansari, 2009; Mundy & Gilmore, 2009) and studies of children with MLD suggest that impairments in mathematics achievement may be better explained by inefficient mapping between symbolic and nonsymbolic representations, rather than by deficits in basic numerosity processing, per se (Iuculano, Tang, Hall, & Butterworth, 2008; Rousselle & Noel, 2007). Dependent variables are mean RT of accurate trials and accuracy for each condition (symbolic and nonsymbolic) at each level of distance (1-6).

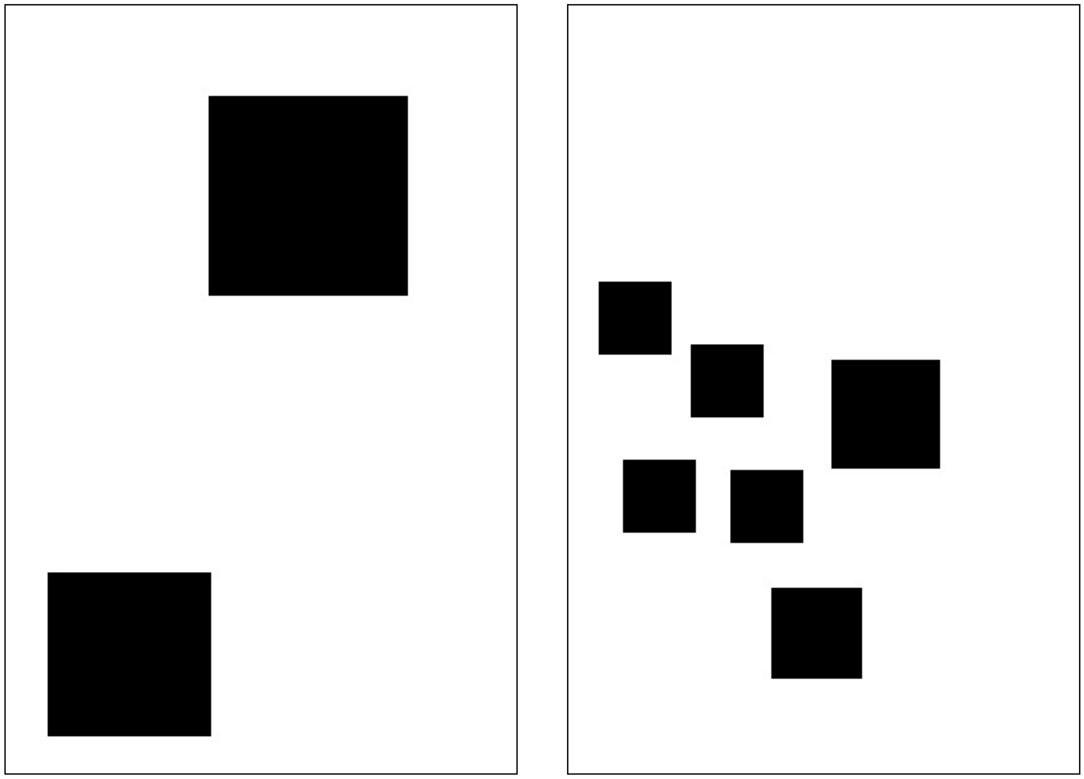


Figure 2. Examples of stimuli presented in the nonsymbolic condition of the Magnitude Judgment (MJ) task (Holloway & Ansari, 2009).

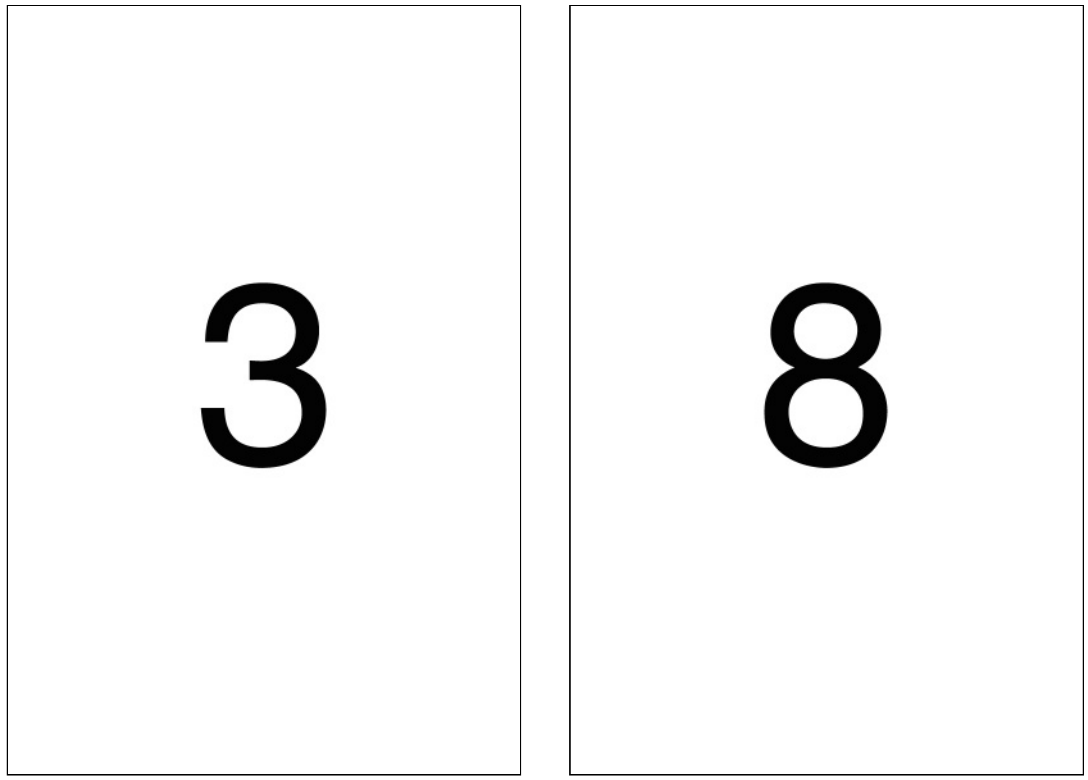


Figure 3. Examples of stimulus pairs presented in the symbolic (i.e. Arabic number) condition of the Magnitude Judgment (MJ) task (Holloway & Ansari, 2009).

Numerical Stroop. In order to assess the automatic processing of numbers, subjects performed a numerical stroop task (Cohen Kadosh et al., 2011). In this task, children were presented with pairs of digits on a computer screen varied in physical size and numerical value. Two conditions were completed: the physical size comparison and the numerical value comparison. For the physical size condition, children were asked to compare the physical sizes of the digits and ignore their numerical value. In the numerical value condition, children were asked to compare the numerical value of the numbers and ignore their physical sizes. Subjects indicated via key press which numeral (right or left) they thought was larger. Each condition was administered separately in a block of 144 trials (total of 288 trials for the task). Each block contained equal numbers of congruent (one number is bigger than the other in both physical size and numerical value), incongruent (one number is bigger in numerical value but smaller in physical size than the other), and neutral stimuli (no variations in physical size, for the value condition, or numerical value, for the size condition; see Figure 4). In addition, three levels of numerical distance were employed (1, 2, 5). Breaks were allowed between test blocks and testing time was approximately 15 minutes. Typically developing children generally produce a size congruity effect (SCE; Henik & Tzelgov, 1982) on the physical size condition, composed of *facilitation* – faster responding to congruent than to neutral trials – and *interference* – slower responding to incongruent than to neutral trials. The SCE suggests that the numerical value of each number is automatically activated to facilitate or to interfere with the physical size comparison task (Ashkenazi et al., 2009; Zhou et al., 2007). In studies of MLD, individuals fail to reproduce this SCE indicating that numerical magnitude is not activated in a way that interferes with (Koontz & Berch, 1996) or facilitates (Ashkenazi et al., 2009; Rubinsten & Henik, 2005) performance of the task. Studies have reported both decreased facilitation (Ashkenazi et al., 2009; Rubinsten & Henik, 2005) as well as decreased interference (Koontz & Berch, 1996) in children with MLD, however decreased facilitation (without effects on interference) appears to be the more robust finding. Dependent variables are RT of accurate trials and accuracy for each comparison condition (physical size and numerical value) at each trial type (congruent, incongruent, and neutral) and numerical distance (1, 2, 5).

Congruent	6 – 3
Incongruent	3 – 6
Neutral (Numerical Value Condition)	3 – 6
Neutral (Physical Size Condition)	3 – 3

Figure 4. Examples of congruent, incongruent, and neutral stimulus pairs presented in the Numerical Stroop task (Cohen Kadosh et al., 2011).

Because children with prenatal alcohol exposure generally demonstrate slowed RT relative to typically developing controls (Burden, Jacobson, & Jacobson, 2005), the Choice Reaction Time (CRT) test from the Cambridge Neuropsychological Test Automated Battery (CANTAB; Limited, 2006) was administered to determine if RT differences are specifically related to impaired numerical processing or if they are a result of more general slowed processing speed characteristic of children with FASD. The CRT is a 2-choice reaction time test in which an arrow-shaped stimulus is displayed on either the left or the right side of the screen. The subject must press the left hand button on the press pad if the stimulus is displayed on the left hand side of the screen, and the right hand button on the press pad if the stimulus is displayed on the right hand side of the screen. The outcome measure utilized in the current study is mean RT for correct trials.

Primary Data Analysis

Prior to any statistical analyses, data was inspected for multivariate outliers and violations of assumptions of normality, homogeneity of variance, and linearity. Multivariate outliers were removed based on Mahalanobis Distance > critical χ^2 value, $p < .001$. Data were not normally distributed; as such, all analyses were conducted both with and without applying data transformation (logarithmic transformation for moderate deviations from normality and inverse transformation for more significant deviations). Findings were largely unchanged after data transformation; data presented below utilize untransformed variables to facilitate meaningful interpretation of findings. Alpha levels of .05 were used to determine statistical significance. All possible main and interaction effects were explored. Statistically significant omnibus and interaction effects were followed up using pairwise comparisons and simple effects tests. For outcome variables without normative information, raw scores were used and age was included as a covariate when appropriate. Appropriateness of a covariate was determined by testing that the covariate was (1) significantly correlated with the dependent variable and (2) did not interact with the independent variable (i.e. group). All analyses utilized analysis of variance (ANOVA) and linear regression techniques, as outlined in detail below.

Aim 1: To examine the hypothesis that children with prenatal alcohol exposure will show impaired mathematics achievement performance relative to controls on the mathematics achievement tests of the WJ-III, data were analyzed as follows:

Hypothesis 1: Overall performance (standard scores) of each group was analyzed using MANOVA with WJ-III test scores as the dependent variables and group as the independent variable.

Support for this hypothesis will be evidenced by a significant group main effect, with the AE group performing more poorly than the CON group on all four WJ-III mathematics tests.

Aim 2: To examine the hypotheses that children with prenatal alcohol exposure will show impairments in aspects of numerical processing relative to controls and that these impairments will contribute to lowered mathematical achievement in children with prenatal alcohol exposure, data were analyzed as follows:

Hypothesis 2a: ANS. Mean RT of correct trials and accuracy (percent correct trials) at each level of task difficulty (ratio between sets) were analyzed separately using a 2x4 mixed model ANOVA. RT and accuracy served as dependent variables with ratio as the within-subject factor and group as the between-subjects factor.

Support for this hypothesis will be evidenced by a significant main effect of ratio and main effect of group. Follow-up tests will indicate that children perform more poorly as the ratio between presented numerosities decreases and that children in the AE group will perform more poorly than the CON group across levels of task difficulty.

Hypothesis 2b: Symbolic and Nonsymbolic MJ. Mean RT of correct trials and accuracy for each condition (symbolic and nonsymbolic) at each level of distance (1-6) was analyzed separately using a 2x2x6 mixed model ANOVA. RT and accuracy served as dependent variables with condition and distance as within-subject factors and group as the between-subjects factor.

Support for this hypothesis will be evidenced by a significant group x condition interaction. Follow-up analyses will indicate a significant effect of group (AE < CON) for both conditions and follow-up tests will support larger group differences on the symbolic condition relative to the nonsymbolic.

Hypothesis 2c: Numerical Stroop. RT and accuracy for each comparison condition (physical size and numerical value) at each trial type (congruent, incongruent, and neutral) and numerical distance (1, 2, 5) were analyzed separately using a 2x2x3x3 mixed model ANOVA. RT and accuracy served as dependent variables with condition, trial type, and distance as the within-subject factors and group as the between-subjects factor.

Support for this hypothesis will be evidenced by a significant group x condition x trial type interaction with follow-up analyses revealing that for only the physical size condition there will be a significant group x trial type interaction: the CON group will demonstrate the SCE and perform worse on incongruent vs. neutral trials and better on congruent vs. neutral trials; however, the AE group will not show the typical SCE and will perform similarly on all trial types.

Hypothesis 2d. In order to evaluate whether performance on number processing tasks is related to global mathematics achievement in the sample, mean RT and accuracy data for all tasks were also included in separate linear regression analyses. Mathematics achievement (WJ-III standard scores) served as the dependent variable and RT and accuracy for each task and group served as independent variables. Numerical processing tasks were entered together on step 1, group was entered on step 2, and the interaction terms were entered on step 3.

Support for this hypothesis will be evidenced by significant and positive associations between all numerical processing performance measures and mathematics achievement scores in both groups.

Other Data Analyses

The Relationship between Numerical Processing and other Domains of Academic Achievement. In order to evaluate the specificity of the relationship between number processing tasks and global mathematics achievement in the sample, mean RT and accuracy data for all tasks were also included in separate linear regression analyses with WJ-III tests of reading and spelling (Letter-Word Identification, Word Attack, Spelling). Reading and spelling achievement (WJ-III standard scores) served as the dependent variables and RT and accuracy for each task and group served as independent variables. Numerical processing tasks were entered together on step 1, group was entered on step 2, and the interaction terms were entered on step 3.

The Contribution of Reaction Time. Because children with prenatal alcohol exposure generally demonstrate slowed RT relative to typically developing controls (Burden et al., 2005), the CRT test from the CANTAB (Limited, 2006) was utilized as a covariate to determine if RT differences are specifically related to impaired numerical processing or if they are a result of more general slowed processing speed characteristic of children with FASD. Data are presented both with and without controlling for RT.

The Contribution of IQ. Given diminished intelligence in individuals with FASD, the issue of IQ is often raised when comparing neuropsychological performance of alcohol-exposed children and non-exposed controls. While we do not minimize the influence of overall level of functioning in determining patterns of performance in FASD, we do suggest that controlling for IQ in primary analyses via IQ-matching or covarying is problematic for several reasons. First, it creates unrepresentative groups of subjects, limiting generalizability of findings and second, it produces overcorrected results by inappropriately removing a proportion of variance explained by the domain of interest (Dennis, Francis, et al., 2009). Given the importance of consideration of these factors when evaluating the current study, data are presented both with and without the inclusion of IQ in statistical models.

Chapter 2, in part, is currently being prepared for submission for publication of the material. Crocker, Nicole; Mattson, Sarah N. The dissertation author was the primary investigator and author of this material.

III. Results

Demographic Variables

Demographic data are listed in Table 2. Groups were similar on sex [χ^2 (df=1) = 1.00, p = .318], race [χ^2 (df=4) = 4.06, p = .398], ethnicity [χ^2 (df=1) = .50, p = .481], and SES [F (1, 57) = 1.743, p = .192]. More children in the AE group were left handed relative to the CON group [χ^2 (df=1) = 3.80, p = .051]. Children in the AE group were older than children in the CON group [F (1, 57) = 6.421, p = .014], and, as anticipated, children in the AE group had significantly lower Full Scale IQ estimates than children in the CON group [F (1,56) = 44.95, p < .001].

Handedness was not significantly correlated with any outcome measure and was not included as a covariate in subsequent data analyses. Age was significantly associated with some outcome variables and was included in the model when appropriate. IQ also was significantly associated with some outcome variables. As described previously, the effects of IQ on mathematics measures were examined in a separate set of analyses.

Table 2. Demographic information for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).

Variable	AE	CON
N	27	32
Sex [N (%) Female]	10 (37.0)	16 (50.0)
Race [N (%) White]	18 (66.7)	26 (81.2)
Ethnicity [N (%) Hispanic]	9 (33.3)	8 (25.0)
Handedness [N (%) Right]*	22 (81.5)	31 (96.9)
Age in years [M (SD)]*	14.0 (2.30)	12.5 (2.34)
SES [M (SD)]+	47.2 (11.01)	51.0 (10.72)
FSIQ [M (SD)]*	86.2 (11.94)	109.7 (14.46)
Diagnosis [N (%) FAS]	11 (40.7)	0 (0)

* significant at the p < .05 level
+ SES, socioeconomic status as measured by Hollingshead

Mathematics Achievement

To examine the hypothesis that children with prenatal alcohol exposure will show impaired mathematics achievement performance relative to controls on the WJ-III tests, data were analyzed using MANOVA with WJ-III test scores as the dependent variables and group as the independent variable. Age was significantly associated with WJ-III test scores [F (1,56) = 5.932, p = .018, partial η^2 = .096] and was included in the analysis. There was a significant main effect of Group [F (1, 56) = 61.749, p < .001, partial η^2 =.775]. Children in the AE group had lower scores on all four WJ-III mathematics achievement tests relative to the CON group (ps < .001). See Table 3.

Table 3. Woodcock Johnson – III test scores for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent means and standard deviations.

Test	**AE**	**CON**
Calculation [M (SD)]*	85.6 (16.57)	115.6 (13.18)
Math Fluency [M (SD)]*	83.7 (15.78)	107.5 (12.34)
Applied Problems [M (SD)]*	85.9 (12.34)	110.3 (11.38)
Quantitative Concepts [M (SD)]*	82.3 (14.52)	109.2 (13.13)

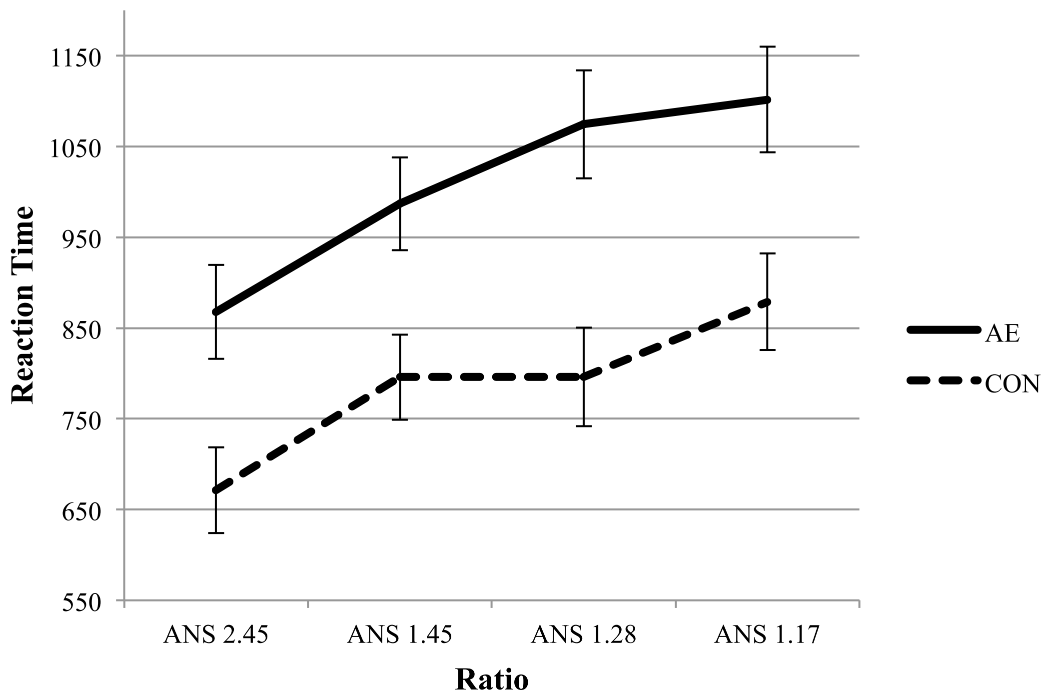
* significant at the p < .001 level

Approximate Number Sense

To examine the hypotheses that children with prenatal alcohol exposure will show impairments in their ability to estimate numerosity, RT and accuracy at each level of ratio (1.17, 1.28, 1.45, and 2.45) were analyzed separately using a 2x4 mixed model ANOVA. RT and accuracy served as dependent variables with ratio as the within-subject factor and group as the between-subjects factor. Unless otherwise indicated, only significant effects are reported.

Reaction Time. Age was significantly associated with ANS RT [F (1,56) = 9.079, p = .004, partial η^2 = .140] and was included in the analysis. A significant main effect of group was observed [F (1, 56) = 9.341, p = .003, partial η^2 = .143]. As hypothesized, children in the AE group performed more slowly than the CON group across all levels of ratio between presented numerosities. There was a significant main effect of ratio [F (3, 54) = 6.815, p = .001, partial η^2 = .275]. As expected, across groups, children's RT increased as the ratio between presented numerosities decreased (ps < .042). See Graph 1.

Graph 1. Approximate Number Sense (ANS) reaction time at each level of ratio between presented numerosities for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.



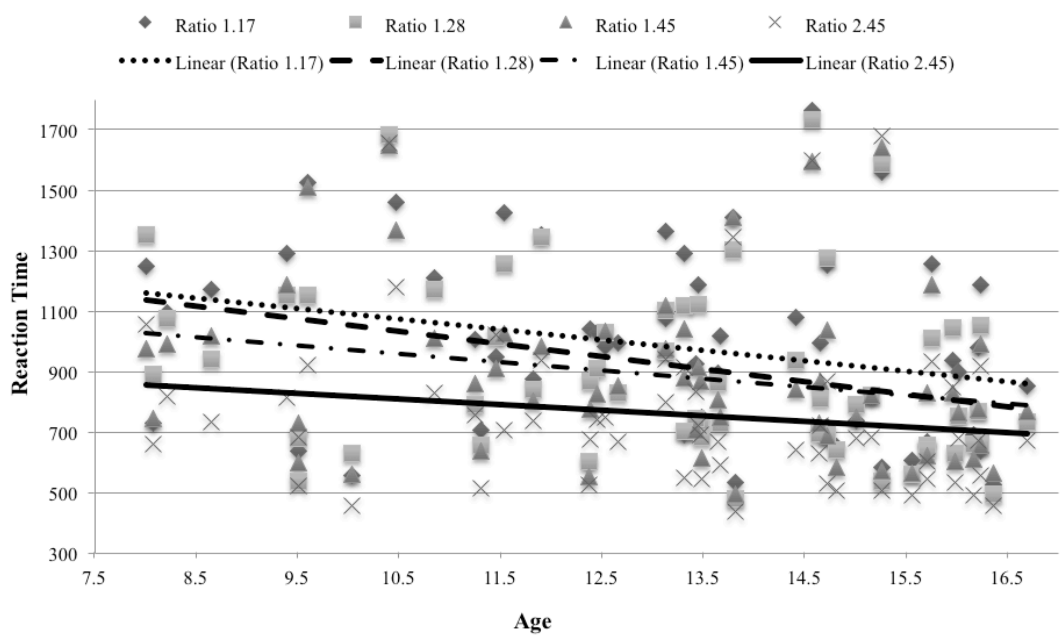
The ratio x age interaction was also significant [F (3, 54) = 2.991, p = .039, partial η^2 = .069]. Follow-up analyses indicated that, across levels of ratio, RT decreased with age (b = -29.763). However, there was a significantly greater effect of age on RT when the ratio between presented numerosities was 1.28 relative to 2.45 [F (1, 56) = 9.138, p = .004, partial η^2 = .140] and relative to 1.45 [F (1, 56) = 4.787, p = .033, partial η^2 = .079]. All other follow-up contrasts were not significant (ps > .058). See Graph 2.

Accuracy. Age was significantly associated with ANS accuracy [F (1,56) = 9.362, p = .003, partial η^2 = .143] and was included in the analysis. A significant main effect of group was observed [F (1, 56) = 7.103, p = .010, partial η^2 = .113]. As hypothesized, children in the AE group performed less accurately than the CON group across all levels of ratio. A significant main effect of ratio was observed [F (3, 54) = 4.109, p = .011, partial η^2 = .186]. As expected, across groups, children's accuracy decreased as the ratio between presented numerosities decreased (ps < .001). See Graph 3.

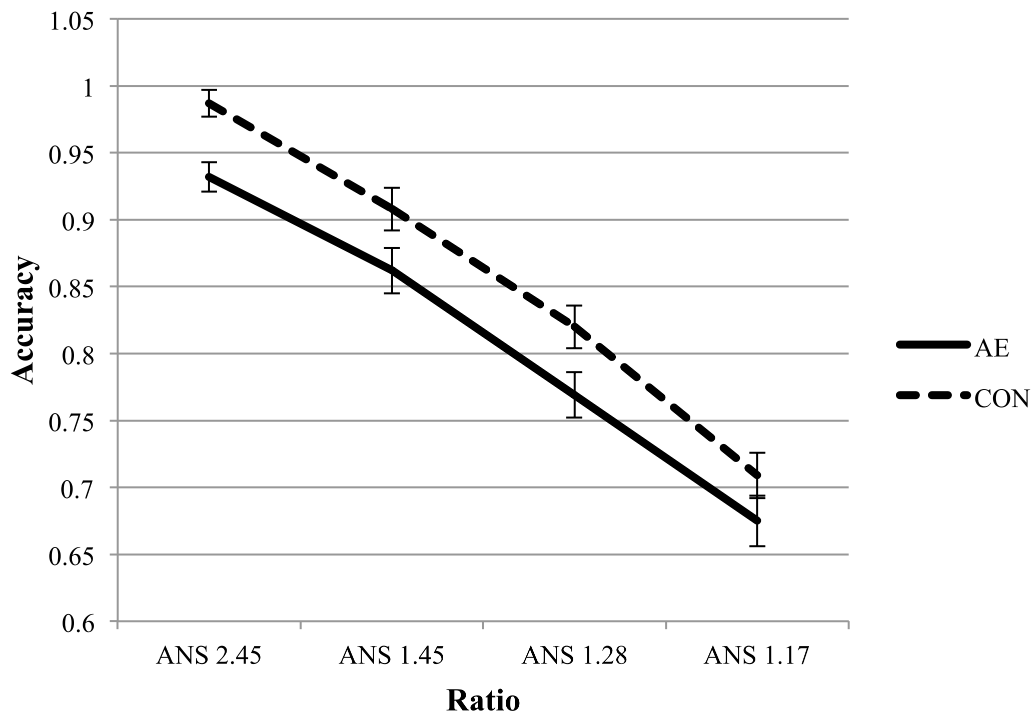
Symbolic and Nonsymbolic Magnitude Judgment

To examine the hypotheses that children with prenatal alcohol exposure will perform more poorly than controls on both conditions of the MJ task and that children with prenatal alcohol exposure will show a relative weakness in symbolic MJ vs. nonsymbolic MJ, mean RT and accuracy for each condition (symbolic and nonsymbolic) at each level of distance (1-6) was analyzed separately using a 2x2x6

Graph 2. Data represent the relationship between reaction time on the Approximate Number Sense (ANS) task and age at each level of ratio between presented numerosities.



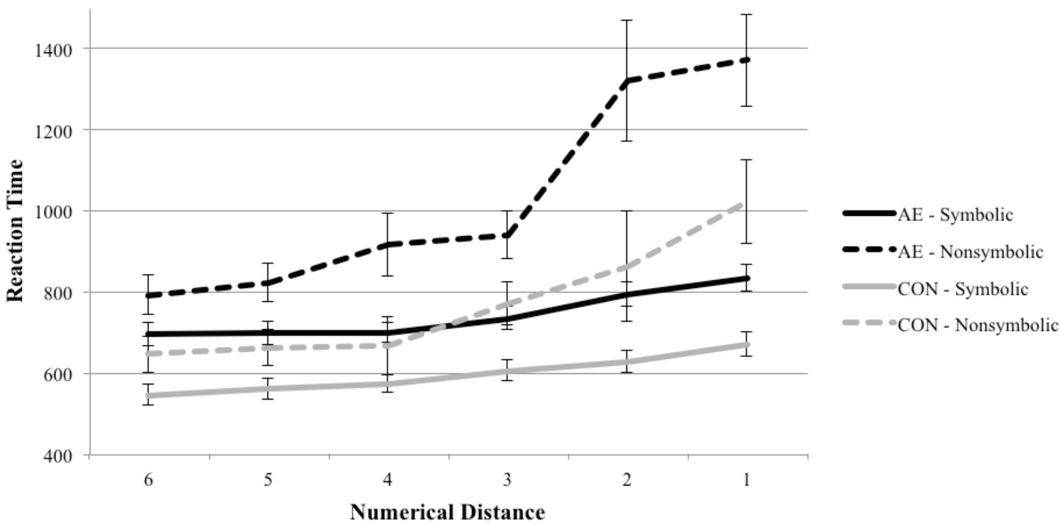
Graph 3. Approximate Number Sense (ANS) accuracy at each level of ratio between presented numerosities for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.



mixed model ANOVA. RT and accuracy served as dependent variables with condition and distance as within-subject factors and group as the between-subjects factor. Unless otherwise indicated, only significant effects are reported.

Reaction Time. Age was significantly associated with MJ RT [F (1, 56) = 17.111, p < .001, partial η^2 = .234] and was included in the analysis. There was a significant main effect of group [F (1, 56) = 9.626, p = .003, partial η^2 = .147]. Across condition and distance, children in the AE group had slower RT than children in the CON group. A significant main effect of condition was observed [F (1, 56) = 7.144, p = .010, partial η^2 = .113]. Children in both groups demonstrated faster reaction times during the symbolic condition than the nonsymbolic condition of the task. There was a significant main effect of distance [F (5, 52) = 6.837, $p < .001$, partial $\eta^2 = .397$]. Across groups, children's reaction time increased as the numerical distance between presented stimuli decreased (ps < .046), with the exception of between distances 5 and 6. There were no reaction time differences between these trials ($p = .133$). The hypothesized group x condition interaction was not significant ($p = .221$). See Graph 4.

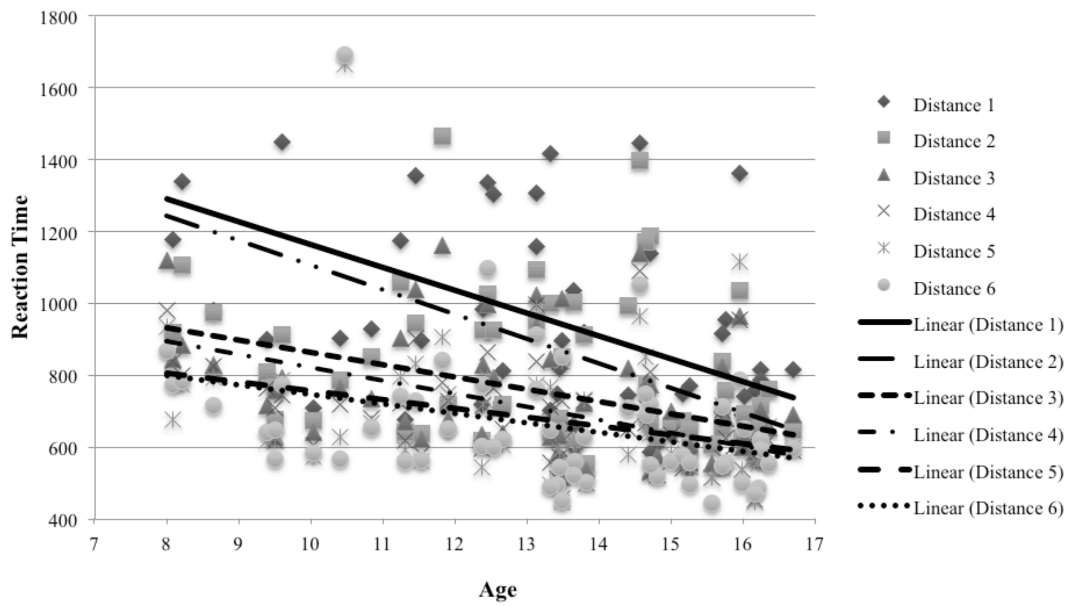
Graph 4. Symbolic and nonsymbolic magnitude judgment (MJ) reaction time at each level of numerical distance between presented stimuli for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.



A condition x distance interaction was observed [F (5, 52) = 3.548, p = .008, partial η^2 = .254]. Follow-up analyses demonstrated that at each level of distance, children demonstrated faster reaction times on the symbolic condition relative to the nonsymbolic condition of the task (ps < .002). On the symbolic condition of the task, RT significantly increased as the distance between presented stimuli decreased (ps < .002), with the exception of between distances 6 and 5 (p = .475), 6 and 4 (p = .192), and 5 and 4 (p = .503). On the nonsymbolic condition of the task, RT significantly increased as the distance between presented stimuli decreased (ps < .022), with the exception of between distances 6 and 5 (p = .205), 5 and 4 (p = .114), and 2 and 1 (p = .057).

The distance x age interaction also was significant [F (5, 52) = 3.536, p = .008, partial η^2 = .254]. Follow-up analyses indicated that RT decreased with age (b = -40.934), however, there was a significantly greater effect of age on RT when the distance between presented numerosities was 6 relative to 4 (p = .041), 2 (p = .003), and 1 (p = .001). The effect of age on RT also was significantly greater when numerical distance was 5 relative to 4 (p = .016), 3 (p = .035), 2 (p = .002), and 1 (p < .001). The effect of age on RT was significantly greater when numerical distance was 4 relative to 2 (p = .006) and 1 (p = .010). Finally, there was a significantly greater effect of age on RT when numerical distance was 3 relative to 2 (p = .005) and 1 (p = .001). All other contrasts were not significant (ps > .089). See Graph 5.

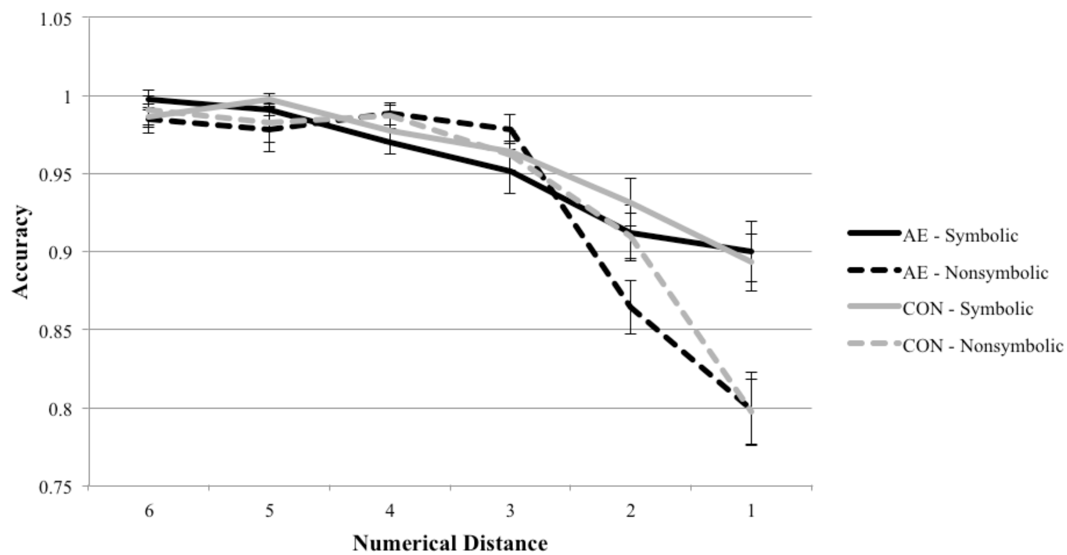
Graph 5. Data represent the relationship between reaction time on the Magnitude Judgment (MJ) task and age at each level of numerical distance between presented stimuli.



Accuracy. Age was not significantly associated with MJ accuracy and was not included in the analysis. A significant main effect of condition was observed [F (1, 57) = 16.660, p = < .001, partial η^2 = .226]. Children in both groups were more accurate during the symbolic condition relative to the nonsymbolic condition of the task. There was a significant main effect of distance [F (5, 53) = 40.125, p < .001, partial η^2 = .791]. Across groups, children's accuracy decreased as the numerical distance between presented stimuli decreased (ps < .05), with the exception of between distances 4 and 5 and 5 and 6. There were no accuracy differences between these trials (ps > .132).

A condition x distance interaction also was observed [F (5, 53) = 8.015, p < .001, partial η^2 = .431]. Follow-up analyses revealed that when the numerical distance between presented stimuli was 2 (p = .019) and 1 (p < .001), children demonstrated greater accuracy on the symbolic condition relative to the nonsymbolic condition of the task. However, when distance between stimuli was 4, children demonstrated greater accuracy on the nonsymbolic condition relative to the symbolic condition (p = .051). There were no significant differences between conditions when numerical distance was 6, 5, and 3 (ps > .146). On the symbolic condition on the task, children performed more accurately as distance between stimuli increased (ps < .012), with the exception of between distances of 6 and 5 (p = .476), 4 and 3 (p = .137), and 2 and 1 (p = .115). On the nonsymbolic condition of the task, children performed more accurately as distance between stimuli increased (ps < .035), with the exception of between distances 6 and 5 (p = .177), 6 and 4 (p = .964), 5 and 4 (p = .334) and

Graph 6. Symbolic and nonsymbolic Magnitude Judgment (MJ) accuracy at each level of numerical distance between presented stimuli for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.



between distances of 5 and 3 ($p = .330$). Hypothesized effects of group and the group x condition interaction were not significant (ps > .505). See Graph 6.

Numerical Stroop

To test the hypothesis that children in the CON group will demonstrate a size congruency effect (SCE; i.e., faster RT/greater accuracy for congruent trials vs. neutral and incongruent trials and slower RT/poorer accuracy for incongruent trials vs. neutral and congruent trials) for both conditions of the numerical stroop task and that children in the AE group will not on the physical size condition, RT and accuracy for each comparison condition (physical size and numerical value) at each trial type (congruent, incongruent, and neutral) and numerical distance (1, 2, 5) were analyzed separately using a 2x2x3x3 mixed model ANOVA. RT and accuracy served as dependent variables with condition, trial type, and distance as the within-subject factors and group as the between-subjects factor. Unless otherwise indicated, only significant effects are reported.

Reaction Time. Age was significantly associated with numerical stroop RT [F (1, 56) = 32.756, $p < .001$, partial $\eta^2 = .369$] and was included in the analysis. A main effect of group was observed [F (1, 56) = 25.942, $p < .001$, partial $\eta^2 = .317$]. Across condition, trial type, and distance, children in the AE group had slower RT than children in the CON group. There was a main effect of trial type [F (2, 55) = 8.023, $p = .001$, partial $\eta^2 = .226$]. Across levels of condition and distance, children in both groups demonstrated the typical SCE (ps < .001). There was a main effect of distance [F (2, 55) = 5.995, $p = .004$, partial $\eta^2 = .179$], such that across conditions and trial types, children in both groups demonstrated longer RT as the distance between presented numerals decreased (*p*s < .001).

The condition x distance interaction was significant [F (2, 55) = 3.198, p = .049, partial η^2 = .104]. Follow-up analyses revealed that across trial types, children in both groups demonstrated longer RT as the distance between presented numerals decreased for only the numerical value condition of the task (*p*s < .001). There was no effect of distance on the physical size condition (*p*s > .444). In addition, children did not display differential RT between conditions, except for when the distance between the numerals was small; when the distance between numbers was 1, children were faster on the physical size condition of the task (p < .001).

The type x distance interaction was significant [F (4, 53) = 4.585, p = .003, partial η^2 = .257]. Follow-up analyses showed that for congruent and neutral trials, children's RT increased as the distance between the numerals decreased (*p*s < .026). However, for incongruent trials, children's RT was only increased when distance between numerals was 1 relative to 5 (p < .001) and 2 (p = .006); children did not demonstrate increased RT on trials where distance between numerals was 5 relative to 2 (p = .070). In addition, when the distance between the numerical stimuli presented were 1 and 2, children did not demonstrate differential RT for congruent and neutral trials (*p*s > .062).

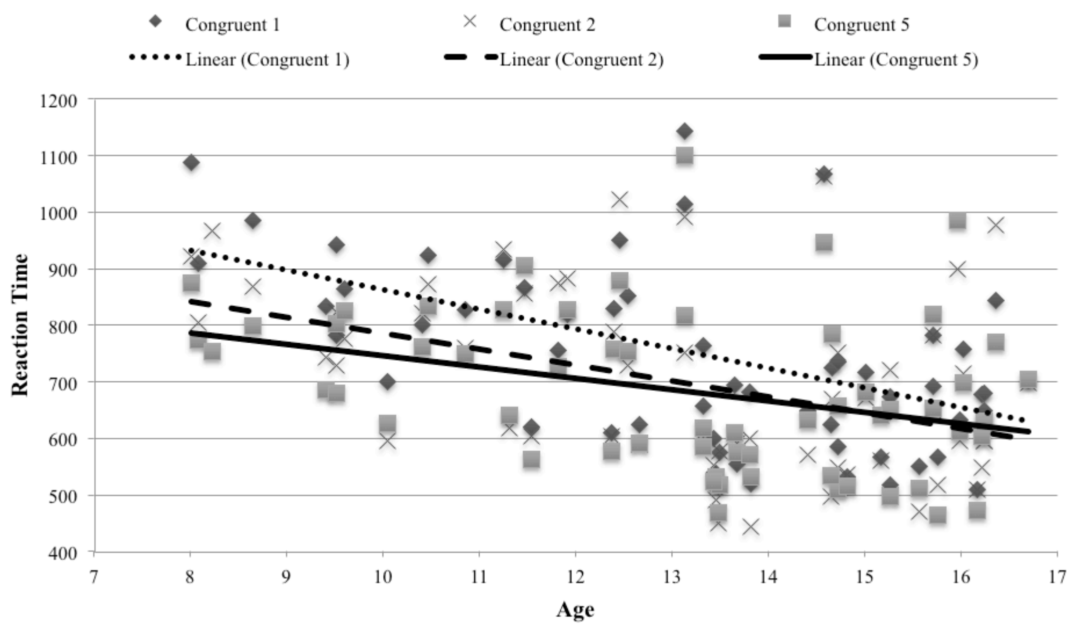
The type x distance x age interaction was also significant [F (4, 53) = 4.012, p = .006, partial η^2 = .232]. Follow-up analyses revealed that the distance x age interaction was only significant for congruent [F (2, 55) = 7.092, p = .002, partial η^2 =

.205] trial types. For congruent trials, RT decreased with age (*b* = -27.655), however, there was a significantly greater effect of age on RT when the distance between presented numerals was 2 relative to 5 [F (1, 56) = 5.756, p = .020, η^2 = .093] and when distance was 1 relative to 5 [F (1, 56) = 12.646, p < .001, η^2 = .184]. The effect of age on RT was similar for distances of 2 and 1 (p = .150). See Graph 7.

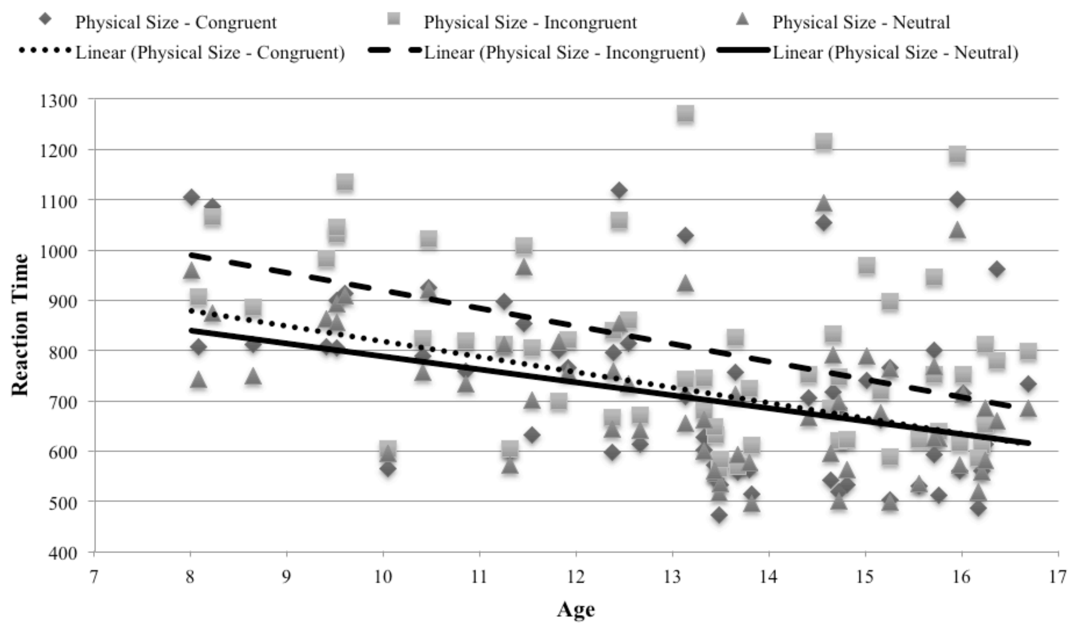
The condition x type x age interaction also was significant [F (2, 55) = 4.012, p = .005, partial η^2 = .176]. Follow-up analyses revealed that the type x age interaction was only significant for the physical size condition of the task [F (2, 55) = 4.686, p = .013, partial η^2 = .146]. On the physical size condition, RT decreased with age (*b* = -30.304), however, there was a significantly greater effect of age for incongruent trials relative to neutral trials [F (1, 56) = 8.550, p = .005, partial η^2 = .132] and for congruent trials relative to neutral trials [F (1, 56) = 4.038, p = .049, partial η^2 = .067]. The effect of age on RT was similar for congruent and incongruent trials (p = .308). See Graph 8.

The group x type [F (2, 55) = 3.834, p = .028, partial η^2 = .122], condition x type [F (2, 55) = 10.665, p < .001, partial η^2 = .279], and group x condition x type [F (2, 55) = 3.501, p = .037, partial η^2 = .113] interactions were significant. Follow-up of the three-way interaction indicated that both groups demonstrated the typical SCE on the numerical value condition of the task (*p*s < .007), and that groups' pattern of performance across trial types differed on the physical size condition of the task, though not as expected. In the CON group, children demonstrated similar reaction times for congruent and neutral trials (p = .453) relative to incongruent trials (*p*s >

Graph 7. Data represent the relationship between reaction time on only congruent trials of the Numerical Stroop task and age at each level of numerical distance between presented stimuli.

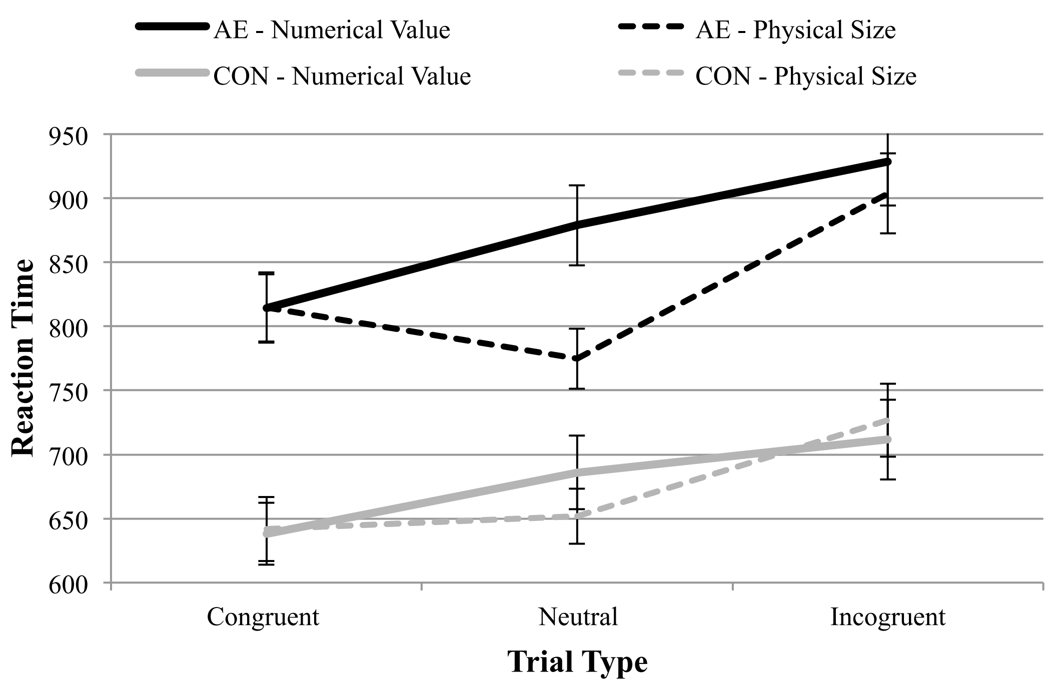


Graph 8. Data represent the relationship between reaction time on the physical size comparison condition of the Numerical Stroop task and age at each trial type (congruent, incongruent, neutral).



.05). In the AE group, children demonstrated differential reaction times for all trial types, however not in the expected direction; children in the AE group demonstrated *slower* RT on congruent trials relative to neutral trials ($p = .007$). They also demonstrated slower RT on incongruent trials relative to neutral and congruent trials (ps < .001). Additionally, children in the CON group did not demonstrate differential RT between the numerical value and physical size condition of the task for any trial type (ps > .174). However, children in the AE group demonstrated faster RT on the physical size condition of the task when the trial type was neutral ($p < .001$). They did not demonstrate differential RT between the numerical value and physical size conditions of the task for congruent and incongruent trials (ps > .475). See Graph 9.

Graph 9. Numerical Stroop reaction time for each condition (numerical value, physical size) at each trial type (congruent, neutral, incongruent) for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.

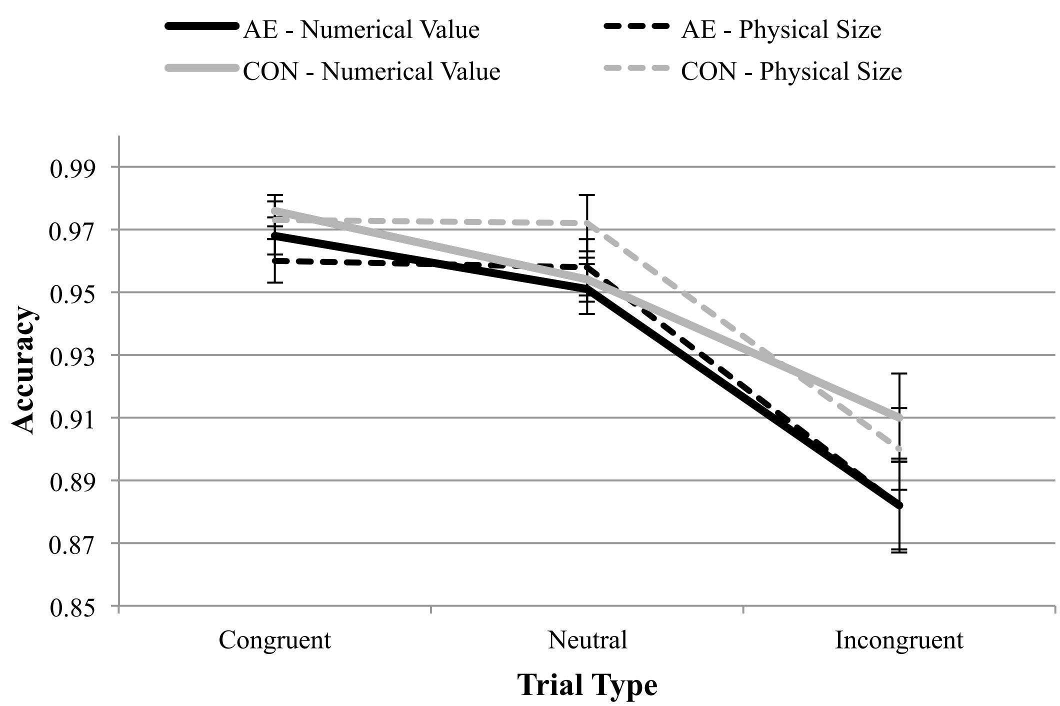


Accuracy. Age was not significantly associated with numerical stroop accuracy and was not included in the analysis. A main effect of trial type was observed [F (2, 56) = 64.509, p < .001, partial η^2 = .697]. Across levels of condition and distance, children in both groups demonstrated the typical SCE (ps < .003). There was a main effect of distance [F (2, 56) = 16.156, p < .001, partial η^2 = .366], such that across conditions and trial types, children in both groups demonstrated decreased accuracy as the distance between presented numerals decreased (ps < .001).

The condition x type [F (2, 56) = 5.244, p = .008, partial η^2 = .158], condition x distance [F (2, 56) = 38.134, p < .001, partial η^2 = .577], and condition x type x distance interactions were significant. Follow-up of the three-way interaction indicated that on the numerical value condition of the tasks, children in both groups demonstrated the typical SCE when the distance between the numerals was 1 and 2 (ps < .021), however when the distance between the numerals was 5, children demonstrated similar accuracy on congruent and neutral trials (p = .106) and performed less accurately on incongruent trials relative to congruent and neutral trials (ps < .004). On the physical size condition of the task, across all trial types, children in both groups demonstrated similar accuracy on congruent and neutral trials (p = .318) and performed less accurately on incongruent trials relative to congruent and neutral trials (ps < .001). In addition, for neutral and incongruent trials, children demonstrated significant differences in accuracy between the numerical value and physical size conditions of the task (physical size > numerical value) when the distance between presented numerals was 1 and 5 (ps < .015); when the distance between numerals was

2, children performed similarly across the two conditions of the task ($p = .321$). However, for congruent trials, there were significant differences in accuracy between the numerical value and physical size conditions of the task (physical size > numerical value) only when the distance between presented numerals was 1 ($p = .001$); there were no differences in accuracy across conditions of the task at distances of 2 and 5 (ps > .058). Hypothesized effects of group and the group x condition x type interaction were not significant (ps > .168). See Graph 10.

Graph 10. Numerical Stroop accuracy for each condition (numerical value, physical size) at each trial type (congruent, neutral, incongruent) for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group). Data represent mean values +/- standard error of the mean.



The Contribution of Reaction Time

CRT was significantly associated with ANS RT, MJ RT, and numerical stroop RT and did not interact with group. Primary data analyses for these dependent variables were repeated with the inclusion of CRT as a covariate to determine if RT differences are specifically related to impaired numerical processing or if they are a result of more general slowed processing speed characteristic of children with FASD.

ANS RT. CRT was significantly associated with ANS RT [F (1,55) = 3.951, p = .052, partial η^2 = .067] and was included in the analysis. A marginally significant main effect of group was observed [F (1, 55) = 3.375, p = .072, partial η^2 = .058]. Children in the AE group performed more slowly than the CON group across all levels of ratio between presented numerosities. The main effect of ratio [F (3, 53) = 1.136, p = .343, partial η^2 = .060] was no longer significant once RT was taken into account. In both groups, children's RT was similar across levels of ratio.

MJ RT. CRT [F (1,55) = 8.226, p = .006, partial η^2 = .130] and age [F (1,55) = 6.568, p = .013, partial η^2 = .107] were significantly associated with MJ RT and were included in the analysis. The main effect of group was no longer significant once RT was controlled [F (1,55) = 2.453, p = .123, partial η^2 = .043]. All other within-subjects effects were also not significant (ps > .087).

Numerical Stroop RT. CRT [F (1,55) = 9.782, p = .003, partial η^2 = .151] and age [F (1,55) = 16.014, p < .001, partial η^2 = .226] were significantly associated with numerical stroop RT and were included in the analysis. A significant main effect of group was observed [F (1,55) = 11.366, p = .001, partial η^2 = .171]. Children in the

AE group performed more slowly than the CON group across levels of condition, distance, and trial type, even after RT was taken into account.

The group x type [F (2,54) = 3.336, p = .043, partial η^2 = .110], condition x type [F (2,54) = 3.136, p = .051, partial η^2 = .104], and the group x condition x type [F (2,54) = 11.366, p = .054, partial η^2 = .102] interactions were statistically significant. Follow-up of the three-way interaction indicated that that both groups demonstrated the typical SCE on the numerical condition of the task (ps < .013). However, groups' pattern of performance across trial types differed on the physical size condition of the task. In the CON group, children demonstrated similar reaction times for congruent and neutral trials (p = .292) relative to incongruent trials (ps < .001). In the AE group, children demonstrated differential reaction times for all trial types, however not in the expected direction; children in the AE group demonstrated *slower* RT on congruent trials relative to neutral trials (p = .004). They also demonstrated slower RT on incongruent trials relative to neutral and congruent trials (ps < .001). Additionally, children in the CON group did not demonstrate differential RT between the numerical value and physical size condition of the task for any trial type (ps > .173). However, children in the AE group demonstrated faster RT on the physical size condition of the task when the trial type was neutral (p = .001). They did not demonstrate differential RT between the numerical value and physical size conditions of the task for congruent and incongruent trial types (ps > .550).

The condition x type x age interaction was statistically significant [F (2, 54) = 4.758, p = .013, partial η^2 = .150]. Follow-up analyses revealed that the type x age interaction was only significant for the physical size condition of the task [F (2, 54) = 4.089, p = .022, partial η^2 = .132]. On the physical size condition, RT decreased with age (b = -20.049), however, there was a significantly greater effect of age for incongruent trials relative to neutral trials [F (1, 55) = 6.413, p = .014, partial η^2 = .104] and for congruent trials relative to neutral trials [F (1, 55) = 4.990, p = .030, partial η^2 = .083]. The effect of age on RT was similar for congruent and incongruent trials (p = .624).

The type x distance x CRT interaction was statistically significant [F (4, 52) = 4.181, p = .043, partial η^2 = .243]. Follow-up analyses revealed that the distance x CRT interaction was only significant for incongruent [F (2, 54) = 3.668, p = .032, partial η^2 = .120] trial types. For incongruent trials, numerical stroop RT increased as CRT increased (b = 1.395), however, there was a significantly greater effect of CRT on numerical stroop RT when the distance between presented numerals was 1 relative to 5 [F (1, 55) = 7.310, p = .009, η^2 = .117]. The effect of CRT on RT was similar for distances of 5 and 2 (p = .066) and 2 and 1 (p = .310).

Relation between Numerical Processing and Mathematics Achievement

In order to evaluate whether performance on numerical processing tasks is related to global mathematics achievement in the sample, mean RT and accuracy data for all tasks were included in separate hierarchical linear regression analyses. Mathematics achievement (WJ-III standard scores) served as the dependent variable and RT and accuracy for each task and group served as independent variables. Age was significantly associated with all WJ-III scores and also was included as an independent variable in all analyses. Numerical processing tasks and age were entered together on step 1, group was entered on step 2, and the interaction terms were entered on step 3. Data are summarized in Table 4 (RT) and Table 5 (accuracy).

Reaction Time. For all four WJ-III indices, model one (age and numerical processing measures) accounted for a significant amount of variance in mathematics achievement. When coefficients for each measure were evaluated, age and numerical stroop RT were significant predictors of all math achievement measures and MJ RT was a significant predictor of Calculation, Applied Problems, and Quantitative Concepts scores. ANS RT was not significantly associated with any WJ-III measure. Also, for all WJ-III indices, model fit improved with the addition of group in model 2; however, the interaction terms included in model 3 did not account for a significant increase in explained variance in mathematics achievement. See Table 4.

Table 4. Summary of the results of hierarchical linear regression analyses evaluating the relationship between reaction time on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and mathematics achievement (WJ-III tests of Calculation, Math Fluency, Applied Problems, and Quantitative Concepts). Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 1	***F* (4, 54) =10.41, R^2 = .394, *p* < .001**		***F* (4, 54) = 13.00, R^2 = .453, *p* < .001**		***F* (4, 54) =18.46, R^2 = .546, *p* < .001**		***F* (4, 54) = 13.32, R^2 = .459, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age	**-5.793**	**< .001**	**-5.202**	**< .001**	**-5.172**	**< .001**	**-5.464**	**< .001**
ANS	0.000	.977	-0.01	.197	-0.004	.505	0.000	.967
MJ	**-0.025**	**.023**	-0.002	.852	**-0.017**	**.029**	**-0.024**	**.012**
Numerical Stroop	**-0.045**	**.010**	**-0.059**	**< .001**	**-0.051**	**< .001**	**-0.048**	**.002**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 2	**ΔR^2 = .170, *p* < .001**		**ΔR^2 = .072, *p* = .005**		**ΔR^2 = .100, *p* < .001**		**ΔR^2 = .170, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Group	**-2.991**	**.005**	**-12.819**	**.005**	**-13.957**	**< .001**	**-17.635**	**< .001**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 3	ΔR^2 = .006, *p* = .936		ΔR^2 = .016, *p* = .765		ΔR^2 = .021, *p* = .495		ΔR^2 = .018, *p* = .657	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age x Group	-0.508	.827	-1.181	.575	-0.091	.956	-2.415	.240
ANS x Group	-0.007	.669	0.002	.867	-0.012	.308	-0.012	.379
MJ x Group	-0.008	.728	0.007	.754	0.012	.484	0.014	.521
Numerical Stroop x Group	0.024	.539	-0.045	.199	-0.029	.286	-0.029	.394

Accuracy. For all four WJ-III indices, model one (age and numerical processing measures) accounted for a significant amount of variance in mathematics achievement. When coefficients for each measure were evaluated, age was a significant predictor of all math achievement measures. ANS accuracy was a significant predictor of Calculation, Applied Problems, and Quantitative Concepts scores, and numerical stroop accuracy was a significant predictor of Calculation and Quantitative Concepts scores. MJ accuracy was not significantly associated with any WJ-III measure. Also, for all WJ-III indices, model fit improved with the addition of group in model 2; however, the interaction terms included in model 3 did not account for a significant increase in explained variance in mathematics achievement, with one exception; when the relationship between numerical processing accuracy and Math Fluency was evaluated, a significant ANS accuracy x group interaction emerged (see Table 5).

To follow up this effect, separate regression analyses examining the relationship between ANS accuracy and Math Fluency were conducted for each group. In the CON group, the model was marginally significant [F (2, 29) = 3.013, R^2 = .172, p = .065]. However neither age (p = .193) nor ANS accuracy (p = .119) were independent significant predictors of Math Fluency. In the AE group, the model did not account for a significant amount of variance in Math Fluency test scores [F (2, 29) = 2.257, R^2 = .158, p = .126].

Table 5. Summary of the results of hierarchical linear regression analyses evaluating the relationship between accuracy on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and mathematics achievement (WJ-III tests of Calculation, Math Fluency, Applied Problems, and Quantitative Concepts). Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 1	***F* (4, 54) = 9.16, R^2 = .360, *p* < .001**		***F* (4, 54) = 5.09, R^2 = .220, *p* = .001**		***F* (4, 54) = 8.08, R^2 = .328, *p* < .001**		***F* (4, 54) = 10.53, R^2 = .396, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age	**-4.743**	**< .001**	**-3.677**	**< .001**	**-3.836**	**< .001**	**-4.327**	**< .001**
ANS	**97.875**	**.009**	32.869	.349	**83.763**	**.007**	**112.419**	**.001**
MJ	3.136	.969	87.022	.262	9.372	.888	48.725	.495
Numerical Stroop	**164.406**	**.012**	89.189	.149	96.688	.070	**114.574**	**.046**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 2	**ΔR^2 = .226, *p* < .001**		**ΔR^2 = .232, *p* < .001**		**ΔR^2 = .242, *p* < .001**		**ΔR^2 = .200, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Group	**-22.608**	**< .001**	**-19.966**	**< .001**	**-18.85**	**< .001**	**-19.427**	**< .001**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 3	ΔR^2 = .021, *p* = .582		**ΔR^2 = .088, *p* = .043**		ΔR^2 = .013, *p* = .785		ΔR^2 = .033, *p* = .318	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age x Group	-2.960	.123	-2.241	.211	-0.203	.897	-3.241	.058
ANS x Group	30.314	.620	**121.157**	**.038**	55.363	.276	66.898	.219
MJ x Group	-68.203	.602	236.326	.058	-16.34	.808	-6.442	.956
Numerical Stroop x Group	-17.751	.884	-167.90	.145	-91.421	.367	-70.351	.514

Relation between Numerical Processing and other Domains of Academic Achievement

In order to test the specificity of the relationships between numerical processing and mathematics achievement measures, additional regression analyses were conducted evaluating the relationship between numerical processing measures and WJ-III tests of reading and spelling (Letter-Word Identification, Word Attack, Spelling). Reading and spelling measures (WJ-III standard scores) served as dependent variables and RT and accuracy for each task and group served as independent variables. Age was significantly associated with all WJ-III scores and also was included as an independent variable in all analyses. Numerical processing tasks and age were entered together on step 1, group was entered on step 2, and the interaction terms were entered on step 3. Data are summarized in Table 6 (RT) and Table 7 (accuracy).

Reaction Time. For all three WJ-III indices, model one (age and numerical processing measures) accounted for a significant amount of variance in reading and spelling achievement. When coefficients for each measure were evaluated, age was a significant predictor of all reading and spelling measures. MJ RT and numerical stroop RT were significant predictors of Letter-Word Identification and Spelling scores. ANS RT was not significantly associated with any WJ-III measure and none of the numerical processing measures were significant predictors of Word-Attack scores. Also, for all WJ-III indices, model fit did not improve with the addition of group in model 2, nor the interaction terms included in model 3. See Table 6.

Table 6. Summary of the results of hierarchical linear regression analyses evaluating the relationship between reaction time on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and reading and spelling achievement (WJ-III Letter-Word Identification, Word Attack, and Spelling). Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 1	**F (4, 54) = 13.83, R^2 = .469, p < .001**		**F (4, 54) = 2.97, R^2 = .119, p = .028**		**F (4, 54) = 7.63, R^2 = .314, p < .001**	
	b	***p***	**b**	***p***	**b**	***p***
Age	**-3.392**	**< .001**	**-1.522**	**.011**	**-3.061**	**< .001**
ANS	-.002	.579	-.006	.229	-.002	.764
MJ	**-.017**	**.003**	-.007	.257	**-.019**	**.024**
Numerical Stroop	**-.017**	**.047**	-.009	.343	**-.034**	**.013**
	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 2	ΔR^2 = .006, p = .420		ΔR^2 = .000, p = .990		ΔR^2 = .029, p = .116	
	b	***p***	**b**	***p***	**b**	***p***
Group	-2.304	.420	-.040	.990	-6.792	.116
	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 3	ΔR^2 = .019, p = .747		ΔR^2 = .060, p = .431		ΔR^2 = .021, p = .786	
	b	***p***	**b**	***p***	**b**	***p***
Age x Group	-.431	.754	1.249	.423	2.289	.270
ANS x Group	.007	.476	.006	.553	.010	.468
MJ x Group	-.011	.443	-.026	.115	-.005	.816
Numerical Stroop x Group	-.014	.533	.016	.532	.015	.661

Accuracy. For all three WJ-III indices, model one (age and numerical processing measures) accounted for a significant amount of variance in reading and spelling achievement. When coefficients for each measure were evaluated, age was a significant predictor of all reading and spelling measures. ANS accuracy and numerical stroop accuracy were significant predictors of Letter-Word Identification and Spelling scores. MJ accuracy was not significantly associated with any WJ-III measure and none of the numerical processing measures were significant predictors of Word-Attack scores. Also, for both reading measures, model fit did not improve with the addition of group in model 2; however for Spelling test scores, the addition of group led to a significant increase in explained variance. Across all WJ-III measures the interaction terms did not significantly improve model fit when included in model 3. See Table 7.

Table 7. Summary of the results of hierarchical linear regression analyses evaluating the relationship between accuracy on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and reading and spelling achievement (WJ-III Letter-Word Identification, Word Attack, and Spelling). Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 1	**F (4, 54) = 10.20, R^2 = .388, p < .001**		**F (4, 54) = 5.04, R^2 = .218, p = .002**		**F (4, 54) = 8.51, R^2 = .341, p < .001**	
	b	***p***	**b**	***p***	**b**	***p***
Age	**-2.803**	**< .001**	**-1.274**	**.015**	**-2.254**	**.002**
ANS	**52.571**	**.008**	36.121	.065	**72.219**	**.009**
MJ	-29.629	.485	69.465	.106	69.599	.240
Numerical Stroop	**88.304**	**.011**	62.293	.069	**135.072**	**.005**
	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 2	ΔR^2 = .038, p = .057		ΔR^2 = .003, p = .657		**ΔR^2 = .070, p = .011**	
	b	***p***	**b**	***p***	**b**	***p***
Group	-5.011	.057	-1.189	.657	**-9.122**	**.011**
	Letter-Word Identification		**Word Attack**		**Spelling**	
Model 3	ΔR^2 = .044, p = .371		ΔR^2 = .013, p = .919		ΔR^2 = .022, p = .721	
	b	***p***	**b**	***p***	**b**	***p***
Age x Group	-1.200	.323	-.102	.937	-1.208	.471
ANS x Group	55.555	.157	12.165	.770	45.107	.403
MJ x Group	48.691	.559	-42.644	.633	93.837	.417
Numerical Stroop x Group	53.009	.495	65.024	.435	13.448	.900

The Contribution of IQ

Given group differences on IQ, it was evaluated for appropriateness of inclusion as a covariate in data analyses. Overall, IQ was significantly associated with all four WJ-III mathematics achievement subtests and this relationship did not interact with group. Therefore, primary data analyses for these dependent variables were repeated with the inclusion of IQ as a covariate in order to evaluate the effect of global intellectual function on mathematics achievement.

When correlations between IQ and numerical processing measures were evaluated, IQ was not associated with ANS reaction time or with accuracy scores on any numerical processing measure, and these relationships were similar in both groups. However, for symbolic and nonsymbolic MJ and both the numerical value and physical size conditions of the numerical stroop task, group significantly interacted with the relationship between these numerical processing measures and IQ. Given differences in the relationships between numerical processing and IQ, both across measures and between groups, it was determined that inclusion of IQ as a covariate in the original mixed model ANOVA analyses was inappropriate.

Instead, the relationship between IQ and MJ RT and IQ and numerical stroop RT was modeled separately for each group using linear regression analyses, with each numerical processing measure as the independent variable and IQ and age as the dependent variables. Because ANS RT and accuracy, MJ accuracy, and numerical stroop accuracy were not correlated with IQ in either group, analyses utilizing these measures as independent variables were not conducted. Correlations between mathematics achievement and numerical processing measures and IQ are presented in Table 8.

Table 8. Correlations (r) between mathematics achievement and numerical processing measures and IQ estimate for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).

Variable	**AE**	**CON**
WJ-III Calculation	.325	.538**
WJ-III Math Fluency	.222	.452*
WJ-III Applied Problems	.635**	.728**
WJ-III Quantitative Concepts	.564**	.576**
ANS RT	-.082	-.073
ANS Accuracy	.331	.068
Symbolic MJ RT	-.444*	-.007
Symbolic MJ Accuracy	-.194	-.067
Nonsymbolic MJ RT	-.398*	-.181
Nonsymbolic MJ Accuracy	-.154	.005
Numerical Stroop - Numerical Value RT	-.488**	.085
Numerical Stroop - Numerical Value Accuracy	.154	.103
Numerical Stroop - Physical Size RT	-.533**	-.075
Numerical Stroop - Physical Size Accuracy	.142	.252

** significant at the $p < .001$ level
* significant at the $p < .05$ level

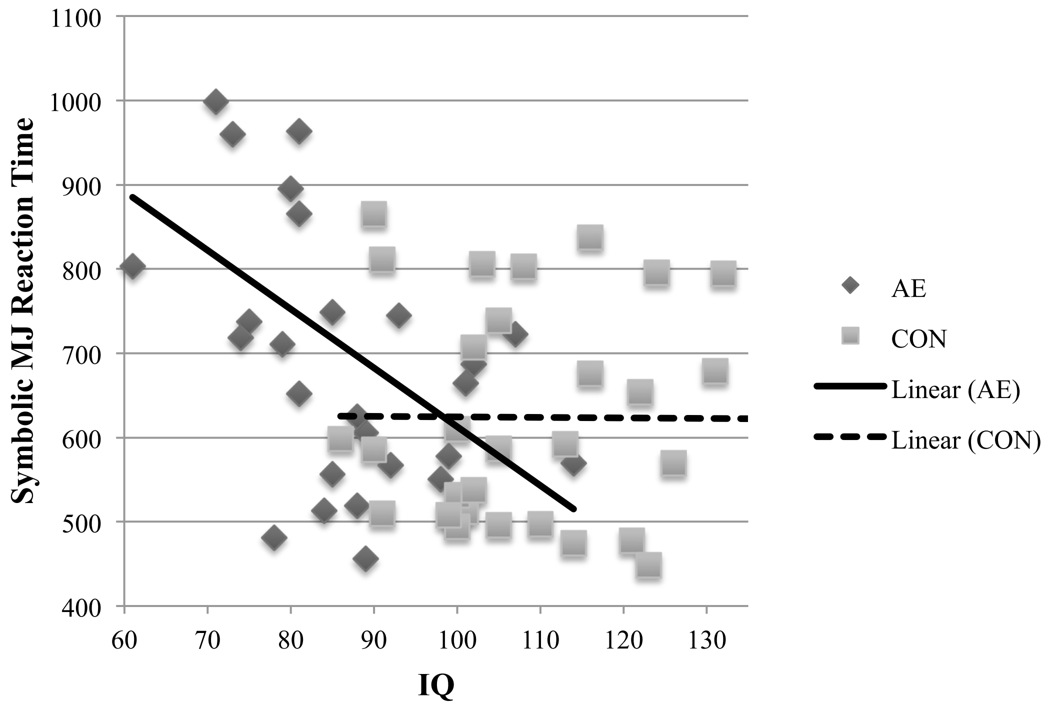
In addition, the contribution of IQ to the relationship between numerical processing measures and mathematics achievement was evaluated using hierarchical linear regression techniques. Mathematics achievement (WJ-III standard scores) served as the dependent variable and RT or accuracy for each task, age, IQ, group and the interaction between them served as independent variables.

Mathematics Achievement. To examine the effect of IQ on WJ-III mathematics achievement tests, data were analyzed using MANOVA with WJ-III test scores as the dependent variables and group as the independent variable. IQ was significantly associated with WJ-III scores [F (1, 55) = 28.259, $p < .001$, partial η^2 = .339] and was included in the analysis. There was a significant main effect of Group [F (1, 55) = 17.785, $p < .001$, partial $\eta^2 = .244$]. Children in the AE group had lower scores on all four WJ-III mathematics achievement tests relative to the CON group (*p*s $< .003$), even after controlling for IQ.

Symbolic and Nonsymbolic MJ RT. To examine the relationship between IQ and MJ RT, linear regression analyses were conducted separately for each group. Symbolic and nonsymbolic MJ RT each served as independent variables and age and IQ served as dependent variables.

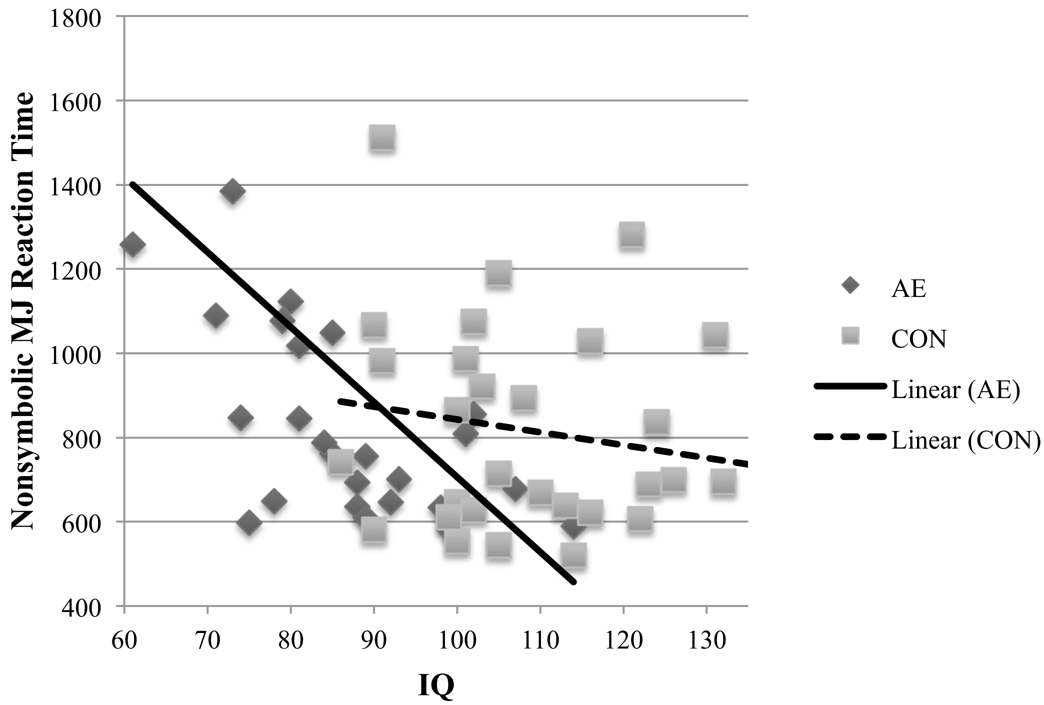
For symbolic MJ RT, the model accounted for a significant amount of variance in numerical processing in the AE group [F (2, 26) = 11.964, $R^2 = .458$, $p < .001$] and the CON group [F (2, 30) = 15.344, $R^2 = .489$, $p < .001$]. In the AE group, when regression coefficients for each dependent variable were examined both age (b = -44.845, β = -.550, $p = .001$) and IQ (b = -7.325, β = -.466, $p = .004$) were significant predictors of symbolic MJ RT. However, in the CON group, only age (b = -42.257, β = -.771, $p < .001$), and not IQ (b = -2.409, β = -.275, $p = .058$), was significantly associated with MJ RT. See Graph 11.

Graph 11. Data represent the relationship between IQ and reaction time on the symbolic condition of the Magnitude Judgment (MJ) task for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).



For nonsymbolic MJ RT, the model accounted for a significant amount of variance in numerical processing in the AE group [F (2, 26) = 11.770, R^2 = .453, p < .001], however was not significant for the CON group [F (2, 30) = 1.660, R^2 = .042, p = .208]. In the AE group, when regression coefficients for each dependent variable were examined both age (b = -134.662, β = -.580, p = .001) and IQ (b = -18.833, β = -.422, p = .008) were significant predictors of symbolic MJ RT. See Graph 12.

Graph 12. Data represent the relationship between IQ and reaction time on the nonsymbolic condition of the Magnitude Judgment (MJ) task for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).

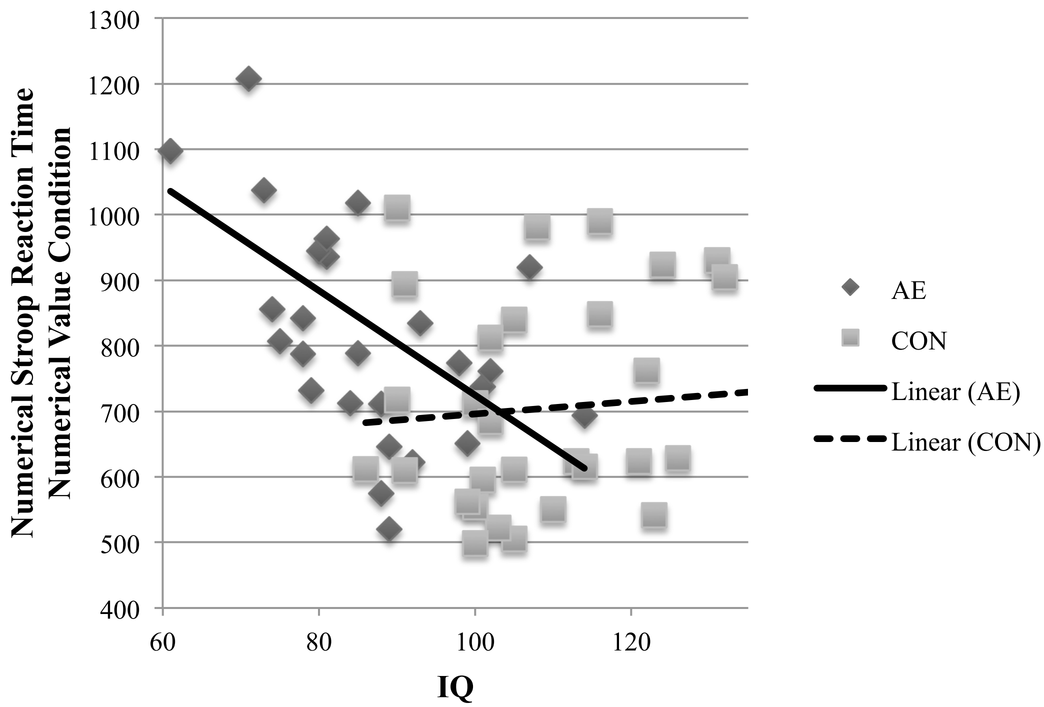


Numerical Stroop RT. To examine the relationship between IQ and numerical stroop RT, linear regression analyses were conducted separately for each group. Mean RT from the numerical value and physical size comparison conditions each served as independent variables and age and IQ served as dependent variables.

For the numerical value comparison condition of numerical stroop task, the model accounted for a significant amount of variance in numerical processing in the AE group [F (2, 26) = 7.182, R^2 = .322, p = .004] and the CON group [F (2, 30) = 22.238, R^2 = .586, p < .001]. In the AE group, when regression coefficients for each dependent variable were examined both age (b = -31.271, β = -.369, p = .032) and IQ (b = -8.215, β = -.503, p = .005) were significant predictors of symbolic MJ RT.

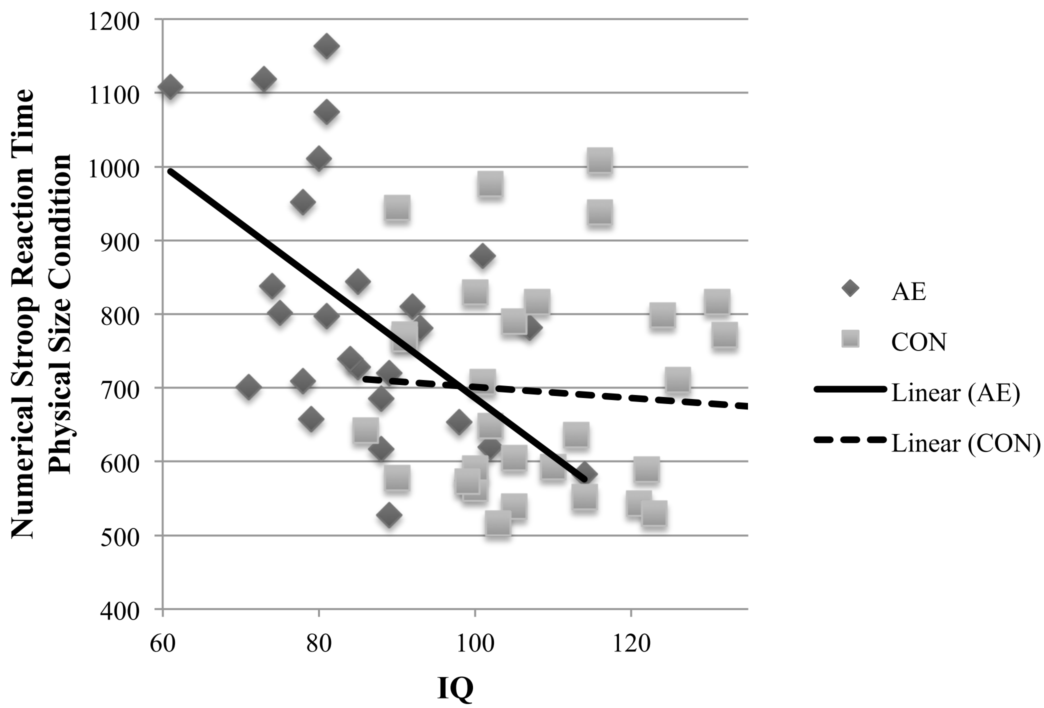
However, in the CON group, only age (b = -58.197, β = -.830, p < .001), and not IQ (b = -2.282, β = -.204, p = .115), was significantly associated with MJ RT. See Graph 13.

Graph 13. Data represent the relationship between IQ and reaction time on the numerical value condition of the Numerical Stroop task for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).



For the physical size comparison condition of numerical stroop task, the model accounted for a significant amount of variance in numerical processing in the AE group [F (2, 26) = 13.271, R^2 = .486, p < .001] and the CON group [F (2, 30) = 20.030, R^2 = .559, p < .001]. In the AE group, when regression coefficients for each dependent variable were examined both age (b = -31.685, β = -.491, p = .002) and IQ (b = -8.164, β = -.553, p = .001) were significant predictors of symbolic MJ RT. In the CON group, both age (b = -51.035, β = -.814, p < .001) and IQ (b = -3.584, β = -.358, p = .010) also were significantly associated with MJ RT. See Graph 14.

Graph 14. Data represent the relationship between IQ and reaction time on the physical size condition of the Numerical Stroop task for children with histories of prenatal alcohol exposure (the AE group) and controls (the CON group).



Relation between IQ, Numerical Processing, and Mathematics Achievement. In order to evaluate the relationship between IQ, numerical processing, and mathematics achievement, hierarchical linear regression analyses were conducted. Mathematics achievement (WJ-III standard scores) served as the dependent variable and RT and accuracy for each task, group, IQ and their interactions served as independent variables. Age was significantly associated with all WJ-III scores and also was included as an independent variable in all analyses. Numerical processing tasks, age, and IQ were entered together on step 1, group was entered on step 2, and the interaction terms were entered on step 3. Data are summarized in Table 9 (RT) and Table 10 (accuracy).

Reaction Time. For all four WJ-III indices, model one (age, IQ, and numerical processing measures) accounted for a significant amount of variance in mathematics achievement. When coefficients for each measure were evaluated, age was a significant predictor of all math achievement measures and IQ was a significant predictor of Calculation, Applied Problems, and Quantitative Concepts scores. In addition, numerical stroop RT was significantly associated with Math Fluency scores. ANS RT and MJ RT were not significantly associated with any WJ-III measure. Also, for all WJ-III indices, model fit improved with the addition of group in model 2; however, the interaction terms included in model 3 did not account for a significant increase in explained variance in mathematics achievement. See Table 9.

Table 9. Summary of the results of hierarchical linear regression analyses evaluating the relationship between reaction time on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and mathematics achievement (WJ-III tests of Calculation, Math Fluency, Applied Problems, and Quantitative Concepts), with the inclusion of IQ in the model. Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 1	***F* (5, 52) = 11.578, R^2 = .481, *p* < .001**		***F* (5, 52) = 10.741, R^2 = .461, *p* < .001**		***F* (5, 52) = 28.610, R^2 = .708, *p* < .001**		***F* (5, 52) = 17.328, R^2 = .589, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age	**-2.587**	**.054**	**-3.426**	**.004**	**-2.166**	**.009**	**-2.297**	**.038**
IQ	**.591**	**.001**	.289	.061	**.586**	**< .001**	**.611**	**< .001**
ANS	.002	.804	-.008	.278	-.003	.543	.001	.888
MJ	-.013	.243	.005	.573	-.005	.462	-.011	.197
Numerical Stroop	-.013	.469	**-.044**	**.008**	.019	.095	-.015	.326
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 2	**ΔR^2 = .100, *p* = .001**		**ΔR^2 = .049, *p* = .021**		**ΔR^2 = .031, *p* = .012**		**ΔR^2 = .053, *p* = .006**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Group	**-18.579**	**.001**	**-11.125**	**.021**	**-8.445**	**.012**	**-12.447**	**.006**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 3	ΔR^2 = .017, *p* = .814		ΔR^2 = .049, *p* = .356		ΔR^2 = .028, *p* = .308		ΔR^2 = .035, *p* = .369	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age x Group	-2.449	.361	-4.183	.086	-1.633	.327	-4.067	.070
IQ x Group	-.257	.519	-.663	.068	-.165	.505	-.152	.644
ANS x Group	-.011	.486	.001	.955	-.016	.116	-.017	.192
MJ x Group	-.013	.598	-.006	.788	.011	.487	.012	.555
Numerical Stroop x Group	.011	.787	-.073	.051	-.039	.132	-.038	.265

Accuracy. For all four WJ-III indices, model one (age, IQ, and numerical processing measures) accounted for a significant amount of variance in mathematics achievement. When coefficients for each measure were evaluated, IQ was a significant predictor of all math achievement measures and age was significantly associated with Calculation and Quantitative Concepts scores. In addition, MJ accuracy was a significant predictor of Math Fluency and Quantitative Concepts scores. ANS accuracy and numerical stroop accuracy were not significantly associated with any WJ-III measure. Also, for all WJ-III indices, model fit improved with the addition of group in model 2; however, the interaction terms included in model 3 did not account for a significant increase in explained variance in mathematics achievement, with one exception. When the relationship between numerical processing accuracy and Math Fluency was evaluated, a significant MJ accuracy x group interaction emerged (see Table 10).

To follow up this effect, separate regression analyses examining the relationship between MJ accuracy and Math Fluency were conducted for each group. In the CON group, the model was not significant [F (3, 27) = 2.477, R^2 = .129, p = .083]. In the AE group, the model accounted for a significant amount of variance in Math Fluency test scores [F (3, 26) = 4.199, R^2 = .270, p = .017]. When coefficients for each measure were evaluated, only MJ accuracy (b = 275.469, β = .510, p = .008) was a significant predictor of Math Fluency test scores in the AE group. IQ (p = .060) and age (p = .079) did not account for a significant amount of variance in Math Fluency test scores.

Table 10. Summary of the results of hierarchical linear regression analyses evaluating the relationship between accuracy on numerical processing tasks (Approximate Number Sense [ANS], symbolic and nonsymbolic Magnitude Judgment [MJ], and Numerical Stroop) and mathematics achievement (WJ-III tests of Calculation, Math Fluency, Applied Problems, and Quantitative Concepts), with the inclusion of IQ in the model. Data represent model fit statistics at each step of the analyses and regression coefficients for each predictor variable.

	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 1	***F* (5, 52) = 13.983, R^2 = .532, *p* < .001**		***F* (5, 52) = 8.837, R^2 = .407, *p* < .001**		***F* (5, 52) = 28.893, R^2 = .328, *p* < .001**		***F* (5, 52) = 22.567, R^2 = .654, *p* < .001**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age	**-2.314**	**.020**	-1.348	.150	-1.131	.072	**-1.762**	**.024**
IQ	**.614**	**< .001**	**.569**	**< .001**	**.721**	**< .001**	**.675**	**< .001**
ANS	45.657	.180	-12.730	.695	17.090	.431	51.177	.060
MJ	55.792	.427	**131.784**	**.054**	78.921	.083	**112.141**	**.047**
Numerical Stroop	87.771	.125	15.421	.777	11.840	.744	34.007	.449
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 2	**ΔR^2 = .084, *p* = .001**		**ΔR^2 = .078, *p* < .005**		**ΔR^2 = .035, *p* = .007**		**ΔR^2 = .041, *p* = .008**	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Group	**-16.473**	**.001**	**-13.505**	**.005**	**-8.667**	**.007**	**-10.587**	**.008**
	Calculation		**Math Fluency**		**Applied Problems**		**Quantitative Concepts**	
Model 3	ΔR^2 = .026, *p* = .590		**ΔR^2 = .098, *p* = .046**		ΔR^2 = .010, *p* = .838		ΔR^2 = .034, *p* = .286	
	b	***p***	**b**	***p***	**b**	***p***	**b**	***p***
Age x Group	-3.545	.075	-2.408	.182	.027	.984	-3.215	.045
IQ x Group	-.174	.584	.067	.818	.162	.453	.090	.723
ANS x Group	15.892	.803	86.463	.144	22.122	.609	36.200	.481
MJ x Group	-43.824	.743	**295.191**	**.019**	57.410	.526	57.298	.593
Numerical Stroop x Group	1.733	.988	-165.599	.137	-87.330	.285	-63.875	.508

Chapter 3, in part, is currently being prepared for submission for publication of

the material. Crocker, Nicole; Mattson, Sarah N. The dissertation author was the primary investigator and author of this material.

IV. Discussion

The current study utilized a *domain specific* model of mathematics abilities to evaluate the nature of math difficulties in children with heavy prenatal alcohol exposure and typically developing controls by testing their core capacity to represent and process numerical information. Overall, data are consistent with previous literature reporting deficits in mathematics in children with prenatal alcohol exposure. Data also suggest that children with prenatal alcohol exposure have impairments in basic numerical processing skills; however, based on the current findings, the extent to which these skills specifically relate to mathematics achievement in this population is less clear. More general cognitive functions may also be important explanatory factors in understanding mechanisms of mathematics performance in children with FASD.

Mathematics Achievement

When children with prenatal alcohol exposure were compared with typically developing controls on measures of mathematics achievement, alcohol-exposed children performed more poorly than controls on WJ-III tests of Calculation, Math Fluency, Applied Problems, and Quantitative concepts, even after statistically controlling for global intellectual function. In addition, children in the AE group did not show differential patterns of performance across these measures, each of which taps slightly different aspects of mathematical functioning, suggesting widespread difficulties across a broad range of mathematical thinking and problem solving skills. These findings are consistent with previous studies suggesting that mathematics is a particular area of weakness in children with FASD (Crocker, Riley, & Mattson, in press; Goldschmidt et al., 1996; Howell et al., 2006; Jacobson et al., 2011; Streissguth et al., 1990; Streissguth et al., 1994). Several studies utilizing broad assessment batteries have demonstrated that mathematics scores are among the outcomes most strongly associated with prenatal alcohol exposure across development (Coles et al., 1991; Jacobson, Jacobson, Sokol, Chiodo, & Corobana, 2004; Streissguth et al., 1994; Streissguth, Barr, & Sampson, 1990) and that mathematics is affected to a greater extent than reading and spelling domains in children with FASD (Goldschmidt et al., 1996; Kerns, Don, Mateer, & Streissguth, 1997).

ANS

As hypothesized, children in the AE group were slower and less accurate in their ability to estimate numerosity. Children in both groups demonstrated the NDE (i.e. longer reaction times and decreased accuracy as the ratio between presented numerosities decreased). Because an interaction effect was not observed for either reaction time or accuracy, children in the AE group did not appear to display disproportionately impaired performance as ratio decreased, but rather a uniform deficit in ANS across all levels of task difficulty. These data are consistent with the limited literature on basic numerical processing in FASD (Jacobson et al., 2011; Kopera-Frye et al., 1996; Meintjes et al., 2010) and in select studies of children with MLD (Landerl et al., 2004; Mazzocco, Feigenson, & Halberda, 2011; Piazza et al., 2010).

Though this is the first study to utilize this particular ANS measure to examine numerical processing in children with histories of prenatal alcohol exposure, previous studies of numerical processing in this population that have included some form of cognitive estimation or magnitude comparison task have shown that alcohol-exposed children are deficient in these skills relative to typically developing controls (Burden et al., 2005; Jacobson et al., 2011; Kopera-Frye et al., 1996; Meintjes et al., 2010). In addition, select studies of children with MLD that have employed similar nonsymbolic numerosity comparison tasks demonstrate that their numerical acuity is impaired in relation to age- and IQ-matched peers (Gilmore, McCarthy, & Spelke, 2010; Mazzocco et al., 2011; Piazza et al., 2010).

Symbolic and Nonsymbolic MJ

Subjects were compared on a symbolic and nonsymbolic magnitude judgment task in order to evaluate whether children with prenatal alcohol exposure have difficulty accessing meaning from Arabic numerical symbols. As expected, children with histories of prenatal alcohol exposure were slower than controls on both symbolic and nonsymbolic conditions of the magnitude judgment task and children in both groups exhibited the NDE, demonstrating longer reaction times as the numerical distance between presented stimuli decreased. However, contrary to hypotheses, children in the AE group did not demonstrate disproportionately longer reaction times on the symbolic condition of the task, suggesting that children with prenatal alcohol exposure do not exhibit a specific deficit in accessing magnitude information from Arabic numerals. In fact, across groups, children demonstrated longer reaction times for the nonsymbolic condition relative to the symbolic condition of the task. The AE group's performance on the nonsymbolic condition of the MJ task and on the ANS measure points to an impairment at the level of basic internal magnitude representation rather than a deficit that occurs when children must access that representation through numerical symbols.

No other studies have compared symbolic and nonsymbolic magnitude judgment in children with FASD and studies of children with MLD have yielded mixed results. As described, some investigations have found that children with MLD demonstrate deficits in their ability to discriminate approximate numerosities (Landerl et al., 2004; Mazzocco et al., 2011; Mussolin, Mejias, & Noel, 2010; Piazza et al., 2010), however, others have not (Holloway & Ansari, 2009; Iuculano et al., 2008; Rousselle & Noel, 2007). Rousselle and Noel (2007) compared children with developmental dyscalculia to typically developing children on symbolic and nonsymbolic number comparison tasks. In contrast to the current findings in children with prenatal alcohol exposure, results indicated that children with dyscalculia were slower and less accurate only when comparing Arabic numerals; on nonsymbolic comparison trials, children with MLD preformed comparably to their typically achieving peers. These data suggest that the core deficit in MLD is deficient access to magnitude representation (Rousselle & Noel, 2007), whereas children with prenatal alcohol exposure appear to have deficits arising from more basic numerical processing. These findings highlight the importance of studying low-level numerical processing and the development of symbol-to-referent connections to better understand mathematical competence, and suggest differences in the nature of the deficit in numerical processing between children with prenatal alcohol exposure and other groups at risk for low mathematics achievement.

Findings of impaired numerosity in children with prenatal alcohol exposure in the present study are likely related to aberrant parietal lobe functioning. As described, parietofrontal brain regions thought to support mathematics abilities are abnormal in children with FASD (Archibald et al., 2001; Fryer et al., 2009; Lebel et al., 2010; Lebel et al., 2008; Meintjes et al., 2010; Santhanam et al., 2009; Sowell et al., 2008). In the only known neuroimaging study to specifically investigate symbolic magnitude judgment in children with histories of prenatal alcohol exposure, (Meintjes et al., 2010), authors utilized fMRI to demonstrate that while control children activated expected frontal and parietal regions to perform symbolic number processing tasks, alcohol-exposed children recruited a broader range of regions to complete the same tasks, likely to compensate for alcohol-related deficits in brain functioning. In addition, the more diffuse parietal pathways recruited by children with prenatal alcohol exposure, including the right and left angular gyrus and posterior cingulate/precuneus, have been suggested to be related to more verbally mediated aspects of numerical processing, such as recitation of numbers to assess relative numerical distance. Reliance on verbal compensatory strategies may help explain the AE group's inefficiency in magnitude judgment in the current study. To date, no known studies have examined the neural correlates specifically related to nonsymbolic magnitude judgment in children with FASD, however studies of children with MLD suggest that decreased activation of the intraparietal sulcus may underlie deficits on these tasks (Price, Holloway, Rasanen, Vesterinen, & Ansari, 2007) and studies of normal adults suggest that the right posterior superior parietal lobe may be more involved in nonsymbolic processing relative to symbolic processing (Holloway, Price, & Ansari, 2010). Future neuroimaging investigations of children with prenatal alcohol exposure should examine both symbolic and nonsymbolic magnitude judgment tasks to better understand the neural substrates underlying numerical processing in this population.

The finding that children in the current study performed more poorly on the nonsymbolic condition of the magnitude judgment task relative to the symbolic condition is somewhat surprising given the prevailing notion that intact development of internal magnitude representation is a requisite for efficient access to magnitude representation via numerical symbols. Given this assumption, the expectation might be that children would perform either similarly across conditions or worse on symbolic relative to nonsymbolic conditions, depending on the presence of a deficit in numerical processing and at what level of processing this impairment occurs. However, there is some evidence to suggest that symbolic and nonsymbolic processing are independent of each other (Cohen, 2009), rely on separate neural networks (Bulthe, De Smedt, & Op de Beeck, 2014; Holloway et al., 2010), and that the development of the relationship between approximate magnitudes and their precise symbolic representations is actually reciprocal (Mundy & Gilmore, 2009; Noel & Rousselle, 2011).

Several studies have examined mapping of numerical magnitude representations in a single direction by asking subjects to generate a symbol as a reference for a given nonsymbolic representation or by inferring the efficiency of mapping via performance on symbolic magnitude comparison tasks. However, in order to assess whether this relationship occurs bi-directionally, Mundy and Gilmore (2009) developed and administered a novel mapping task to children ages 6-8. On half of all trials, children were presented with an Arabic symbol and had to choose which of two dot arrays was the same in quantity to the symbol (symbolic to nonsymbolic). On the other half of trials, children were presented with a dot array and had to choose which of two Arabic numerals represented the same quantity as the nonsymbolic array. Children in the study were more accurate at choosing a symbolic label to match a nonsymbolic target than the reverse; subjects were actually unable to map from symbolic to nonsymbolic representations when the ratio between nonsymbolic representations was .67 (difficult) relative to when it was .50 (easy).

The authors hypothesized that this asymmetry in mapping ability may be related to differences in precision between symbolic and non-symbolic representations. A symbolic stimulus is associated with a precise quantity or precise point on a number line, whereas nonsymbolic stimuli (with the exception of very small sets of objects) are processed as approximate and imprecise magnitudes representing a general area on a mental number line and, by nature, may introduce increased opportunity for error. The symbolic to nonsymbolic condition of the task involves activation of one precise (Arabic numeral target) and two approximate (nonsymbolic response options) areas of the number line, whereas the nonsymbolic to symbolic condition involves only one approximate representation and two that are precise. As such, children may be more proficient at the task when they are required to process fewer approximate representations (i.e. mapping from nonsymbolic to symbolic stimuli; Mundy & Gilmore, 2009). Better performance on the symbolic condition relative to nonsymbolic condition of the MJ task observed in the current study may be explained by a similar phenomenon whereby children are faster and more accurate at comparing precise relative to approximate quantities.

Interestingly, despite showing slower reaction times, children with prenatal alcohol exposure were not less accurate than controls in comparing magnitude of either nonsymbolic stimuli or Arabic numerals, suggesting inefficiency but not an inability to process numerical information. It is possible that difficulty with the magnitude judgment task arises as a result of alcohol-exposed children's difficulty in coordinating a response rather than by differences in numerical representation. Perhaps numerosity is similarly developed across groups, and it is the meaningful use of this numerosity that is impaired in children with prenatal alcohol exposure. Thus, given more time, alcohol-exposed children are able to perform the task to the same degree as their typically developing counter parts.

Support for this hypothesis is found in a study comparing children and adult's brain activation in an fMRI adaptation paradigm (Cantlon, Brannon, Carter, & Pelphrey, 2006). In this study, subjects did not have to complete a task, but instead were asked to passively view a stream of visual arrays, primarily consisting of the same number of the same element shape (e.g. 16 circles). However, occasionally, individuals would be presented with a stimulus that deviated from the standard stimuli in either number (e.g. 32 circles) or shape (e.g. 16 squares). When changes in brain activation in response to the deviant stimuli were examined, the intraparietal sulcus showed greater activation in response to numerical deviants versus shape deviants. These activation patterns were similar for both children and adults, suggesting that children may have numerical representation abilities that are as well developed as adults, but that deficits emerge at the level of response coordination. Accordingly, the current findings of alcohol-exposed children's increased reaction time but similar accuracy compared with controls on the magnitude judgment task may be explained by similar difficulties with response selection in the presence of intact numerical processing abilities.

In our study, when reaction time was included in the model, effects of group on magnitude judgment (both on the ANS task and the symbolic and nonsymbolic MJ task) were attenuated, lending further support to the notion that deficits on this task could be related to difficulties in response coordination rather than a pure deficit in numerical magnitude representation. However, when processing efficiency in individuals with histories of prenatal alcohol exposure was investigated using a paradigm that allowed for separation of the effects of generalized processing *speed* and task specific processing *efficiency*, performance on a symbolic magnitude comparison measure was the only task (of four administered) in which a specific effect of prenatal alcohol exposure was found for processing *efficiency*. In other words children with prenatal alcohol exposure demonstrated impairments in magnitude judgment that were not solely attributable to a generalized deficit in processing speed (Burden et al., 2005). Perhaps differences in methodology and data analyses can account for these differences; however, conflicting findings indicate that further study regarding the effects of processing speed on numerical cognition in children with prenatal alcohol exposure is warranted.

Numerical Stroop

To evaluate the extent to which children with prenatal alcohol exposure automatically activate numerical magnitude information, subjects were compared on a numerical stroop task. Children with histories of prenatal alcohol exposure were slower than controls at determining which of two digits was larger in either numerical value or physical size. In addition, as hypothesized, a group x condition x trial type interaction was observed. On the numerical value condition, children in both groups demonstrated the typical SCE, demonstrating faster reaction times for congruent vs. neutral trails (*facilitation*) and longer reaction times for incongruent vs. neutral trials (*interference*). Groups' patterns of performance across trial types differed on the physical size condition of the task, though not as expected. Contrary to our hypotheses, control children demonstrated similar reaction times for congruent and neutral trials, whereas alcohol-exposed children demonstrated differential reaction times for all trial types. Interestingly, children in the AE group actually performed more *slowly* on congruent relative to neutral trials, as well as slower on incongruent trials relative to neutral and congruent trials. Thus, while children in the AE group were impaired in the speed with which they made physical size comparisons, it is less clear that automatic processing of numerical information is specifically affected in this group, given that children in both groups demonstrated decreased facilitation effects on the physical size comparison condition of the task.

Though no other studies have examined numerical stroop tasks in children with FASD, findings from studies of children with MLD have been equivocal. Several investigations have demonstrated that individuals with mathematics difficulties demonstrate decreased facilitation and fail to produce a SCE on the physical size condition of the task, suggesting that numerical magnitude representations are not being automatically activated in a way that allows them to benefit from congruent trials (Ashkenazi et al., 2009; Rubinsten & Henik, 2005) or, in some studies, interferes with responding on incongruent trials (Koontz & Berch, 1996). Cohen Kadosh and colleagues (2007, 2012) were actually able to reproduce a decrease in the SCE in the physical size condition of a numerical stroop task by applying transcranial magnetic stimulation to right intraparietal regions of originally well-performing adults (Cohen Kadosh, Bien, & Sack, 2012; Cohen Kadosh et al., 2007). However, there have been mixed findings and the aforementioned studies are in contrast with others comparing children with MLD and controls that have shown decreased SCE in both groups (Landerl et al., 2004; as is the case with the current findings), while others have shown intact SCE in both groups (Rousselle & Noel, 2007). Thus, results of the current study as well as mixed findings from the MLD literature make understanding the nature of automatic numerical processing in FASD and its role in their mathematical functioning challenging.

Some investigators have suggested that consideration of both the SCE and the NDE together might actually be a more sensitive measure of automaticity of numerical processing. For example, several studies utilizing a numerical stroop task have demonstrated a *reversed* NDE for incongruent trials of the physical size comparison, such that larger numerical distance actually results in longer reaction times (Girelli et al., 2000; Heine et al., 2010; Szucs & Soltesz, 2007; Szucs, Soltesz, Jarmi, & Csepe, 2007; Tang, Critchley, Glaser, Dolan, & Butterworth, 2006). Because subjects are better at making a judgment based on numerical value when distance between numbers is larger, this actually leads to increased interference when numerical value is the task irrelevant stimuli. It also suggests that numerical value is being automatically activated even when it is irrelevant for the task. Even so, when the SCE and NDE of children in three different mathematics achieving groups (high, typical, and low) were compared, it did not prove to be helpful in distinguishing between them (Heine et al., 2010). Children in all three groups showed a typical SCE, and children in both typically achieving and low achieving groups demonstrated a reversed NDE, further obscuring the nature of the relationship between numerical stroop performance and mathematics impairments. In the present study, neither the condition x type x distance nor the condition x type x distance x group interactions were statistically significant, indicating the lack of an observed reversed NDE for either group.

Because children must inhibit task irrelevant dimensions in order to perform efficiently on the numerical stroop task, the current findings of impaired performance in children in the AE group may be related to deficits in executive function commonly reported in this population (Coles et al., 1997; Connor, Sampson, Bookstein, Barr, & Streissguth, 2000; Green et al., 2009; Kodituwakku, Handmaker, Cutler, Weathersby, & Handmaker, 1995; Mattson, Goodman, Caine, Delis, & Riley, 1999; Mattson & Riley, 2000; McGee, Schonfeld, Roebuck-Spencer, Riley, & Mattson, 2008; Rasmussen, Wyper, & Talwar, 2009; Vaurio, Riley, & Mattson, 2008). Children with FASD often have difficulty on tasks involving stimulus or response conflict, such as traditional color-word stroop tasks and the Wisconsin Card Sorting Test; alcohol-exposed children tend to make more errors than their typically developing peers, particularly on interference conditions and when the task requires subjects to switch between sets (Connor et al., 2000; Mattson et al., 1999; McGee et al., 2008; Vaurio et al., 2008). Further, when inhibitory control in FASD has been examined utilizing neuroimaging methods, children have been reported to demonstrate greater neural activation than controls on Go/No-Go tasks, suggesting the need to employ greater cognitive effort to perform similarly to controls on these measures (Burden et al., 2009; Fryer et al., 2007).

In a study by Kooistra and colleagues (2011), children with FASD, ADHD, and typically developing controls were compared using the attention network test (ANT). Similarly to the numerical stroop task, the ANT employs congruent, incongruent, and neutral stimuli in order to assess three related but distinct aspects of attention – alerting, orienting, and executive control. Performance of children with FASD was more impaired by incongruent trials than congruent or neutral trials relative to controls and they received significantly lower executive control network scores. In addition, children with FASD were not impaired in their overall accuracy relative to control children. While there was no numerical processing element in this study, alcohol-exposed children's impaired executive abilities and increased response conflict at a more basic level would be expected to interfere with their performance on a task involving those skills *and* numerical processing demands (e.g. the numerical stroop task). Indeed, findings from the current study are consistent with those reported by Kooistra et al. (2011) and point to the importance of executive abilities in understanding alcohol-exposed children's performance on the numerical stroop task.

A small number of studies have begun to investigate the relationship between performance on numerical processing tasks and inhibitory control and how the relationship between them might affect mathematical functioning. In their study combining ERP and behavioral data in children and adults, Soltesz, Goswami, White, and Szucs, (2011) suggest that children have equally fast access to numerical representations as adults, but that because children have a less developed ability to inhibit irrelevant information, they perform more poorly on the task (Soltész, Goswami, White, & Szűcs, 2011). This hypothesis was more recently tested by Gilmore, Attridge, Clayton, et al (2013). They suggest that the perceptual controls often employed by dot comparison measures of ANS acuity inadvertently introduce congruent and incongruent trial types into the task. Their findings demonstrated that the relationship between performance on these measures and mathematics achievement in their sample was being driven by children's performance on incongruent trials only. In addition, they showed that the relationship between ANS and mathematics achievement was no longer significant once inhibitory control (measured via the NEPSY-II Inhibition test) was considered in the model. Similarly, Fuhs and McNeil (2013) found that performance on inhibition tasks reduced the relationship between dot comparison scores and early mathematics abilities (measured using the TEMA-3) in a sample of low-income preschoolers.

Although the focus of the current study was to investigate the extent to which abnormalities in fundamental numerical processing are related to mathematics impairment in FASD, competing theories have been proposed, and several researchers suggest that multiple pathways to mathematics difficulties can exist (Dennis, Berch, et al., 2009; Fuchs et al., 2010; Rubinsten & Henik, 2009; Spelke & Kinzler, 2007). The *domain-general* view of mathematics, for example, focuses on the contribution of higher order cognitive processes to the development of mathematical ability (Geary, 1993, 2004). Studies utilizing this model have demonstrated that executive function and cognitive control measures are related to emerging mathematics ability in preschool children (Espy et al., 2004), kindergarteners (Blair & Razza, 2007), and school-aged children (St Clair-Thompson & Gathercole, 2006), and certainly, the above studies that evaluated the relationship among numerical processing tasks, inhibitory control, and mathematics ability also support this link (Fuhs & McNeil, 2013; Gilmore et al., 2013; Soltész et al., 2011). Perhaps a framework that incorporates multiple models of mathematics functioning, including both domain *specific* and *domain general* approaches, will provide important information regarding mathematics abilities in children with FASD.

As in the magnitude judgment task, despite showing slower reaction times, children with prenatal alcohol exposure were not less accurate than controls on the numerical stroop task. This again points to inefficiency in responding but not a lack of ability to adequately perform the task. For this measure, when reaction time was included in the model, children with prenatal alcohol exposure still performed significantly more poorly than controls. This suggests that difficulty in response coordination arising from overall reduced processing speed in children with prenatal alcohol exposure is not a likely explanation for the observed discrepancy in reaction time and accuracy on the numerical stroop task. Overall, both groups made few errors, perhaps rendering accuracy an insufficiently sensitive measure of numerical stroop performance in this instance.

Relationship with Mathematics Achievement

Overall, children's numerical processing skills were related to mathematics achievement in our sample. This finding is consistent with previous studies of children with FASD (Jacobson et al., 2011), MLD (Mazzocco et al., 2011) and typically developing children (Halberda et al., 2008). However, there was not clear evidence of a specific pattern to these relationships, both in terms of relative contribution of each numerical processing skill to mathematics achievement and lack of differential relationships among numerical processing and distinct aspects of math achievement (i.e. calculation, math fluency, quantitative concepts, and applied problems). Further, when numerical processing measures were evaluated as predictors of other domains of academic achievement, significant relationships with reading and spelling scores were observed.

Comorbidity between MLD and reading disorders (RD) is common (Landerl & Moll, 2010; Willcutt et al., 2013) and, analogous to the current findings, studies have demonstrated that core mechanisms of reading, such as rapid automatic naming, may also relate to mathematics abilities (Mazzocco & Grimm, 2013). Some studies suggest that presence of a common predictor in RD and MLD does not necessarily indicate that similar neural networks mediate the two (Mazzocco & Grimm, 2013). In other words, lack of specificity in the relationship between numerical processing and mathematics achievement demonstrated in the current study does not necessarily refute the notion that unique neural substrates underlie mathematics difficulty in this population. The tasks used in the current investigation are cognitively complex and rely on several skills for successful completion, in addition to simple judgment of magnitude (e.g. cognitive control, processing speed). Perhaps these auxiliary skills are what are driving the significant associations between numerical processing and reading and spelling scores. Further, numerical tasks were not related to Word Attack scores, a measure of phonological processing, which is also thought to represent a core mechanism of reading abilities.

Conversely, lack of specificity of the relationship between numerical processing and mathematics achievement may point to the utility of investigating other, more *domain general*, cognitive capabilities in order to understand mathematics achievement in children with histories of heavy prenatal alcohol exposure. As discussed, executive functioning has been related to mathematics achievement (Blair & Razza, 2007; Espy et al., 2004; St Clair-Thompson & Gathercole, 2006) and studies suggest that working memory may be an especially relevant executive ability underlying mathematics performance (Floyd, Evans, & McGrew, 2003; Kyttala, Aunio, & Hautamaki, 2010; McLean & Hitch, 1999; Meyer, Salimpoor, Wu, Geary, & Menon, 2010; Rosselli, Matute, Pinto, & Ardila, 2006; Zheng, Swanson, & Marcoulides, 2011). In a study that examined working memory and mathematics performance in children with FASD and controls (Rasmussen & Bisanz, 2011), authors demonstrated that math performance was correlated with 5 of the 6 working memory and attention variables they selected and that group differences in math performance were reduced with the addition of three of the measures as covariates. Similarly, visuospatial skills have been demonstrated to support mathematics performance (Bachot, Gevers, Fias, & Roeyers, 2005; Geary, 2004; Mazzocco, Singh Bhatia, & Lesniak-Karpiak, 2006; McCloskey, Caramazza, & Basili, 1985; Vuilleumier, Ortigue, & Brugger, 2004; Zorzi, Priftis, Meneghello, Marenzi, & Umilta, 2006) and a recent study of children with FASD suggests that these abilities may also be particularly significant in understanding their mathematics function (Crocker et al., in press). In this investigation, measures of spatial attention, spatial working memory, and spatial recognition memory were related to mathematics achievement scores in children with histories of heavy prenatal alcohol exposure.

Thus, while studies are limited, these findings lend support for the *domain general* model of mathematics function in FASD.

In the current investigation, the addition of group on step 2 of the linear regression analyses resulted in a significant increase in explained variance in mathematics achievement in the sample. This reflects the specific effect of prenatal alcohol exposure on mathematics ability that has been robustly reported in the literature; however, it may also lend further support to the notion that numerical processing skills are not a sufficient explanatory mechanism of math performance in FASD and that other aspects of cognition should be considered. Interestingly, these findings are in contrast to one of the only other studies of numerical processing in this population, where the effect of prenatal alcohol exposure on calculation was completely mediated by magnitude comparison performance (Jacobson et al., 2011). Differences in study design and analytic strategy may account for this discrepancy, and it is possible that the extent to which *domain specific* and *domain general* abilities relate to mathematics depend on the specific type of math problems under investigation. For example, Fuchs et al. (2010) demonstrated that for both procedural calculations and word problems, *domain specific* numerical cognition was uniquely predictive of performance. However, for only word problems, a set of *domain general* abilities provided additional unique explanatory value. Future studies should take a more comprehensive approach, including both *domain general* and *domain specific* factors together in order to understand the relative importance of these models in explaining mathematics deficits in FASD.

While poor mathematics appears to be a core deficit in children with FASD, what is less clear is the extent to which children with prenatal alcohol exposure meet criteria for MLD. There is some preliminary evidence to indicate that children with FASD meet criteria for MLD at a higher rate than their non-exposed peers (Infante et al., 2011), however the issue has not been well investigated and is complicated by disagreement in the field regarding the adequacy of widely used diagnostic criteria as a marker for the disorder (Fletcher et al., 2005). However, some studies that have evaluated numerical processing in children with MLD relative to other low achieving groups have found that numerical processing skills only differentiated children with MLD from typically achieving peers, but not children with moderately low achievement (Mazzocco et al., 2011). Thus it is possible that more specific relationships between numerical processing measures and mathematics achievement would emerge in a subset of children with prenatal alcohol exposure that meet criteria for MLD. Though not possible to examine in the current study, as children were excluded from participation based on presence of either MLD or RD, future studies should investigate the possibility that separate pathways to mathematics performance could exist for alcohol-exposed children with and without MLD.

Relationship between IQ, Numerical Processing, and Mathematics Achievement

Children with prenatal alcohol exposure were significantly impaired on measures of mathematics achievement relative to typically developing controls even when IQ was considered in statistical analyses. As discussed, this finding is consistent with several previous investigations suggesting that mathematics abilities are disproportionately affected by heavy prenatal alcohol exposure (Coles et al., 1991; Goldschmidt et al., 1996; Howell et al., 2006; Jacobson et al., 2011; Streissguth et al., 1994; Streissguth et al., 1994). IQ was also differentially related to numerical processing abilities between groups. In typically developing children, there was no relationship between measures of numerical processing and IQ. However, in children with FASD, IQ was significantly correlated with RT indices of both symbolic and nonsymbolic MJ and both conditions of the numerical stroop task. While numerical processing is generally thought to be independent of IQ (Landerl et al., 2004), perhaps as a result of deficient skills in this domain, children with prenatal alcohol exposure need to rely more heavily on other cognitive processes to support performance on numerical processing tasks (e.g. verbal counting, response conflict), making IQ a more salient predictor of numerical processing in that group.

The relationship between numerical processing measures and mathematics achievement was also affected by the inclusion of IQ in the statistical model, with many numerical processing indices failing to account for a unique amount of variance in mathematics achievement measures. However, numerical stroop RT and MJ accuracy were significantly associated with Math Fluency scores, and MJ accuracy also accounted for a significant amount of variance in Quantitative Concepts scores. This may indicate that there is some effect of numerical processing measures on mathematics achievement in children with prenatal alcohol exposure, independent of IQ, however, these limited findings do not appear to provide entirely compelling evidence that there is a specific link between numerical processing and later mathematics achievement in this population.

These findings are not consistent with those reported by Jacobson et al. (2011), as they demonstrated that the effect of prenatal alcohol exposure on calculation abilities was entirely mediated by performance on a magnitude judgment task and that IQ did not mediate the relationship between prenatal alcohol exposure and calculation or magnitude judgment. Clearly further investigation needs to be done and these discrepant findings highlight the importance of investigating the contribution of both numerical processing skills and abilities in other cognitive domains when investigating mathematics in children with FASD.

Limitations

Previous studies of children with prenatal alcohol exposure have often utilized one gross measure of mathematics achievement to assess mathematical function and its relationship with other variables. While the current study attempted to improve upon this by including four separate measures of mathematics in order to assess different aspects of performance (i.e. Calculation, Math Fluency, Applied Problems, and Quantitative Concepts), each of the measures utilized still required children to drawn upon a broad range of abilities and it is possible that different patterns in their relationships with numerical processing would emerge when examining even more specific types of mathematical skills. Similarly, although measures of basic numerical processing are generally more focused than measures of mathematics achievement, as discussed, they too may rely on a combination of cognitive abilities (e.g. numerical processing and executive control) leaving some question as to which specific functions are driving relationships with mathematics achievement. Future studies should include a more detailed analysis of mathematics and numerical processing in order to better understand the complex relationships among these skills. Also, this study utilized a *domain specific* model of mathematics development to evaluate the nature of mathematics difficulty in children with prenatal alcohol exposure and typically developing controls. However, the current findings, as well as data from previous investigations, suggest that both *domain specific* and *domain general* models could provide useful information regarding mathematics abilities in children with FASD. Future investigations should be more comprehensive in their approach to assessment of mechanisms of mathematics function and may help to reconcile some of the differences between the current findings and the existing literature.

A broad age range was targeted for inclusion in the current study and performance on some numerical processing measures differed as a function of age. The varying capabilities of subjects, due to differences in level of cognitive development as well as grade level and amount of instruction in mathematics, may limit understanding of the relationship between numerical processing and mathematics achievement in our sample. In general, our data show that older children were faster and more accurate at estimating numerical magnitude than younger children and that this relationship with age occasionally varied depending on level of task difficulty and condition of the measure. This is in line with findings from investigations that have evaluated the development of numerical processing over time, which suggest an ontogenic increase in precision of the ANS, manifesting as decreased reaction times and increased accuracy on numerical processing measures as children age (Halberda, Ly, Wilmer, Naiman, & Germine, 2012). Future investigations might consider examining alcohol-exposed children within a focused age range or grade level to gain a more specific understanding of mechanisms that underlie mathematics function at a specific time in development. Conversely, longitudinal studies would allow for evaluation of the trajectory of numerical processing abilities and their relationship with mathematics achievement across development.

Given the cross-sectional and retrospective nature of the study design, we are not able to make *causal* inferences about the role of numerical processing in later mathematics achievement in alcohol-exposed children. Again, longitudinal studies utilizing prospectively identified samples may be more helpful for understanding causal mechanisms of mathematics deficits in children with histories of prenatal alcohol exposure. Finally, although consistent with other studies of mathematics in children affected by prenatal alcohol exposure, the sample used in this study was relatively small in size, and therefore results must be interpreted cautiously. Replication of these findings is critical to better understand the nature of mathematics functioning in children with FASD.

Implications and Future Directions

Recent neuroimaging investigations of children with prenatal alcohol exposure have begun to examine the brain mechanisms underlying mathematics, including calculation abilities and symbolic numerical processing (Lebel et al., 2010; Meintjes et al., 2010; Santhanam et al., 2009). However continued study is necessary, particularly as no investigations have evaluated functional differences in nonsymbolic magnitude judgment or the automaticity of numerical magnitude processing. Understanding how these neural pathways are similar or different to typically developing children and other groups at risk for mathematics difficulties may provide helpful information regarding how mathematics abilities develop in FASD, including what kinds of compensatory mechanisms children might be utilizing, and whether *domain general* or *domain specific* theories are best suited for understanding mathematics in this population.

Findings from the current study may have implications for improvement of academic interventions available for children with histories of prenatal alcohol exposure. Empirically based interventions for this population are limited, however there is some evidence to suggest that a program focused specifically on improvement of mathematics skills may be helpful for children with FASD (Coles et al., 2009; Kable et al., 2007). This intervention was designed specifically to compensate for the neurodevelopmental difficulties commonly observed in children affected by prenatal alcohol exposure and focused on slower pace of mathematics instruction, use of tangible objects to aid in calculations, repetitive experiences, and real time feedback regarding patterns of errors. After six weeks of tutoring services, 58% of children in the intervention group made clinically significant gains on mathematics achievement measures, relative to only 23% of children in a psychoeducational contrast condition

(Kable et al., 2007); importantly, these gains were maintained at 6-month follow-up (Coles et al., 2009).

Because children with prenatal alcohol exposure were found to be deficient in numerical processing it is possible that they would also benefit from interventions targeted directly at the enhancement of these skills. Several intervention studies, using both symbolic and non-symbolic stimuli, have demonstrated improvement in non-exposed children's performance on numerical processing tasks that has also generalized to more global measures of mathematical skills, such as calculation (Hyde, Khanum, & Spelke, 2014; Obersteiner, Reiss, & Ufer, 2013; Ramani & Siegler, 2008; Siegler & Ramani, 2008; Wilson, Dehaene, Dubois, & Fayo, 2009). However, further study regarding the underpinnings of mathematics in FASD should be considered first, given the limited evidence regarding the specificity of these deficits and their relationship with mathematics achievement noted in the current study. It is also possible that interventions focused on improvement of more general cognitive abilities would result in improvements in mathematics function in children with prenatal alcohol exposure. Two known studies have focused on intervention for children with histories of prenatal alcohol exposure in cognitive domains that, while not specifically related to mathematics abilities, may be particularly relevant (Loomes, Rasmussen, Pei, Manji, & Andrew, 2008; Wells, Chasnoff, Schmidt, Telford, & Schwartz, 2012). The first utilized rehearsal training and demonstrated improvement in working memory abilities in children with prenatal alcohol exposure (Loomes et al., 2008) and a more recent investigation employed neurocognitive habilitation to increase executive function skills in exposed children (Wells et al., 2012). Future studies and follow-up investigations of these existing interventions should include outcome measures that evaluate the effect that enhancement of general cognitive function may have on mathematics achievement in children with FASD.

In summary, this study adds to the robust literature indicating that mathematics is a specific area of weakness in FASD. It is also one of a very limited set of investigations that have started to elucidate the mechanisms of mathematics difficulties in children with prenatal alcohol exposure. It is the first known study to examine both symbolic and nonsymbolic aspects of numerical processing and the extent to which numerical magnitude information is automatically activated in children with prenatal alcohol exposure. Consistent with existing findings, we demonstrated that children with prenatal alcohol exposure have difficulties in numerical processing relative to non-exposed peers. However, in contrast, our data do not provide compelling evidence that these abilities are specifically related to higher level mathematics achievement in our sample and leave room for the consideration of alternative explanatory mechanisms. Several differences in study design, including use of different numerical processing tasks, and analytic strategy could account for these discrepant results, and, as such, continued evaluation of mechanisms of mathematics in FASD is critical.

Chapter 4, in part, is currently being prepared for submission for publication of the material. Crocker, Nicole; Mattson, Sarah N. The dissertation author was the primary investigator and author of this material.

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