Prenatal Alcohol Exposure-related Reading and Phonological Processing Deficits Mediated by Working Memory

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COMPULSORY DECLARATION: This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and quotation in, this dissertation from the work, or works, of other people has been attributed, cited, and referenced.

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Date: 13/03/2017

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ABSTRACT

Few research studies have investigated the effects of prenatal alcohol exposure (PAE) on reading ability and/or on phonological processing. Most published studies have only included measures of single-word reading. This choice means those studies may lack ecological validity in that they might not have adequately captured the real-life reading difficulties experienced by individuals with PAE. Furthermore, only a handful have considered the possible mediating roles of those higher-order cognitive functions (e.g., working memory (WM)) that are known to be affected by PAE. The current research employed an extensive battery of phonological processing measures, as well as a reading test that featured measures of reading accuracy, reading rate, and comprehension. A sample of 159 children between 9 and 14 years of age, with varying degrees of PAE, including heavily exposed children and non- or minimally-exposed controls, were tested. The design also considered the potential for a mediating role of WM on performances on these tests. Overall, results showed performance deficits in children with either fetal alcohol syndrome or partial fetal alcohol syndrome on reading comprehension and on four measures of phonological processing, after control for potential confounders. Additional analyses showed that performance within all five of these reading-related domains were at least partially mediated by WM performance. I discuss these results in the context of previous findings in this literature, and describe their implications for reading interventions in children and adolescents with PAE.

INTRODUCTION

Considering the amount of time people spend interacting with written text in their daily lives, there can be little doubt that reading ability has far-reaching value in our information-driven society, stretching from the professional to the social spheres. Those who struggle with reading impairments may experience poor scholastic achievement, and may later endure unemployment and earning difficulties (Caspi, Wright, Moffitt, & Silva, 1998). Besides these external achievement hurdles, at the internal level individuals with reading impairments frequently experience strong feelings of shame, anger, and frustration. These feelings may lead to low self-esteem and behavioral problems (Margalit & Al-Yagon, 2002).

Relatively few studies have investigated reading difficulties in individuals with fetal alcohol spectrum disorders (FASD). This paucity of research stands in contrast to the wealth of investigations focused on intellectual, arithmetic, learning and memory, attention, processing speed, and executive functioning deficits in FASD (e.g., Burden, Jacobson, & Jacobson, 2005; Goldschmidt, Richardson, Stoffer, Geva, & Day, 1996; Howell, Lynch, Platzman, Smith, & Coles, 2006; Jacobson, Jacobson, & Sokol, 1994; Jacobson, Jacobson, Sokol, Chiodo, & Corobana, 2004; Jacobson, Jacobson, Sokol, Martier, & Ager, 1993; Kable & Coles, 2004; Kodituwakku, 2007; Lewis et al., 2015; Lewis et al., 2016; Mattson, Calarco, & Lang, 2006; Mattson, Crocker, & Nguyen, 2011; Mattson, Goodman, Caine, Delis, & Riley, 1999; Mattson, Riley, Gramling, Delis, & Jones, 1997; Rasmussen, 2005; Rasmussen & Bisanz, 2009; Willoughby, Sheard, Nash, & Rovet, 2008). Among those studies that have investigated reading in FASD samples, only a handful have included cognitive variables known to be affected in FASD as potential mediators of the effects of prenatal alcohol exposure (PAE) on reading outcomes (i.e., Dodge, Molteno, Sokol, Jacobson, & Jacobson, 2014; Glass, Graham,

Akshoomoff, & Mattson, 2015; Molteno, Bromley, Thomas, Jacobson, & Jacobson, 2011). A better understanding of the ways in which reading performance is influenced by the effects of PAE on working memory could, for example, help guide future intervention programs.

Mechanisms of Skilled Reading

To grasp the meaning of a text, readers rely on the interactive processes of lower-order word recognition and higher-order meaning-making (Cain, Oakhill, & Bryant, 2004; Verhoeven, Reitsma, & Siegel, 2011). One of the first steps in reading acquisition involves the elementary decoding of written letters into speech sounds (also called phonological recoding), a process that occurs with increasing speed and accuracy as reading experience increases. Eventually, skilled readers are able to automatically recognize multi-letter units and whole words, allowing them to focus more on the meaning of text than on the recognition of words (Samuels & Flor, 1997). This early ability to map orthographic units to familiar phonological forms requires a certain level of phonological awareness - an understanding of how oral language can be divided into progressively smaller units of words and phonemes (Wagner et al., 1997). Research has shown, repeatedly, that individuals with reading disorders often experience phonological awareness deficits (e.g., Bruck, 1992; Kirby, Parrila, & Pfeiffer, 2003).

Besides the fundamental auditory and visual perception processes that are necessary for reading, a multitude of cognitive processes also come into play (Verhoeven et al., 2011). As with other cognitive tasks, attention is considered a prerequisite for skilled reading, allowing for the top-down control of, for example, saccadic eye movements and information processing (Schuett, Heywood, Kentridge, & Zihl, 2008). Furthermore, complex cognitive tasks like reading rely heavily on other, high-level, aspects of executive functioning (EF; an umbrella term for cognitive skills involving self-regulation and mental control), such as working memory (WM) capacity

(Baddeley, 2003). WM is defined, generally, as the ability to temporarily store and manipulate information. With specific regard to reading, adequate WM capability allows the reader to: (1) rehearse phonological information, necessary for word decoding and reading comprehension, using the phonological loop component; (2) maintain visual representations of the text layout, using the visuospatial sketchpad component; and (3) switch between the processing and storing aspects of information processing using the central executive system that allows for attentional control of WM. WM capacity has been found to be a robust predictor of reading comprehension (Cain et al., 2004; Carretti, Borella, Cornoldi, & De Beni, 2009), and a WM-based intervention with special-needs children improved their reading comprehension (Dahlin, 2011).

Fetal Alcohol Spectrum Disorders (FASD)

FASD: Diagnosis and associated cognitive impairments. FASD is an umbrella term used to describe a range of adverse physical, cognitive, and behavioral effects that may occur when a fetus is exposed to alcohol prenatally (Hoyme et al., 2005). At the most severe end of the FASD continuum is *fetal alcohol syndrome* (FAS), which is characterized by a consistent pattern of facial anomalies (e.g., short palpebral fissures, thin upper lip, flat or smooth philtrum, and flat nasal bridge), with accompanying pre- or post-natal growth retardation and deficits in central nervous system (CNS) development and functioning. Except in the case of FAS, an FASD diagnosis can only be made when there is a confirmed history of maternal drinking during pregnancy. *Partial FAS* (PFAS) is characterized by the presence of at least two of the characteristic facial anomalies, and either growth retardation, deficits in CNS development, or cognitive-behavioral deficits. *Alcohol-related birth defects* (ARBD) refer to the presence of PAE-related congenital structural defects (e.g., cardiac, renal, or skeletal defects) in the absence of other FAS-related deficits. Finally, *alcohol-related neurodevelopmental disorder* (ARND)

refers to the presence of PAE-related CNS development and/or cognitive-behavioral deficits in the absence of other FAS-related deficits. ARND is the most difficult of these disorders to identify, due to a lack of agreement regarding a specific neurobehavioral phenotype or behavioral profile. Given the diverse and, as yet, unspecified range of outcomes potentially associated with a diagnosis of ARND, the current research, therefore, grouped heavily exposed children who did not meet criteria for FAS or PFAS into a single group termed *nonsyndromal heavily exposed* (HE).

The diversity of manifestations that fall within the FASD classification scheme is due to differences in the timing and level of PAE, as well as the presence of maternal risk factors (e.g., maternal age at conception; Jacobson et al., 2004; May et al., 2005) and genetic differences (Dodge, Jacobson, & Jacobson, 2014; Jacobson et al., 2006; see review by Warren & Li, 2005). The resulting cognitive-behavioral profiles found in individuals with FASD show similar degrees of variability, with the most severely affected being those who have the characteristic FAS facial anomalies. Those without those facial anomalies are usually less severely impaired. A recent study using innovative 3D technology has, however, shown that some HE children whose facial anomalies were not detected during clinical dysmorphology examinations may, nonetheless, have cognitive deficits similar to those of children with FAS and PFAS (Suttie et al., 2013). Hence, contemporary research studies of FASD should, if possible, include an HE or ARND comparison group alongside the FAS and PFAS groups.

There is a rich literature describing, in children on the FASD continuum, impaired general intellectual functioning (Jacobson et al., 2004; Mattson et al., 1997), as well as specific deficits in arithmetic (Goldschmidt et al., 1996; Howell et al., 2006; Rasmussen & Bisanz, 2009), verbal learning and memory (Lewis et al., 2015; Lewis et al., 2016; Mattson et al., 2011;

Mattson, Riley, Gramling, Delis, & Jones, 1998; Willoughby et al., 2008), language and speech (see Kodituwakku, 2007, for a review), attention (Mattson et al., 2006), processing speed (Burden et al., 2005; Jacobson et al., 1994; Jacobson et al., 1993; Kable & Coles, 2004), and executive functions (Kodituwakku, 2007; Mattson et al., 2011; Mattson et al., 1999; Rasmussen, 2005). However, relatively few studies have focused on reading performance in FASD.

FASD: Reading performance. A relatively small literature describes FASD-related reading deficits. In a large Australian sample (N = 4056), 8- to 9-year-olds with heavy alcohol exposure during the first trimester of pregnancy were twice as likely to fail to attain the benchmark for reading on a national test (O'Leary, Taylor, Zubrick, Kurinczuk, & Bower, 2013). Such research provides valuable insight into the real-world reading performance of individuals with PAE. Unfortunately, it does not provide insight into their specific areas of difficulty. To identify exactly where breakdowns occur, it is necessary to employ measures designed specifically to investigate the various aspects of reading.

The four studies described immediately below investigated PAE effects on letter identification and single-word reading using the *Wide Range Achievement Test-Revised* (WRAT-R; Jastak & Wilkinson, 1984). The first study included 482 school-aged children with moderate PAE (Streissguth, Barr, & Sampson, 1990). Binge drinking (defined, in this case, as 5 or more drinks per occasion) in the month before pregnancy recognition was related to a 3-point deficit in reading scores at age 7.5 years. The second study, a longitudinal design, assessed a sample of 512 children (M age = 6.5 years; Goldschmidt et al., 1996). It found that deficits in reading ability were associated with alcohol exposure during the second trimester of pregnancy. These effects remained only marginally significant after controlling for IQ, but a subsequent analysis showed effects over and above IQ when alcohol use was dichotomized at 1 drink per day. The

authors interpreted their findings in terms of a threshold effect, where second trimester PAE-related reading deficits only became evident at 1 drink or more per day. The third study investigated a sample of 50 children, aged between 5 and 16 years (Mattson et al., 1998). It found that children with PAE (*M* age = 9.1 years) and FAS (*M* age = 10.8 years) performed significantly more poorly than controls (*M* age = 10.2 years) on this test of letter identification and single-word reading, but that the performances of alcohol-exposed groups did not differ from each other. Finally, Sowell et al. (2008) compared the reading performance of 17 children and adolescents with FASD (*M* age = 10.5 years) to that of 19 typically developing age- and gender-matched controls (*M* age = 11.2 years). They reported that FASD participants performed significantly more poorly than controls on the third edition of the WRAT (WRAT-3; Wilkinson, 1993).

Treit et al. (2013) used the *Word Identification* subtest from the *Woodcock Reading Mastery Tests-Revised* (WRMT-R; Woodcock, 1987) to investigate the ability to identify and pronounce single words of increasing difficulty in 17 children with FASD at two different points (*M* age = 8.2 years at first assessment; *M* age = 11.4 years at second assessment). Performance by the FASD sample was significantly below the population norm at the initial assessment (p = .011), but not at the subsequent assessment (p = .083), indicating a degree of 'catch-up' in word-reading performance over time. This finding may be related to the fact that word-reading becomes more automatic as reading experience increases (Samuels & Flor, 1997), so that younger children with word-reading deficits experience delays that might not be evident later on.

Together, the studies reviewed above suggest that PAE effects on word-reading may be sensitive to both the dose and timing of exposure and may be less evident at later ages, as reading experience increases. It is not known, however, to what degree children with PAE catch

up and attain the same level of reading proficiency as non-exposed children. In addition, successful word-reading can be achieved in multiple ways: the reading of unfamiliar words can rely on processes of phonological recoding, analogizing (the unfamiliar word is compared to a familiar word with similar spelling), or predicting (guessing based on letter clues and context). In contrast, the reading of familiar words relies more on whole-word retrieval from long-term memory (Ehri, 2005). Hence, scores on the word-reading tests described above do not permit differentiation between the contributions to final outcome of various word-reading processes.

Reading tests that aim specifically to measure phonological processing skills typically use non-words (strings of consonants and vowels that are not real words) to establish how well readers can phonologically decode words with which they are not familiar. The WRMT-R *Word Attack* subtest (Woodcock, 1987) is one such test. This test assesses phonological processing and reading decoding skills using 45 non-words, thereby avoiding other reading dimension confounds, such as comparisons with familiar words or guessing from context. Non-word pronunciations must follow the grammatical rules of English to be scored correctly. Streissguth et al. (1994) used that subtest to assess phonological processing in a cohort of 462 alcohol-exposed adolescents at age 14 years. They found dose-dependent effects, with higher levels of exposure related to larger performance deficits and binge drinking showing the strongest effects. A later study also employed the Word Attack subtest to compare the performance of 9 adolescents with FAS (14-16 years old) with data from a non- or minimally-exposed cohort of 174 adolescents (14-15 years old; Carmichael Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998). That study did not find significant between-group differences in phonological processing, although it must be noted that that FAS sample might have been too small to detect effects.

Adnams et al. (2007) investigated reading ability and phonological awareness in a South African sample of 9- to 10-year old children. They assessed reading ability using *The University of Cape Town Reading Test* and phonological awareness using an adapted and Afrikaans-translated version of the *Phonological Awareness and Early Literacy Test* (PAELT; Byrne & Fielding-Barnsley, 1993). The PAELT contains multiple subtests measuring different aspects of phonological awareness (e.g., segmentation of sounds, syllable and phoneme blending, syllable and phoneme manipulation, and letter sounds). Children with FASD (n = 36) performed significantly more poorly than non-exposed controls (n = 23) on measures of both reading ability and phonological awareness. Furthermore, phonological awareness deficits persisted after controlling for verbal IQ.

Given that skilled readers eventually progress from more basic word-recognition stages to higher-order stages where comprehension becomes a key factor (Verhoeven et al., 2011), it is surprising that not many studies have investigated PAE effects on reading comprehension. One measure that includes basic reading (phonological processing and single-word reading) and comprehension subtests is the reading component of the *Wechsler Individual Achievement Test* (WIAT; Wechsler, 1992). A study that employed only the WIAT basic reading subtest also obtained results of standardized, school-administered tests of reading from participants' school records (Howell et al., 2006). This study included two groups with PAE, one with the physical effects related to exposure (n = 46; M age = 15.1 years) and one without (n = 82; M age = 14.9 years), as well as a non-exposed control group (n = 53; M age = 14.9 years) and a comparison group that featured children receiving special education services (n = 84; M age = 15.5 years). On average, the group with physical features of PAE and the special education group performed significantly more poorly than the other two groups on the school-administered reading tests.

However, only the special education group performed significantly more poorly than the other groups on the WIAT basic reading subtest. These discrepant findings (reading difficulties in the most severely affected PAE group on school-administered reading tests but not on the WIAT basic reading subtest) suggest that this adolescent sample's reading difficulties may be explained by factors other than those examined by that subtest.

I mentioned earlier that reading (and reading comprehension especially) involves a multitude of higher-order cognitive processes (e.g., attention and WM) that extend beyond phonological processing (e.g., Cain et al., 2004; Verhoeven et al., 2011). As also mentioned earlier, many of those higher-order processes are known to be affected in FASD (e.g., Burden et al., 2005; Kodituwakku, 2007; Mattson et al., 2006; Mattson et al., 2011; Rasmussen, 2005). However, only a few studies have investigated whether these higher-order cognitive processes might serve as potential mediators of PAE effects on reading outcomes.

Dodge et al. (2014) included both the basic reading and comprehension subtests from the WIAT and found, in a sample of 282 adolescents (*M* age = 14.4 years), that PAE was related to deficits in reading comprehension. However, they also found no basic reading deficits in their sample. Furthermore, poorer reading comprehension was not attributed to a lowered IQ, but was mediated by PAE-related processing speed and attention deficits. The researchers noted that PAE effects on basic reading skills may have been evident at younger ages, but were no longer present in their adolescent sample.

Another study employed a word-reading subtest from the second edition of the WIAT (WIAT-II; Wechsler, 2005) to assess single-word reading in children with heavy PAE (n = 49) and children with minimal or no PAE (n = 47), all aged between 8 and 16 years (M = 12.5; Glass et al., 2015). In addition, the researchers used the NEPSY-II (Korkman, Kirk, & Kemp, 2007)

subtests assessing phonological processing, speeded naming, and word-list interference (WM measure) to investigate the associations of these cognitive variables with word-reading. They found that children with heavy PAE performed significantly more poorly on the word-reading subtest than those with minimal or no PAE. Furthermore, although phonological processing, speeded naming, and WM all contributed significantly to word-reading performance across both groups, there was a significant WM x Group interaction: The relation between WM and word-reading was much stronger for the children with heavy PAE. However, that study did not investigate reading comprehension, which may also be affected by PAE-related WM deficits.

In a sample of 47 children (*M* age = 11.3 years), the effects of heavy PAE on reading comprehension were mediated by both reading speed and phonological awareness deficits (Molteno et al., 2011). Reading comprehension effects remained significant after controlling for IQ. This study measured reading speed, accuracy, and comprehension using the *Neale Analysis of Reading Ability* (NARA; Neale, 1997) and phonological awareness using the *Phonological Assessment Battery* (PhAB; Frederickson, Frith, & Reason, 1997). Of interest here is that the Spoonerisms subtest of the PhAB was the phonological awareness component that mediated the effect of alcohol on reading comprehension in children with PAE. This subtest measures the ability to segment single-syllable words and to then build new words, or word combinations, by combining those segments. Some have argued that the Spoonerisms subtest does not only involve phonological awareness but also relies on WM (Varvara, Varuzza, Sorrentino, Vicari, & Menghini, 2014), because it requires the segmentation of words into sound units (phonological awareness), holding those segments in mind (WM phonological loop component), and then combining those segments into new words (phonological awareness and WM central executive

component). Thus, in addition to reading speed, WM and phonological awareness, rather than pure phonological awareness, may have mediated reading comprehension in this sample.

The previously-mentioned study by Carmichael Olson et al. (1998) also investigated reading speed and comprehension in their adolescent sample, using the *Rapid Single Visual Presentation Task* (RSVP; Kintsch & VanDijk, 1978). The RSVP measures reading speed, memory, and comprehension. It is a computer-administered task in which a story is presented, one word at a time, in the middle of the screen. The reader controls the rate of presentation by pressing the space bar. Memory and comprehension are tested by the interjection of multiple-choice questions between passages. The 9 adolescents with FAS performed more poorly than a minimally- or non-exposed cohort group (n = 174) on the comprehension component of the RSVP, but their performance was similar to that of an IQ comparison subgroup from the larger cohort (n = 52). In this study, there were no between-group differences in reading speed. However, the fact that the FAS group and the IQ comparison group performed more poorly on the comprehension component than the larger cohort, despite having similar reading speeds, suggests that comprehension deficits may have been related to a relatively impaired general intellectual functioning in this sample. Or, comprehension may have been mediated by other, more specific cognitive variables, resulting in similar performances by the FAS and IQ comparison groups.

Rationale, Specific Aims and Hypotheses

In summary, the literature reviewed above suggests that PAE is associated with academic reading difficulties (O'Leary et al., 2013; Howell et al., 2006), as well as with specific deficits in letter identification and single-word reading (Glass et al., 2015; Goldschmidt et al., 1996; Mattson et al., 1998; Sowell et al., 2008; Streissguth et al., 1990; Treit et al., 2013); phonological

processing (Adnams et al., 2007; Glass et al., 2015; Molteno et al., 2011; Streissguth et al., 1994); sentence reading (Adnams et al., 2007); and reading comprehension (Carmichael Olson et al., 1998; Dodge et al., 2014; Molteno et al., 2011). However, deficits in letter identification, single-word reading, and phonological processing may not be evident at later ages (Carmichael Olson et al., 1998; Dodge et al., 2014; Howell et al., 2006; Treit et al., 2013). PAE-related reading comprehension difficulties have been reported to be mediated by lower IQ (Carmichael Olson et al., 1998) and by deficits in phonological awareness, processing speed, and attention, over and above IQ (Molteno et al., 2011; Dodge et al., 2014). Finally, deficits in single-word reading following heavy PAE appear to be related to deficits in phonological processing, speeded naming, and WM (Glass et al., 2015).

Many of the extant studies in this literature employed tests of single-word reading only. These tests do not provide a sufficiently broad scope to accurately capture where breakdowns in reading might be occurring, especially at older ages when word-reading becomes more automatic. The real-world reading difficulties that these children experience may be more strongly impacted by deficits at the sentence level, and in reading comprehension. Furthermore, some higher-order cognitive functions that have repeatedly been shown to be affected in PAE are also known to be important components in skilled reading (e.g., attention, WM, and other EF skills), yet very few studies have considered these cognitive functions in PAE-related reading research. To my knowledge, no study has investigated the role of WM in PAE-related reading deficits beyond single-word reading.

Hence, the first purpose of the current study was to establish whether children with a history of PAE exhibit deficits in phonological processing and reading ability, as measured by comprehensive assessments of those two constructs. Furthermore, the study aimed to determine

whether any observed deficits in phonological processing and reading ability were mediated by WM deficits.

The study therefore tested the following hypotheses:

1. Children with a history of PAE will show impaired performance, relative to that of non-exposed or minimally exposed, demographically similar, controls, on measures of reading ability and phonological processing. Furthermore, any observed deficits will be due to the effects of PAE and not be attributable to the effects of potential confounding variables (e.g., prenatal smoking and child's age at testing).
2. PAE-related deficits in reading ability and phonological processing will be mediated by WM deficits.

METHODS

Design and Setting

The current study employed a cross-sectional design and was part of an on-going prospective longitudinal cohort study (Jacobson et al., 2008).

All study procedures were conducted at the Child Development Research Laboratory in the University of Cape Town, Faculty of Health Sciences.

Participants

The research sample consisted of 159 Cape Coloured (mixed ancestry) children whose mothers were prospectively recruited into the parent study during pregnancy. The children were assessed during infancy, and at 5, 9, and 13 years of age. The current research is based on data obtained at their 9-year follow-up assessment.

Recruitment. The children's mothers were recruited between July 1999 and January 2002 at the antenatal clinic of a midwife obstetric unit that serves an economically disadvantaged, predominantly Cape Coloured, population (Jacobson et al., 2008). Each gravida was interviewed by a research nurse at her first antenatal visit. A timeline follow-back interview, adapted for use with women in this community, focused on the mother's alcohol use, both at the time of recruitment and at conception (Jacobson, Chiodo, Jacobson, & Sokol, 2002).

Inclusion criteria. Any woman averaging at least 1.0 oz of absolute alcohol (AA)/day (i.e., the equivalent of 2 standard drinks/day), or reporting at least two incidents of binge drinking (5 standard drinks/occasion),[1] during the first trimester of pregnancy was invited to participate in the study. Women who abstained from drinking any alcohol during pregnancy or who drank only minimally (< 0.5 oz AA/day and no binge drinking during the first trimester) were invited to participate as part of the control group.

Exclusion criteria. Women younger than 18 years of age and those with diabetes, epilepsy, or cardiac problems requiring treatment were not included. Religiously observant Muslim women were also excluded because their religious practices prohibit alcohol consumption, and they would, therefore, have been disproportionately represented among the controls. Infant exclusionary criteria included major chromosomal anomalies, neural tube defects, multiple births, and seizures.

FASD diagnoses. In September 2005, a 6-day clinic was organized at a local church in a neighborhood where many of the children live. During the clinic, each child was examined for

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[1]At the time of participant recruitment, binge drinking was defined as 5 drinks/occasion. The definition of binge drinking for women has since been changed to 4 drinks/occasion (National Institute of Alcohol Abuse and Alcoholism, 2004). Thus, for recruitment purposes, a cut-off of 5 drinks/occasion was used, but subsequent analyses will employ a binge drinking cut-off of 4 drinks/occasion.

growth and FAS anomalies by two expert, U.S.-based, FAS dysmorphologists using a standard diagnostic protocol (Hoyme et al., 2005). There was substantial agreement between the two U.S.-based dysmorphologists on their assessments of all dysmorphic features, including palpebral fissure length and philtrum and vermilion ratings based on the Astley and Clarren (2001) rating scales (r = .80, .84, and .77, respectively). There was also substantial agreement between them and a Cape Town-based FAS dysmorphologist (median r = .78), who evaluated 8 children who could not be seen at the clinic. The two dysmorphologists who attended the clinic (and who were blind to the alcohol exposure history) subsequently participated in case conferences with S. and J. Jacobson and C. Molteno. At those case conferences, each child was classified as FAS, PFAS, HE, or non-exposed control.

Materials

Maternal alcohol and drug use. In the timeline follow-back interview administered at recruitment, the mother was asked about her drinking on a day-by-day basis during a typical 2-week period around the time of conception, with recall linked to specific times of day and activities (Jacobson et al., 2008). If she reported that her drinking had changed since conception, she was also asked about when it had changed and about her usage pattern over the previous 2 weeks. At the follow-up antenatal visit, the mother was again asked about her drinking during the previous 2 weeks. At the 1-month postpartum visit, she was asked about her drinking during a typical 2-week period during the latter part of her pregnancy.

Volume was recorded for each type of alcoholic beverage consumed each day and converted to oz of AA using weights that reflect AA concentration in Cape Town: liquor = 0.40, beer = 0.05, wine = 0.12, and ciders = 0.06. Thereafter, six summary measures were constructed:

average oz AA⁄day, average oz AA/occasion, and number of drinking days/week (frequency) at conception and across pregnancy.

The mothers were also asked how many cigarettes they smoked per day, and whether they used marijuana, methaqualone ("mandrax"), cocaine, or any other illicit drugs, during pregnancy.

Neale Analysis of Reading Ability (NARA). This instrument measures reading accuracy, reading rate, and comprehension, and has good reliability and validity (Neale, 1997). Bower and Hartman (2006) translated and adapted the NARA into an Afrikaans version that is used by South African clinicians for the purposes of neuropsychological and educational assessment.

Participants are required to read six increasingly difficult text passages out loud, while the examiner notes any reading errors on a copy of the same text and records the time taken to read each passage. Hence, the examiner is able to obtain measures of reading accuracy and speed. Reading errors are organized into six categories: mispronunciations (phonetic errors), substitutions (words in passage replaced by real words), refusals (pauses of 4-6 seconds and failures to attempt words), additions (words/word parts inserted into passage), omissions (words are omitted from passage), and reversals (letters in words are swopped around). At the conclusion of each passage, participants answer comprehension questions related to that passage. Once a participant exceeds the maximum number of allowed errors on a passage (16 errors for passages 1 to 5; 20 errors for passage 6), the test is discontinued, no comprehension questions for that passage are administered, and only the passages leading up to that one are scored.

Phonological Assessment Battery (PhAB). Phonological processing ability was assessed using scores obtained from the *Phonological Assessment Battery* (PhAB; Frederickson

et al., 1997). The PhAB is an English-language instrument used for purposes of neuropsychological and educational assessment, and has good reliability and validity. Two Afrikaans-speaking members of the parent study's research team adapted and translated the PhAB into Afrikaans, for assessment in that language. (See Appendix A for original and Afrikaans-translated and -adapted PhAB subtests.)

The PhAB provides a comprehensive assessment of phonological processing across six subtests:

(1) The Alliteration Test measures the ability to identify the initial sounds in single syllable words. The examiner reads three words aloud, and the child has to repeat the two words with the same initial sound (e.g., lot, *mess, mud*).

(2) The Rhyme Test measures the ability to detect rhyming in single syllable words. The examiner reads three words aloud, and the child has to repeat the two words that end with the same sound (e.g., *sail*, boot, *nail*).

(3) The Spoonerisms Test measures the ability to segment single-syllable words and to then build new words, or word combinations, by combining those segments. Part 1 of the test requires the participant to replace the first sound of a word with another sound (e.g., replacing the first sound of *cat* with an */f/* makes *fat*). Part 2 requires the participant to switch the first sounds of two words (e.g., *lazy dog* becomes *dazy log*). The resulting target words can be either real words or nonsense words.

(4) The Non-Word Reading Test measures the ability to phonologically decode letter strings. Participants are required to read non-words (rather than real words) so that they rely only on their phonological processing skills and knowledge of letter-sound correspondence, without the help of visual vocabulary recognition or spoken vocabulary cues that may feature when

reading phonetically regular words. Part 1 consists of 10 one-syllable items (e.g., *gat*) and Part 2 consists of 10 two-syllable items (e.g., *ropsatch*).

(5) The Naming Speed Test, which requires retrieval of whole-word phonological coding, measures phonological production speed. The test contains two subtests in which two different stimulus types are used: line drawings of five common objects (*The Picture Naming Test*) and the numbers 1 to 9 (*The Digit Naming Test*). Each test consists of two trials. During each of these, the participant is asked to name 50 randomly presented items, in sequence, as quickly as possible.

(6) The Fluency Test measures the ability to retrieve phonological information from long-term memory. It contains three subtests, in which participants are required to name as many words as possible within 30 seconds. The *Semantic Fluency* test requires participants to name words from a given semantic category (e.g., *animals*), whereas the *Alliteration Fluency* and *Rhyme Fluency* tests require them to name words that either start or end with the same sounds (similar to the alliteration and rhyme tests above). The *Semantic Fluency* subtest measures semantic, rather than phonological, processing. Hence, results from this subtest can be contrasted with those from the *Alliteration Fluency* and *Rhyme Fluency* subtests, in order to distinguish performance on semantic processing tasks from that on phonological processing tasks.

General intellectual functioning (IQ). IQ was assessed using the *Wechsler Intelligence Scale for Children* (WISC-IV), which has good reliability and validity (Wechsler, 2003). The WISC was translated into Afrikaans by a Master's level clinical psychologist who was a native Afrikaans speaker. The *Junior South African Individual Scales* (JSAIS; Madge et al., 1981) instrument was also administered at the children's 5-year assessment visit. The JSAIS, a locally normed and standardized battery, is available in Afrikaans and English. JSAIS IQ scores

obtained at the 5-year assessment visit were strongly correlated with their 9-year WISC scores, $r = .71$, $p < .001$, thus providing validation for the translated subtests.

Working memory (WM). A measure of verbal WM was obtained from the WISC-IV *Digit Span Backward* subtest. This task requires participants to repeat strings of digits of increasing length in reverse order to that presented. The examiner reads each number at a rate of one per second and discontinues the test when the participant is not able to repeat both items from a given sequence length correctly.

Table 1 presents details of the potential mediator and outcome variables that were included in subsequent statistical analyses.

Procedure

Ethical considerations. This research was approved by the UCT Department of Psychology Research Ethics Committee and adhered to the ethical guidelines outlined by the UCT Codes for Research. The UCT Faculty of Health Sciences Research Ethics Committee and the Wayne State University Institutional Review Board provided ethical approval for the parent study (See Appendix B for relevant ethical approval letters.)

Written informed consent was obtained from each mother at recruitment and at subsequent visits, and written assent was obtained from those participants who were between 13 and 17 years old. The consent and assent forms were administered in either Afrikaans or English, depending on the language preference of the mother or the language of instruction in the child's school, respectively (see Appendix C). Participants were informed that participation was voluntary and that they were able to withdraw at any stage. If participants had any concerns or questions, they were able to discuss these with Prof. Molteno, a developmental pediatrician, who oversees the Cape Town study.

Table 1
Potential Mediator and Outcome Variables Included in Analyses

Variable	Definition
Instrument /Outcome variable	
NARA	
Reading Accuracy	Summed total of maximum score/passage (16 for passages 1 to 5; 20 for passage 20) minus amount of errors/passage. Score is then converted to an age equivalent score using norms tables.
Reading Rate	Words/minute: Total number of words in passages administered, multiplied by 60, divided by total reading time of passages (in seconds). Score is then converted to an age equivalent score using norms tables.
Comprehension	Total number of correctly answered comprehension questions across passages administered. Score is then converted to an age equivalent score using norms tables.
PhAB	
Alliteration	Total correct responses from Part 1 and Part 2 of subtest (max = 10).
Rhyme	Total correct responses from Part 1 and Part 2 of subtest (max = 21).
Spoonerisms	Total correct responses from Part 1 and Part 2 of subtest (max = 30).
Non-word Reading	Total correct responses from Card 2 and Card 3 of subtest (max = 20).
Picture Naming	Total time (in seconds) taken to name pictures from Picture Naming Card 1 and Picture Naming Card 2.
Digit Naming	Total time (in seconds) taken to name digits from Digit Naming Card 1 and Digit Naming Card 2.
Alliteration Fluency	Total correct responses given across 2 trials.
Rhyme Fluency	Total correct responses given across 2 trials.
Semantic Fluency	Total correct responses given across 2 trials.
WISC-IV IQ	
FSIQ	Full Scale IQ score derived from performance on 10 subtests.
Working Memory	Maximum number of digits recalled backwards on WISC-IV Digit Span Backwards subtest.

Note: NARA = Neale Analysis of Reading Ability; PhAB = Phonological Assessment Battery; WISC-IV = Wechsler Intelligence Scale for Children–Fourth Edition; FSIQ = Full-Scale IQ.

All data collected were identified only by code numbers to ensure confidentiality and to protect the anonymity of participants. The data files are kept in locked cabinets in the UCT Child Development Research Laboratory. Unless mothers provide written consent, no information is released for medical or other purposes. No identifiable details of participants are used in publications or presentations, except that photos may be used for scientific or teaching purposes if (and only if) the mother provides written permission to do so.

All women who reported drinking during pregnancy were advised that stopping or reducing their drinking would reduce the risk to their baby. They were also referred to the South African National Council on Alcoholism and Drug Dependence or the Department of Psychiatry and Mental Health at Groote Schuur Hospital for treatment, if they wanted it. After the high incidence of maternal alcoholism in the Cape Town Longitudinal Cohort was recognized, an intervention was implemented in which both drinking and nondrinking mothers in the study were invited to participate in a home visitor program run by the Parent Centre, a non-profit organization based in Cape Town, shortly after being recruited into the study. The program involved meeting with a home visitor 1-2 times per week during pregnancy and for 6 months postpartum. The home visitors were trained to use motivational interviewing techniques to support and encourage mothers to talk about their use of alcohol and other stressors in their everyday lives, with the aim of helping them find ways to reduce their alcohol intake and/or be referred for treatment for alcoholism. The home visitors were supervised by and met weekly with a licensed clinical psychologist and/or a senior social worker at the Parent Centre. Arrangements were made with the UCT Department of Psychiatry and Mental Health for referral for treatment of severe depression and/or alcohol abuse or dependence, if requested by the mother.

None of the study procedures put any of the participants at risk. The mothers and participants incurred no participation-related costs. After each testing session, the mother received ZAR 150 (at the time of study, approximately US$ 20) compensation for their participation. At the conclusion of the second session, she received a photo of the child and the child received a small age-appropriate gift.

Testing procedure. The cognitive tests relevant to the current study formed part of larger neuropsychological batteries, administered at the participants' 9-year follow-up visits (between

2009 and 2015). Testing occurred in three phases. A number of children completed all of their testing sessions during one phase, before the next group of children were tested during the following phase. Table 2 depicts the timeline and order of cognitive testing. Only the tests relevant to the current study are included in the table.

Participants and their mothers were transported from their homes to the UCT Child Development Research Laboratory, and back home again, in a research-dedicated van. Prior to beginning testing, a member of the research team explained the study procedures in detail to the mother, who was asked to sign an informed consent document, and to the child, who was asked to sign a written assent document (if they were between 13 and 17 years old at the time; see Appendix C). Each testing session took about 3-4 hours, including breakfast, a 20-minute break for a mid-morning snack, and a light lunch. Standard procedure was followed for administration in both Afrikaans and English. All the examiners were MA-level research assistants who were blind to FASD diagnoses and to the alcohol exposure history of participants.

Data Management and Statistical Analyses

Variables. The effects of PAE on the developing fetus may vary depending on, for instance, dose, timing, maternal age at delivery, and genetic variability (Jacobson et al., 2004). The predictor variables for the current study, therefore, included both continuous measures of PAE (oz AA/day, oz AA/occasion, and number of drinking days/week) and categorical measures of FASD diagnosis (FAS/PFAS, HE, or non-exposed Control). The outcome variables included: indices of reading performance, as measured by NARA Reading Accuracy, Reading Rate, and Comprehension scores; and indices of phonological processing, as measured by the PhAB Alliteration, Rhyme, Spoonerisms, Non-word Reading, Picture Naming, Digit Naming, Alliteration Fluency, and Rhyme Fluency subtests. These scores were not combined into

Table 2

Timeline and Order of Cognitive Test Administration

2009	2010	2011	2012	2013	2014	2015
Phase 1			Phase 2		Phase 3	
Session 1	Session 2		Session 1		Session 1	Session 2
Day 1			Day 1		Day 1	
WISC-IV	NARA		WISC-IV		WISC-IV	NARA
Similarities	PhAB		Similarities		Similarities	PhAB
Block Design			Block Design		Block Design	
Picture Completion			Picture Completion		Picture Completion	
Digit Span			Digit Span		Digit Span	
Coding			Coding		Coding	
			NARA			
Day 2			PhAB		Day 2	
WISC-IV					WISC-IV	
Vocabulary			Day 2		Matrix Reasoning	
Matrix Reasoning			WISC-IV		Arithmetic	
Arithmetic			Vocabulary		Symbol Search	
Comprehension			Matrix Reasoning		Comprehension	
Symbol Search			Arithmetic		Vocabulary	
			Comprehension			
			Symbol Search			

Note. Different testing sessions occurred months apart, whereas testing days within a single session occurred, whenever possible, on consecutive days. WISC-IV = Wechsler Intelligence Scale for Children–Fourth Edition; NARA = Neale Analysis of Reading Ability; PhAB = Phonological Assessment Battery.

composite scores, so that potentially varying PAE effects on different aspects of reading and phonological processing could be explored independently. Scores on the PhAB Semantic Fluency subtest (a test of semantic processing, as opposed to phonological processing) served as an additional outcome variable, to compare with scores on the Alliteration Fluency and Rhyme Fluency subtests. The potential mediating variable under consideration was WM, as measured by scores obtained on the WISC-IV Digit Span Backwards subtest.

Given the potential influences of extraneous variables in developmental teratology research (Jacobson & Jacobson, 2005), I constructed a correlation matrix to identify potential confounding variables. Any control variable that was related even weakly to an outcome variable (i.e., at $p <$ .10) was considered a potential confounder of PAE effects on that outcome and was statistically controlled for in subsequent analyses. The potential confounding variables included the child's age at testing, sex of child, primary caregiver's years of education, and maternal smoking during pregnancy. None of the mothers reported using cocaine, and methaqualone ($n = 4$) and marijuana ($n = 14$) use during pregnancy were too rare for statistical adjustment. Associations between PAE and outcome variables were, therefore, rerun omitting children with either prenatal methaqualone or marijuana exposure.

Descriptive statistics. I calculated descriptive statistics for continuous measures of PAE, reading performance and phonological processing, IQ, and WM, to explore the data and to determine whether assumptions underlying parametric statistical tests were met. I also constructed a sample characteristics table to describe the sample's sociodemographic characteristics and scores on other prenatal exposure variables.

Inferential statistical analyses. I used SPSS version 23 to analyze the data. Unless otherwise stated, the threshold for statistical significance was set at $\alpha = .05$. Traditional hypothesis testing emphasizes the importance of avoiding Type I errors (i.e., reporting a relation between variables where no relation exists). But, when it comes to public health research, missing a relation

between variables and thereby underestimating a real risk is of greater concern (Jacobson & Jacobson, 2005). The clinically important effects of PAE on cognitive functioning are often subtle and associated with small effect sizes. The current research was therefore more concerned with avoiding Type II errors (i.e., rejecting a relation between variables where one does exist) in data analyses and interpretation.

I employed three methods of statistical analysis to explore relations between predictor variables and outcome variables. First, analyses of covariance (ANCOVAs) explored relations between FASD diagnosis and phonological processing and reading performance outcomes, with potential confounding variables included as covariates. Least-Significant Difference (LSD) tests were used where post-hoc comparisons of statistically significant results were warranted.

Second, I ran simple regressions with continuous measures of PAE entered as predictors of phonological processing and reading performance outcomes. Third, I tested the same models, but this time using multiple regression analyses with potential confounders added in. AA/day was significantly positively skewed and was, therefore, normalized using a natural log transformation ($ln[x + 1]$) before being included in any regression analyses. Hierarchical multiple regression analyses were run only in cases where simple regressions identified significant or near-significant relations. In each multiple regression analysis, I entered PAE at the first step and potential confounding variables at the second step as a block, to partial out their effects. I conducted additional simple and multiple regression analyses (as suggested by Baron & Kenny, 1986) to determine whether observed relations between FASD diagnoses and reading performance and phonological processing were mediated by WM, before assessing the statistical significance of mediation effects using the Sobel Test (Sobel, 1982).

RESULTS

Sample Characteristics

For the purposes of the current analyses, and in a manner consistent with previous studies in the field (Lewis et al., 2015; Lewis et al., 2016), I combined the FAS and PFAS groups to form a larger group (FAS/PFAS; $n = 39$) more comparable in size to the HE ($n = 58$) and Control ($n = 62$) groups. Evidence that this was a judicious decision is provided by the results of one-tailed independent sample *t*-tests showing that the FAS and PFAS groups differed from each other on only two of the outcome measures: Picture Naming, $t(37) = -2.75$, $p = .005$; and Digit Naming, $t(36) = -1.80$, $p = .041$. On all other reading and phonological processing outcomes, $p > 0.2$.

Maternal sample characteristics. Table 3 presents sociodemographic and substance-use characteristics for mothers of children in the three diagnostic groups. There were significant between-group differences for all sociodemographic and substance-use variables, except for marijuana and methaqualone usage, both occurred too rarely for statistical adjustment.

The between-group differences in mother's/primary caregiver's years of education were associated with a medium effect size. Post-hoc pairwise comparisons suggested that mothers of children in the FAS/PFAS group had achieved significantly lower levels of education than those in both the HE and Control groups, $p = .002$ and $p < .001$, respectively. The analyses detected no significant difference in level of education for mothers of children in the HE and Control groups, $p = .148$.

Regarding the three continuous measures of PAE, between-group differences were associated with large effect sizes. Post-hoc pairwise comparisons suggested that mothers of children in the FAS/PFAS group had marginally, but non-significantly, larger AA/day values than those in the HE group, $p = .070$, and significantly greater values than those in the Control group, $p < .001$. Another pairwise comparison suggested that mothers of children in the HE group also had significantly greater AA/day values than those in the Control group, $p < .001$. Regarding drinking

Table 3
Sample Characteristics (N = 159)

Variable	FAS/PFAS (*n* = 39)	HE (*n* = 58)	Control (*n* = 62)	*F* or χ^2	*p*	*ESE*
Maternal characteristics						
Education (years)[a]	7.95 (2.62)	9.41 (2.30)	10.00 (1.80)	10.50	< .001***	.34
Prenatal alcohol exposure						
AA/day (oz)[b]	1.09 (1.23)	0.78 (0.89)	0.00 (0.00)	25.38	< .001***	.50
AA/occasion (oz)	4.09 (1.89)	3.65 (2.50)	0.03 (0.16)	87.05	< .001***	.73
Drinking days/week	1.69 (1.17)	1.31 (0.99)	0.00 (0.02)	61.02	< .001***	.66
Prenatal smoking (cigarettes/day)	6.73 (5.46)	6.43 (5.92)	3.15 (5.35)	7.01	.001**	.29
Prenatal drug use[c]						
Marijuana (days/month)	1.60	2.87	2.23	-	-	-
Methaqualone (days/month)	0.61	1.90	0.00	-	-	-
Child characteristics						
Sex (% male)	58.97	50.00	46.77	1.46	.482	.10
Age at testing (years)	11.66 (1.19)	12.06 (1.00)	12.08 (1.18)	1.95	.146	.16
WISC-IV Full Scale IQ	64.41 (10.43)	75.44 (13.84)	76.15 (13.51)	11.43	< .001***	.36

Note. Means are presented with standard deviations in parentheses. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed nonsyndromal; ESE = effect size estimate; AA = absolute alcohol (0.5 oz AA ≈ 1 standard drink); WISC-IV = Wechsler Intelligence Scale for Children–Fourth Edition. The test statistic was either *F* or χ^2 depending on whether the variable under consideration was continuous or categorical. The estimate of effect size was calculated using either *eta squared* or *Cramer's V* depending on whether a one-way ANOVA or chi-squared test of contingency was employed. [a]Primary caregiver's years of completed education. [b]Data presented for the non-logged variable. [c]Means displayed for users only. Three women in the FAS/PFAS group reported marijuana use during pregnancy, 9 in the HE group did so, as did 2 in the Control group. One woman in the FAS/PFAS group reported methaqualone use during pregnancy, 3 in the HE group did so, and none in the Control group did so.
$^{**}p < .01$. $^{***}p < .001$.

frequency, mothers of children in the FAS/PFAS group had significantly more drinking days/week than those in both the HE and Control groups, $p = .028$ and $p < .001$, respectively. Mothers of children in the HE group also had more drinking days/week than those in the Control group, $p < .001$. Finally, mothers of children in both the FAS/PFAS and HE groups had significantly greater AA/occasion values than those in the Control group, $p < .001$ in both cases, but there was no significant difference in the average AA/occasion values for those in the FAS/PFAS and HE groups, $p = .228$.

In summary, although mothers of children in the FAS/PFAS and HE groups drank similar amounts of alcohol per occasion, those in the FAS/PFAS group drank more frequently than those in the HE group. Of note here too is that only two Control women (3.23%) consumed any alcohol during pregnancy (*M* AA/day = 0.01 in both cases; *M* AA/occasion = 1.16 and 0.59, respectively; and number of drinking days/week = 0.07 and 0.15, respectively).

Regarding prenatal smoking, between-group differences were associated with a medium effect size. Post-hoc pairwise comparisons suggested that mothers of children in both the FAS/PFAS and HE groups smoked significantly more cigarettes per day than those in the Control group, $p = .002$ in both cases. However, the analysis detected no significant difference in the amount of cigarettes smoked per day during pregnancy for mothers of children in the FAS/PFAS and HE groups, $p = .797$.

Child sample characteristics. Table 3 presents sociodemographic and cognitive characteristics for the three groups of children. Analyses detected no significant between-group differences in terms of sex distribution or age at testing.

Regarding WISC-IV performance, the omnibus *F* test detected significant between-group differences for FSIQ, associated with a medium effect size. Post-hoc pairwise comparisons suggested that children in the FAS/PFAS group obtained significantly lower FSIQ scores than

children in both the HE and Control groups, $p < .001$ in both cases, but that there was no significant difference in the scores of children in the HE and Control groups, $p = .768$.

Testing Hypothesis 1

My first hypothesis predicted that children with a history of PAE would show impaired performance, relative to that of non-exposed or minimally exposed, demographically similar, controls, on measures of reading ability and phonological processing. The hypothesis further stated that any observed deficits would be due to the effects of alcohol exposure and would not be attributable to the effects of potential confounding variables (e.g., prenatal smoking and child's age at testing). I tested this hypothesis using both one-way ANCOVAs and multiple regression analyses. Prior to conducting these analyses, I conducted a series of bivariate correlational analyses to assess relations between potential confounding variables and reading and phonological processing outcomes (see Appendix D). Given that some of the variables were non-normally distributed (see Appendix E), I used Pearson, Spearman, and Kendall correlation coefficients to capture these relationships. If a non-normal variable (potential confounder/outcome) was correlated with another variable (outcome/potential confounder) at a significant or near-significant level ($p < .10$) for any of the three types of correlation analyses, then the potential confounding variable was included in subsequent analyses of that outcome.

One-way ANCOVAs. Table 4 presents results from the one-way ANCOVAs. For the sake of brevity, only significant findings are discussed here. Details of post hoc pairwise comparisons are presented in Appendix F. After the addition of potential confounders to the models, there remained significant between-group differences for NARA Comprehension, and for PhAB Alliteration, Spoonerisms, Alliteration Fluency, and Rhyme Fluency outcomes. All of these between-group differences were associated with small effect sizes.

***Reading outcomes*.** Regarding NARA Comprehension scores, children in the FAS/PFAS group performed significantly more poorly than those in both the HE and Control groups (see

Table 4
Relation of FASD Diagnosis to NARA and PhAB Outcomes: Results of ANCOVAs (N = 159)

	Diagnostic group					
Outcome variable	FAS/PFAS (n = 39)	HE (n = 58)	Control (n = 62)	F	p	η_p^2
NARA						
Reading Accuracy[a]	8.16 (2.27)	9.47 (2.15)	9.11 (2.40)	1.64	.198	.02
Reading Rate[b]	7.67 (1.77)	9.10 (2.12)	9.20 (2.41)	2.40	.094†	.03
Comprehension[c]	7.65 (1.89)	9.31 (1.89)	9.28 (2.42)	3.75	.026*	.05
PhAB						
Alliteration[d]	6.38 (3.68)	8.48 (2.20)	8.03 (2.72)	3.19	.044*	.04
Rhyme[e]	11.95 (6.51)	15.26 (5.05)	14.21 (5.65)	1.95	.147	.03
Spoonerisms[f]	7.92 (8.52)	14.72 (8.32)	14.68 (8.71)	3.81	.024*	.05
Non-Word Reading[g]	10.85 (6.57)	14.28 (5.29)	12.45 (5.98)	2.76	.066†	.04
Picture Naming[h]	109.85 (19.25)	97.90 (23.17)	95.95 (20.33)	1.49	.228	.02
Digit Naming[i]	71.66 (23.08)	58.29 (19.20)	59.94 (18.58)	1.72	.183	.02
Alliteration Fluency[j]	8.18 (4.24)	11.43 (3.72)	11.13 (4.49)	3.61	.029*	.05
Rhyme Fluency[k]	3.64 (2.58)	6.57 (3.44)	6.18 (2.97)	7.01	.001**	.08
Semantic Fluency[l]	14.21 (3.40)	17.24 (6.07)	17.85 (6.27)	1.68	.191	.02

Note. Means are presented with standard deviations in parentheses. NARA = Neale Analysis of Reading Ability; PhAB = Phonological Assessment Battery; FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed nonsyndromal. [a]Potential confounders included primary caregiver's years of education and child's age at testing. [b]Potential confounders included primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. [c]Potential confounders included primary caregiver's years of education and child's age at testing. [d]Potential confounders included primary caregiver's years of education, sex of child, and child's age at testing. [e]Potential confounders included primary caregiver's years of education, prenatal smoking, and child's age at testing. [f]Potential confounders included primary caregiver's years of education, prenatal smoking, and child's age at testing. Data missing for 1 child in the HE group. [g]Potential confounders included primary caregiver's years of education and child's age at testing. [h]Means displayed are for completion times. Potential confounders included primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. [i]Means displayed are for completion times. Potential confounders included primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. Data missing for 1 child in the FAS/PFAS group. [j]Potential confounders included primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. Data missing for 1 child in the Control group. [k]Potential confounders included primary caregiver's years of education and child's age at testing. [l]Potential confounders included primary caregiver's years of education, sex of child, and child's age at testing. In all instances where sex of child was a significant confounder, girls outperformed boys.
$^{\dagger}p < .10$. $^{*}p < .05$. $^{**}p < .01$.

Table F1). Significant covariates included child's age at testing (η_p^2 = .07) and primary caregiver's years of education (η_p^2 = .06). These results must be interpreted with caution, however, because some ANCOVA assumptions were violated (see Appendix E). It is worth mentioning here, however, that in instances where parametric test assumptions were not met, more conservative nonparametric tests may have underestimated the effects of PAE on the outcome.

When marijuana users were excluded, children in the FAS/PFAS group still performed significantly more poorly on NARA Comprehension than those in both the HE and Control groups,

p = .023 and .038, respectively. Similarly, when methaqualone users were excluded, children in the FAS/PFAS group still performed significantly more poorly than those in both the HE and Control groups, p = .021 and .045, respectively. Thus, comprehension, as measured by the NARA subtest of that name, appeared to be the only reading outcome for which FASD diagnosis was significantly related to performance after controlling for all potentially confounding variables.

Phonological processing outcomes. Regarding performance on the PhAB Alliteration subtest, post hoc pairwise comparisons suggested that children in the FAS/PFAS group performed significantly more poorly than those in the HE group (see Table F2). Significant covariates included primary caregiver's years of education (η_p^2 = .04) and child's age at testing (η_p^2 = .03). Regarding performance on the PhAB Spoonerisms subtest, post hoc pairwise comparisons suggested that children in the FAS/PFAS group performed significantly more poorly than those in both the HE and Control groups. Significant covariates included child's age at testing (η_p^2 = .11) and primary caregiver's years of education (η_p^2 = .05). Regarding performance on the PhAB Alliteration Fluency subtest, post hoc pairwise comparisons suggested that children in the FAS/PFAS group performed significantly more poorly than those in the HE group. Significant covariates included child's age at testing (η_p^2 = .05), sex of child (η_p^2 = .04), and primary caregiver's years of education (η_p^2 = .03). Regarding performance on the Rhyme Fluency subtest, post hoc pairwise comparisons suggested that children in the FAS/PFAS group performed significantly more poorly than those in both the HE and Control groups. The only significant covariate was primary caregiver's years of education (η_p^2 = .04). All of these results must be interpreted with caution, however, because some ANCOVA assumptions were violated (see Appendix E).

Because some mothers reported prenatal marijuana and methaqualone use, I reran these analyses excluding data from those cases. For Alliteration, when marijuana users were excluded, children in the FAS/PFAS group still performed significantly more poorly than those in the HE

group, $p = .042$. Similarly, when methaqualone users were excluded, this between-group difference remained significant, $p = .018$. For Spoonerisms, when marijuana users were excluded, children in the FAS/PFAS group still performed significantly more poorly than those in both the HE and Control groups, $p = .016$ and $p = .020$, respectively. When methaqualone users were excluded, children in the FAS/PFAS group still performed more poorly than those in both the HE and Control groups, although the latter comparison between-group difference fell just short of statistical significance, $p = .025$ and $p = .051$, respectively. For Alliteration Fluency, when marijuana users were excluded, children in the FAS/PFAS group still performed significantly more poorly than those in the HE group, $p = .010$. Similarly, when methaqualone users were excluded, this between-group difference remained significant, $p = .017$. For Rhyme Fluency, when marijuana users were excluded, children in the FAS/PFAS group still performed significantly more poorly than those in both the HE and Control groups, $p = .003$ in both cases. Similarly, when methaqualone users were excluded, these between-group differences remained significant, $p = .001$ and .008, respectively.

Multiple regression analyses. To narrow down my selection of multiple hierarchical regression models, I first conducted a series of bivariate correlational analyses to assess relations between continuous measures of PAE and reading and phonological processing outcomes (see Appendix D). Given that some of the variables were non-normally distributed (see Appendix E), I used Pearson, Spearman, and Kendall correlation coefficients to capture these relationships. If the non-normal variables were correlated with other variables of interest at significant or near-significant levels ($p < .10$) for any of the three types of correlation analyses, those variables were included in subsequent simple regression analyses. The normally distributed variables were also included in subsequent simple regression analyses if they were correlated with other variables of interest at significant or near-significant levels for Pearson correlation analyses.

Correlation analyses results (see Appendix D) indicated that relations between the following variables warranted further investigation via simple regression analyses: NARA Reading

Accuracy and drinking days/week; NARA Reading Rate and AA/day, AA/occasion, and drinking days/week; NARA Comprehension and AA/day as well as drinking days/week; PhAB Alliteration and AA/day as well as drinking days/week; PhAB Rhyme and drinking days/week; PhAB Spoonerisms and AA/day, AA/occasion, and drinking days/week; PhAB Non-Word Reading and drinking days/week; PhAB Picture Naming and AA/day, AA/occasion, and drinking days/week; PhAB Digit Naming and AA/day as well as drinking days/week; PhAB Alliteration Fluency and AA/day, AA/occasion, and drinking days/week; PhAB Rhyme Fluency and AA/day as well as drinking days/week; and PhAB Semantic Fluency and AA/day, AA/occasion, and drinking days/week.

Table 5 presents the results from subsequent simple regression analyses. Comprehension was the only NARA outcome that was significantly predicted by continuous measures of PAE: Both AA/day and drinking days/week were significant predictors of Comprehension scores, with the latter predictor being slightly stronger. The relation between drinking days/week and Reading Rate approached statistical significance.

Continuous measures of PAE significantly predicted performances on the following PhAB outcome variables: Alliteration (predicted by AA/day); Spoonerisms (predicted by AA/day and drinking days/week); Digit Naming (predicted by drinking days/week); and Alliteration Fluency (predicted by drinking days/week). Relations between the following PhAB outcomes and continuous measures of PAE approached statistical significance: Alliteration (predicted by drinking days/week); Picture Naming (predicted by drinking days/week); Digit Naming (predicted by AA/day); and Alliteration Fluency (predicted by AA/day). The relation between Semantic Fluency and drinking days/week also approached statistical significance.

I conducted subsequent multiple regression analyses only in cases where simple regression analyses identified significant or near-significant relationships between continuous measures of PAE and reading and phonological processing outcomes.

Table 5
Linear Regression Analyses: Continuous alcohol measures predicting NARA and PhAB outcomes (N = 159)

Variables entered							
Outcome	Alcohol measure	*N*	R^2	*B*	*SE B*	*B*	*p*
		Neale Analysis of Reading Ability					
Reading Accuracy	Drinking days/week	159	.01	-1.54	1.17	-.10	.190
Reading Rate	AA/day	159	.01	-0.60	0.44	-.11	.173
	AA/occasion	159	.01	-0.07	0.07	-.07	.354
	Drinking days/week	159	.02	-2.07	1.13	-.15	**.068**†
Comprehension	AA/day	159	.03	-0.93	0.43	-.17	**.032***
	Drinking days/week	159	.04	-2.81	1.10	-.20	**.012***
		Phonological Assessment Battery					
Alliteration	AA/day	159	.03	-1.25	0.57	-.17	**.029***
	Drinking days/week	159	.02	-2.61	1.47	-.14	**.077**†
Rhyme	Drinking days/week	159	.02	-4.49	2.91	-.12	.125
Spoonerisms	AA/day	158	.03	-3.48	1.74	-.16	**.047***
	AA/occasion	158	.002	-0.16	0.28	-.05	.573
	Drinking days/week	158	.04	-11.02	4.46	-.19	**.015***
Non-word Reading	Drinking days/week	159	.01	-3.92	3.03	-.10	.198
Picture Naming	AA/day	159	.004	3.21	4.27	.06	.453
	AA/occasion	159	.001	0.23	0.68	.03	.738
	Drinking days/week	159	.02	19.26	10.95	.14	**.081**†
Digit Naming	AA/day	158	.02	6.95	4.03	.14	**.087**†
	Drinking days/week	158	.03	22.86	10.30	.18	**.028***
Alliteration Fluency	AA/day	158	.02	-1.47	0.85	-.14	**.085**†
	AA/occasion	158	.003	-0.09	0.14	-.05	.525
	Drinking days/week	158	.03	-4.74	2.18	-.17	**.031***
Rhyme Fluency	AA/day	159	.003	-0.40	0.64	-.05	.529
	Drinking days/week	159	.02	-2.51	1.65	-.12	.130
Semantic Fluency	AA/day	159	.003	-0.82	1.13	-.06	.472
	AA/occasion	159	.003	-0.13	0.18	-.06	.476
	Drinking days/week	159	.02	-5.14	2.91	-.14	**.079**†

Note. NARA = Neale Analysis of Reading Ability; PhAB = Phonological Assessment Battery; AA = absolute alcohol.
$^{\dagger}p < .10$. $^{*}p < .05$.

Reading outcomes. Table 6 presents the results from the multiple hierarchical regression models that included continuous measures of PAE as predictors of NARA reading outcomes. Neither of the continuous PAE measures considered in these analyses significantly predicted any of the reading outcomes after potential confounders were added to the models. In all instances, child's age at testing was the strongest significant predictor, and primary caregiver's years of education the second strongest. However, the difference in size of contribution was sometimes negligible. For the Reading Rate model, sex of child was also a significant predictor.

Table 6

Hierarchical Regression Analyses: Continuous alcohol measures predicting NARA outcomes, controlling for potential confounders (N = 159)

	Step 1				Step 2			
Variables entered	*B*	*SE B*	*β*	*p*	*B*	*SE B*	*β*	*p*
Model 1: Reading Rate and drinking days/week[a]								
Drinking days/week	-2.07	1.13	-.15	.068†	-0.79	1.22	-.06	.517
Primary caregiver's education					0.21	0.07	.22	.006**
Prenatal smoking					-0.003	0.03	-.01	.926
Sex of child					0.95	0.33	.21	.004**
Child's age at testing					0.51	0.15	.26	.001**
Model 2: Comprehension and AA/day[b]								
AA/day	-0.93	0.43	-.17	.032*	-0.50	0.41	-.09	.232
Primary caregiver's education					0.26	0.07	.27	.001**
Child's age at testing					0.56	0.14	.28	< .001***
Model 3: Comprehension and drinking days/week[c]								
Drinking days/week	-2.81	1.10	-.20	.012*	-1.42	1.08	-.10	.190
Primary caregiver's education					0.25	0.07	.26	.001**
Child's age at testing					0.55	0.14	.28	< .001***

Note. NARA = Neale Analysis of Reading Ability; AA = absolute alcohol.

[a]R^2 = .02 for Step 1, ΔR^2 = .16 for Step 2 (p < .001).

[b]R^2 = .03 for Step 1, ΔR^2 = .15 for Step 2 (p < .001).

[c]R^2 = .04 for Step 1, ΔR^2 = .14 for Step 2 (p < .001).

$^{\dagger}p$ < .10. $^{*}p$ < .05. $^{**}p$ < .01. $^{***}p$ < .001.

However, one should exercise caution when attempting to generalize these models beyond the current sample, because some regression assumptions were violated (see Appendix E for assumption checks and model diagnostics).

Phonological processing outcomes. Table 7 presents the results from the models that included continuous measures of PAE as predictors of PhAB phonological processing outcomes. Neither of the continuous PAE measures considered in these analyses significantly predicted any of the phonological processing outcomes after potential confounders were added to the models. Child's age at testing was the strongest significant predictor in all models, except for those describing relations between Alliteration and AA/day and Alliteration and drinking days/week, where primary caregiver's years of education was the strongest significant predictor. Primary caregiver's years of education was the second strongest significant predictor in all models, except for those describing relations between Alliteration and AA/day and Alliteration and drinking days/week, where the second strongest significant predictor was child's age at testing. However, the difference in size of contribution was sometimes negligible. Sex of child was also a significant predictor (albeit the weaker one out of the three significant predictors) in the models describing relations between Digit Naming and AA/day, Digit Naming and drinking days/week, Alliteration Fluency and AA/day, and Alliteration Fluency and drinking days/week.

However, one should exercise caution when attempting to generalize these models beyond the current sample, because some regression assumptions were violated (see Appendix E for assumption checks and model diagnostics).

In summary, FASD diagnosis was a better predictor of performance on reading and phonological processing outcomes than continuous measures of PAE, because FASD diagnosis remained a significant predictor on some outcomes, whereas continuous measures of PAE were no longer significant predictors on any outcomes after control for potential confounders.

Table 7

Hierarchical Regression Analyses: Continuous alcohol measures predicting PhAB outcomes, controlling for potential confounders

	Step 1				Step 2			
Variables entered	*B*	*SE B*	*β*	*p*	*B*	*SE B*	*β*	*p*
Model 4: Alliteration and AA/day (*N* = 159)[a]								
AA/day	-1.25	0.57	-.17	.029*	-0.81	0.56	-.11	.150
Primary caregiver's education					0.27	0.10	.22	.006**
Sex of child					0.86	0.44	.15	.050†
Child's age at testing					0.49	0.19	.19	.012*
Model 5: Alliteration and drinking days/week (*N* = 159)[b]								
Drinking days/week	-2.61	1.47	-.14	.077†	-1.02	1.47	-.06	.490
Primary caregiver's education					0.29	0.10	.23	.004**
Sex of child					0.84	0.44	.14	.057†
Child's age at testing					0.49	0.20	.19	.013*
Model 6: Spoonerisms and AA/day (*N* = 158)[c]								
AA/day	-3.48	1.74	-.16	.047*	-1.72	1.81	-.08	.345
Primary caregiver's education					1.00	0.29	.26	.001**
Prenatal smoking					-0.003	0.13	-.002	.983
Child's age at testing					2.68	0.57	.34	< .001***
Model 7: Spoonerisms and drinking days/week (*N* = 158)[d]								
Drinking days/week	-11.02	4.46	-.19	.015*	-5.60	4.78	-.10	.243
Primary caregiver's education					0.97	0.29	.25	.001**
Prenatal smoking					0.01	0.13	.01	.928
Child's age at testing					2.66	0.57	.34	< .001***
Model 8: Picture Naming and drinking days/week (*N* = 159)[e]								
Drinking days/week	19.26	10.95	.14	.081†	5.57	11.49	.04	.629
Primary caregiver's education					-1.66	0.70	-.18	.019*
Prenatal smoking					0.15	0.31	.04	.635
Sex of child					-6.49	3.08	-.15	.037
Child's age at testing					-7.54	1.37	-.39	< .001***
Model 9: Digit Naming and AA/day (*N* = 158)[f]								
AA/day	6.95	4.03	.14	.087†	2.99	3.80	.06	.434
Primary caregiver's education					-2.65	0.62	-.30	< .001***
Prenatal smoking					0.03	0.26	.01	.903
Sex of child					-11.68	2.69	-.29	< .001***
Child's age at testing					-7.02	1.20	-.39	< .001***
Model 10: Digit Naming and drinking days/week (*N* = 158)[g]								

Drinking days/week	22.86	10.30	.18	.028*	7.35	10.02	.06	.464
Primary caregiver's education					-2.63	0.62	-.29	< .001***
Prenatal smoking					0.04	0.27	.01	.897
Sex of child					-11.59	2.69	-.28	< .001***
Child's age at testing					-6.99	1.20	-.38	< .001***
Model 11: Alliteration Fluency and AA/day (N = 158)[h]								
AA/day	-1.47	0.85	-.14	.085†	-0.44	0.92	-.04	.634
Primary caregiver's education					0.41	0.14	.22	.005**
Prenatal smoking					-0.05	0.07	-.07	.433
Sex of child					1.59	0.64	.18	.014*
Child's age at testing					0.90	0.29	.23	.002**
Model 12: Alliteration Fluency and drinking days/week (N = 158)[i]								
Drinking days/week	-4.74	2.18	-.17	.031*	-1.53	2.43	-.06	.531
Primary caregiver's education					0.41	0.15	.22	.006**
Prenatal smoking					-0.05	0.07	-.06	.484
Sex of child					1.58	0.64	.18	.015*
Child's age at testing					0.90	0.29	.23	.002**
Model 13: Semantic Fluency and drinking days/week (N = 159)[j]								
Drinking days/week	-5.14	2.91	-.14	.079*	-2.57	2.68	-.07	.339
Primary caregiver's education					0.33	0.18	.13	.067
Sex of child					2.02	0.80	.18	.012*
Child's age at testing					2.24	0.36	.44	< .001***

Note. PhAB = Phonological Assessment Battery; AA = absolute alcohol.
[a]R^2 = .03 for Step 1, ΔR^2 = .11 for Step 2 (p < .001). [b]R^2 = .02 for Step 1, ΔR^2 = .11 for Step 2 (p < .001).
[c]R^2 = .03 for Step 1, ΔR^2 = .18 for Step 2 (p < .001). [d]R^2 = .04 for Step 1, ΔR^2 = .17 for Step 2 (p < .001).
[e]R^2 = .02 for Step 1, ΔR^2 = .21 for Step 2 (p < .001). [f]R^2 = .02 for Step 1, ΔR^2 = .33 for Step 2 (p < .001).
[g]R^2 = .03 for Step 1, ΔR^2 = .31 for Step 2 (p < .001). [h]R^2 = .02 for Step 1, ΔR^2 = .15 for Step 2 (p < .001).
[i]R^2 = .03 for Step 1, ΔR^2 = .14 for Step 2 (p < .001). [j]R^2 = .02 for Step 1, ΔR^2 = .24 for Step 2 (p < .001).
†p < .10. *p < .05. **p < .01. ***p < .001.

Testing Hypothesis 2

My second hypothesis predicted that PAE-related deficits in reading ability and phonological processing would be mediated by deficits in WM. I tested this hypothesis using both simple and multiple regression analyses (as suggested by Baron & Kenny, 1986), and confirmed mediation effects using the Sobel test (Sobel, 1982).

Given that FASD diagnosis was a stronger predictor of reading and phonological processing outcomes than continuous measures of PAE, I used group status (exposed versus non-exposed) as a dichotomous categorical predictor in these analyses. Only the FAS/PFAS and Control groups were included, so that I could contrast the performances of children whose reading and phonological processing abilities appeared to be impacted by heavy PAE with children who did not have such exposure. I tested mediation only for those reading and phonological processing outcomes that were identified, by the analyses testing Hypothesis 1, as showing FASD-related effects after consideration of potential confounding variables: NARA Comprehension and PhAB Alliteration, Spoonerisms, Alliteration Fluency, and Rhyme Fluency. For each outcome, I first confirmed zero-order relationships among variables, using single regression analyses, before proceeding with multiple regression analyses. For multiple regression analyses, I entered group status at the first step, followed by the WM measure (Digit Span Backwards) at the second step.

Regarding NARA Comprehension, results indicated that group status (FASD/PFAS vs. Control) significantly predicted both Comprehension ($B = 0.05$, $SE = 0.01$, $p = .001$) and WM ($B = 0.03$, $SE = 0.01$, $p < .001$). WM also significantly predicted Comprehension ($B = 0.67$, $SE = 0.08$, $p < .001$). These results therefore supported the mediation hypothesis. Results presented in Table 8 indicate that group status only marginally predicted Comprehension after controlling for

Table 8
Working Memory Mediation of NARA and PhAB Outcome Measures (N = 159)

Outcome	*N*	β^a	β^b	Sobel *z*	*p*
Neale Analysis of Reading Ability					
Comprehension[a]	101	.34**	.18†	3.10	.002**
Phonological Assessment Battery					
Alliteration[b]	101	.25*	.10	2.98	.003**
Spoonerisms[c]	101	.36***	.17*	3.28	.001**
Alliteration Fluency[d]	100	.31**	.14	3.14	.002**
Rhyme Fluency[e]	101	.40***	.26**	2.91	.004**

Note. NARA = Neale Analysis of Reading Ability; PhAB = Phonological Assessment Battery. β^a denotes the standardized regression coefficient describing the association between group status (FASD/PFAS vs. Control) and the various NARA and PhAB outcome measures. B^b denotes the standardized regression coefficient describing the association between group status (FASD/PFAS vs. Control) and the various NARA and PhAB outcome measures after statistical adjustment for working memory (WM), as measured by the Digit Span Backwards subtest of the Wechsler Intelligence Scale for Children–Fourth Edition. [a]R^2 = .32 for the model including both group status and WM as predictors. [b]R^2 = .24 for the model including both group status and WM as predictors. [c]R^2 = .40 for the model including both group status and WM as predictors. [d]R^2 = .32 for the model including both group status and WM as predictors. [e]R^2 = .31 for the model including both group status and WM as predictors.
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

WM, and a subsequent Sobel test confirmed partial mediation. Overall, approximately 32% of the variance in Comprehension scores was accounted for by group status and WM performance.

Regarding PhAB Alliteration, results indicated that group status (FASD/PFAS vs. Control) significantly predicted both Alliteration ($B = 0.05$, $SE = 0.02$, $p = .011$) and WM ($B = 0.03$, $SE = 0.01$, $p < .001$). WM also significantly predicted Alliteration ($B = 0.67$, $SE = 0.12$, $p < .001$). These results therefore supported the mediation hypothesis. Results presented in Table 8 indicate that group status no longer significantly predicted Alliteration after controlling for WM, and a subsequent Sobel test confirmed full mediation. Overall, approximately 24% of the variance in Alliteration scores was accounted for by group status and WM performance.

Regarding PhAB Spoonerisms, results indicated that group status (FASD/PFAS vs. Control) significantly predicted both Spoonerisms ($B = 0.19$, $SE = 0.05$, $p < .001$) and WM ($B = 0.03$, $SE = 0.01$, $p < .001$). WM also significantly predicted Spoonerisms ($B = 2.85$, $SE = 0.33$, $p < .001$). These results therefore supported the mediation hypothesis. Results presented in Table 8 indicate

that group status still significantly predicted Spoonerisms after controlling for WM, and a subsequent Sobel test confirmed partial mediation. Overall, approximately 40% of the variance in Spoonerisms scores was accounted for by group status and WM performance.

Regarding PhAB Alliteration Fluency, results indicated that group status (FASD/PFAS vs. Control) significantly predicted both Alliteration Fluency ($B = 0.08$, $SE = 0.03$, $p = .001$) and WM ($B = 0.03$, $SE = 0.01$, $p < .001$). WM also significantly predicted Alliteration Fluency ($B = 1.32$, $SE = 0.16$, $p < .001$). These results therefore supported the mediation hypothesis. Results presented in Table 8 indicate that group status no longer significantly predicted Alliteration Fluency after controlling for WM, and a subsequent Sobel test confirmed full mediation. Overall, approximately 32% of the variance in Alliteration Fluency scores was accounted for by group status and WM performance.

Regarding PhAB Rhyme Fluency, results indicated that group status (FASD/PFAS vs. Control) significantly predicted both Rhyme Fluency ($B = 0.07$, $SE = 0.02$, $p < .001$) and WM ($B = 0.03$, $SE = 0.01$, $p < .001$). WM also significantly predicted Rhyme Fluency ($B = 0.93$, $SE = 0.13$, $p < .001$). These results therefore supported the mediation hypothesis. Results presented in Table 8 indicate that group status still significantly predicted Rhyme Fluency after controlling for WM, and a subsequent Sobel test confirmed partial mediation. Overall, approximately 31% of the variance in Rhyme Fluency scores was accounted for by group status and WM performance.

In sum, the effects of group membership (FASD/PFAS vs. Control) on NARA Comprehension, PhAB Spoonerisms, and PhAB Rhyme Fluency were partially mediated by WM, while the effects of group membership on PhAB Alliteration and PhAB Alliteration Fluency were fully mediated by WM.

DISCUSSION

This study investigated two broad aims. First, it examined whether children with a history of prenatal alcohol exposure (PAE) exhibited deficits in reading ability and phonological processing, as measured by comprehensive assessments of those two constructs. Second, it sought to determine whether any observed deficits in reading ability and phonological processing were mediated by deficits in working memory (WM). It accomplished these aims by testing two specific hypotheses. The first of these was that children with a history of PAE will show impaired performance, relative to that of non-exposed or minimally exposed, demographically similar, controls, on measures of reading ability and phonological processing. Furthermore, any observed deficits are due to the effects of PAE and are not attributable to the effects of potential confounding variables. The second hypothesis was that PAE-related deficits in reading ability and phonological processing are mediated by deficits in WM. To my knowledge, this is the first study to consider the potentially mediating role of WM in associations between PAE and reading outcomes beyond single-word reading.

In this section, I discuss the findings relating to each of my hypotheses within the context of relevant, previously published literature. The section begins with a discussion of the results from one-way ANCOVAs and multiple regression analyses investigating the associations between PAE and various reading and phonological processing outcomes, while controlling for potential confounding sociodemographic variables (i.e., those relating to Hypothesis 1). I then discuss the results from additional single and multiple regression analyses and tests of mediation that aimed to investigate the potentially mediating role of WM in the associations between PAE and reading and phonological processing outcomes (i.e., those relating to Hypothesis 2). Finally,

I address the limitations of this study, directions for future research, and the clinical significance of these findings.

Relations Between PAE and Reading and Phonological Processing Outcomes

My first hypothesis predicted that (a) children with a history of PAE would show impaired performance, relative to that of non-exposed or minimally exposed, demographically similar, controls, on measures of reading ability and phonological processing, and (b) any observed deficits would be due to the effects of PAE and would not be attributable to the effects of potential confounding variables. The predictor variables for the current study included both continuous measures of PAE (oz AA/day, oz AA/occasion, and number of drinking days/week) and a categorical variable describing group status as it related to FASD diagnosis (i.e., FAS/PFAS, HE, or non-exposed Control).

I tested this hypothesis using both one-way ANCOVAs (with group status as the between-group factor) and multiple regression analyses (with continuous measures of PAE as predictors) to predict performances on reading and phonological processing outcomes while controlling for the effects of potential confounding variables. I conducted hierarchical multiple regression analyses only in cases where prior simple regression analyses identified significant or near-significant relationships between continuous measures of PAE and reading and phonological processing outcomes. Because some mothers reported prenatal marijuana and methaqualone use, I reran analyses for principal findings excluding data from those cases.

This hypothesis was confirmed for some of the reading and phonological processing outcomes when FASD diagnosis was used as the between-group factor, but for none of the outcomes when continuous PAE measures were used as predictors. Influential confounders and the findings for relevant outcomes are discussed below.

An important note here is that, due to the theoretical, methodological, and statistical issues involved in controlling for IQ in neurodevelopmental research, IQ was not controlled for in the current research. Dennis et al. (2009) argue that the practice of controlling for IQ differences when studying neurocognitive outcomes in children with neurodevelopmental disorders is generally misguided:

IQ cannot be a discriminant measure in models of neurocognitive outcomes. To the extent that IQ represents the same processes as the construct of interest, then controlling for IQ removes variability in the outcome measure that is directly related to the construct of interest. Under such circumstances, IQ serves as a poor covariate, making any conclusions about specific cognitive processes more difficult and increasing interpretive complexity by removing some unspecified aspect of the dependent measure from itself. Even when the goal of including IQ as a covariate is to more clearly elucidate a theoretical question, frequently it either fails to do so, or it is less appropriate than alternative methods not including IQ at answering the question. (Dennis et al., 2009, pp. 340)

This research, therefore, considered only the following potential confounding variables: primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. Three of these variables significantly predicted performances on reading and phonological processing outcomes. Given that the cognitive components involved in reading and phonological processing reach maturity at different developmental stages (Wolf, Bowers, & Biddle, 2000), it is not surprising that child's age was the strongest predictor across all reading and most phonological processing outcomes. Primary caregiver's level of education was also a strong predictor and was significant for all outcomes. This finding is consistent with multiple lines of research that have demonstrated associations between parental education and child academic

achievement (e.g., Davis-Kean, 2005; Guryan, Hurst, & Kearney, 2008; Haveman & Wolfe, 1995). Mothers with higher levels of education tend to spend more time teaching their children, reading to them, and helping them with their homework, all of which contribute to their later academic achievement (Guryan et al., 2008). Interestingly, sex of child was a significant predictor only for outcomes involving timed tasks, and for all of the timed tasks except for rhyme fluency. In all cases, girls outperformed boys. This finding is consistent with other reports of females outperforming males in reading skills, speeded naming tasks, and processing speed tasks involving alphabets and digits (for a review, see Roivainen, 2011).

Reading outcomes. In the current sample, neither FASD diagnosis nor continuous PAE measures significantly predicted either reading accuracy or reading rate after control for potential confounders. Regarding reading comprehension, FASD diagnosis did significantly predict comprehension after control for potential confounders, but continuous PAE measures did not.

These findings stand in contrast to those of others who reported PAE-effects on both reading accuracy and reading rate. Specifically, Sowell et al. (2008) reported that a group of 17 children and adolescents with FASD (*M* age = 10.5 years) performed significantly more poorly on a test of letter identification and single-word reading than a group of 19 controls (*M* age = 11.2 years) who were matched on age, gender, handedness, and maternal education. Similarly, Mattson et al. (1998) found PAE-related effects on letter identification and single-word reading at 5 to 16 years of age, despite matching groups on sex, age, handedness, and ethnicity, and controlling for socioeconomic status (SES).

Regarding continuous PAE measures and reading accuracy, Streissguth et al. (1990) reported PAE-related effects on letter identification and single-word reading in a cohort of 482 children (*M* age = 7.5 years) with exposure captured as binge drinking (defined as 5 or more

drinks/occasion) in the month before pregnancy recognition. Goldschmidt et al. (1996) found similar effects with increasing amounts of alcohol per day during the second trimester of pregnancy in a cohort of 512 children (*M* age = 6.5 years). They included the following significant confounders in their statistical modeling: home environment factors relating to cognitive development in low-SES samples, maternal education and work/school status, and child's sex and grade in school. Even after including these confounders, the average daily volume of alcohol consumed during the second trimester of pregnancy significantly predicted letter identification and single-word reading scores.

These two studies may have been more able to detect alcohol effects, compared to the current study, due to their larger sample sizes. However, Glass et al. (2015) reported word reading effects for a smaller sample, after controlling for potential confounders. Their sample included children with heavy PAE (*n* = 49) and controls with minimal or no PAE (*n* = 47), all aged between 8 and 16 years (*M* = 12.5). The minimum required levels of exposure for inclusion in their HE group (> 4 drinks/occasion at least once/week, or at least 14 drinks/week during pregnancy) were slightly higher than those for the current study (at least 2 incidents of 4 or more drinks/occasion during the 1st trimester of pregnancy, or an average of at least 2 drinks/day), which may have driven the stronger effects found in their study. Another possible reason for U.S.-based studies detecting PAE-related effects on reading accuracy where the current study did not, may be because their control groups were not as sociodemographically and educationally disadvantaged, and were likely performing better than the Cape Town controls in terms of reading skills, therefore serving as a better comparison group. Furthermore, reading accuracy effects may depend on the timing of exposure, or interactions between dose and timing of exposure, as suggested by the findings of the former two studies described above.

It might also be the case that deficits in reading accuracy become less prominent at later ages as word reading becomes more automatic. The ability to achieve automaticity in specific cognitive domains is a useful adaptation that allows for the reassignment of cognitive resources to other tasks (Samuels & Flor, 1997). Automaticity in word reading, for example, allows for the reassignment of attentional resources to reading comprehension.

Word reading typically becomes automatic with repeated exposure and practice. Although age does not directly represent word reading experience, it does serve as a reasonable proxy for such experience, especially when it can be assumed that children of similar ages have experienced the same number of years of education within similar schooling systems, and that they are from families who are similarly involved in their children's education. Findings from a study involving children with FASD indicated that initial reading accuracy deficits may improve at later ages, possibly as word reading becomes more automatic with additional reading experience. Treit et al. (2013) found that 17 children with FASD (*M* age = 8.2 years) performed significantly below the population norm in terms of single-word reading at initial assessments ($p = .011$), but not at subsequent assessments ($p = .083$) occurring, on average, 3.2 years later (*M* age = 11.4 years). Although the change in scores over time did not reach statistical significance, it did indicate a degree of ‘catch-up’ in word reading over time, as reading experience increased. Some children with heavy PAE may therefore have reading accuracy deficits at earlier ages but subsequently catch up to their peers, so that reading accuracy deficits at later ages are only observed in those who were more severely affected by PAE (i.e., those at the more severe end of the FASD continuum).

Consistent with the current research, Molteno et al. (2011) and Dodge et al. (2014) also found no significant association between average oz AA/day and reading accuracy after control

for confounders. In a sample older than the current one, Howell et al. (2006) compared reading accuracy performances of two groups with PAE, one with the physical features related to PAE (*n* = 46; *M* age = 15.1 years) and one without (*n* = 82; *M* age = 14.9 years), as well as a non-exposed control group (*n* = 53; *M* age = 14.9 years) and a comparison group that featured children receiving special education services (*n* = 84; *M* age = 15.5 years). The special education group performed significantly more poorly on a test of single-word reading than all three of the other groups, whose performances did not differ from each other. However, data obtained from the children's school records showed that both the special education group and the most severely affected alcohol-exposed group (i.e., the one with PAE-related physical features) performed significantly more poorly than the other two groups on school-administered standardized reading tests. The fact that the group with PAE-related physical features showed deficits on school-administered reading tests, but not on the single-word reading test, suggests that their reading deficits might have involved areas of difficulty not tapped by that test, at an age where word reading had possibly already become automatic.

As word reading becomes more automatic, reading speed increases (Samuels & Flor, 1997). In the current sample, then, reading rate performances may have followed the pattern of reading accuracy performances for that reason. (Recall that PAE was not significantly associated with either reading rate or reading accuracy after control for confounders.) However, some poor readers do present with slowed reading speeds despite age-appropriate word accuracy scores, possibly due to a general underlying processing speed deficit (Wolf et al., 2000). Processing speed deficits have repeatedly been observed in individuals with PAE (Burden et al., 2005; Jacobson et al., 1994; Jacobson et al., 1993; Kable & Coles, 2004), and some research has identified PAE-related deficits in reading rate.

Specifically, Molteno et al. (2011) found that average oz AA/day significantly predicted reading rate in a sample of 47 children (*M* age = 11.3), after control for child's age and prenatal smoking. However, the mothers of children with heavy PAE in their sample (*n* = 31) consumed an average of 2.6 oz AA/day, whereas in the current sample mothers of HE children consumed an average of 0.78 oz AA/day and those of children in the FAS/PFAS group consumed an average of 1.09 oz AA/day. The average level of PAE in the Molteno sample was therefore considerably higher than that of even the most severely affected group in the current sample, which possibly allowed them to better detect effects on reading rate. Although PAE-related effects on reading rate did not reach statistical significance in the current sample, the statistical trends were stronger for reading rate than for reading accuracy, suggesting that reading rate might be relatively more sensitive to alcohol effects than reading accuracy at this age.

Consistent with the current research, Carmichael Olson et al. (1998) reported that 14-16-year-old adolescents with FAS (*n* = 9) performed in the average range on tests of letter identification and single-word reading, and had similar reading speeds on a story reading task to a larger cohort of minimally- or non-exposed control children (*n* = 174). Although their FAS group may have been too small to detect deficits in reading accuracy and reading speed, the adolescents with FAS did show deficits in reading comprehension compared to controls, a finding mirrored in the current research.

In the current research, children in the FAS/PFAS group performed significantly more poorly than those in both the HE and control groups on a measure of reading comprehension. Children in the HE and control groups performed similarly. However, continuous PAE measures did not significantly predict reading comprehension after the inclusion of potential confounding variables. These findings partly support those presented by Molteno et al. (2011), who also found

PAE-related deficits in reading comprehension. However, Molteno et al. (2011) reported that average oz AA/day was significantly associated with poorer reading comprehension, even after controlling for child's age and prenatal smoking. As mentioned before, the ability of those researchers to detect effects using continuous measures of PAE may have been due to the fact that the average level of PAE in their sample was considerably higher than that of the current one. Also consistent with the current research, Dodge et al. (2014) reported PAE-related deficits in reading comprehension after controlling for confounders in a sample of 282 adolescents (*M* age = 14.4 years). This sensitivity of reading comprehension to alcohol effects may be due to the multiple cognitive processes involved in reading comprehension, such as attention, processing speed, WM, and other EF processes (Cain et al., 2004; Verhoeven et al., 2011; Wolf et al., 2000), that are also known to be affected by PAE (e.g., Burden et al., 2005; Kodituwakku, 2007; Mattson et al., 2006; Mattson et al., 2011; Rasmussen, 2005).

In sum, the current research and those of others reviewed here suggest that PAE-related deficits in reading accuracy and reading rate may or may not be present at later ages (i.e., towards adolescence), depending on factors such as dose and timing of exposure and the contribution of other sociodemographic factors. Reading comprehension, on the other hand, appears to be much more sensitive to the effects of PAE at this age.

Phonological processing outcomes. Regression analyses suggested that continuous PAE measures did not significantly predict performance on any of the phonological processing outcomes after control for potential confounders. Analyses of covariance, on the other hand, detected significant between-group differences on the PhAB Alliteration, Spoonerisms, Alliteration Fluency, and Rhyme Fluency subtests. These between-group differences survived the addition of potential confounders to the models.

Regarding the PhAB Alliteration and Rhyme subtests (both tasks of basic phonological awareness), only one pairwise comparison remained significant after the inclusion of potential confounders: The HE group significantly outperformed the FAS/PFAS group on the Alliteration subtest. These tasks required children to identify the initial sounds (on the Alliteration subtest) or the final sounds (on the Rhyme subtest) in single syllable words. The examiner read three words aloud, and the child had to repeat the two words with the same initial sound (e.g., lot, *mess, mud*) or final sound (e.g., *sail*, boot, *nail*). Although both of these tasks are considered to be tests of basic phonological awareness, Rhyme appears to be relatively easier than Alliteration, because the average Rhyme subtest scores in the current sample were higher than the average Alliteration subtest scores across all groups, and children have been found to attain rhyme skills at earlier ages: Stanovich, Cunningham, and Cramer (1984) administered ten different tasks of phonological awareness to children at 6 years of age and found that performances on all rhyme tasks in their study were already at ceiling by that age. However, there was more variation in performances on a task very similar to the Alliteration subtest used in the current study. Furthermore, there might also be differences in the intrinsic difficulty of these tasks. There might, for example, be a recency effect in the Rhyme task, which required children to match words based on their final sounds (that are more recent in memory and thus easier to recall) whereas the Alliteration task required matching of initial sounds. These apparent differences in age of acquisition and level of difficulty may help explain why PAE-related group differences were observed on the Alliteration subtest but not the Rhyme subtest in the current sample.

Findings for the Rhyme subtest, in the current sample, are consistent with those of Molteno et al. (2011), who found that AA/day did not significantly predict Rhyme in their sample (n = 47; M age = 11.3). However, in contrast to the current findings, AA/day did not

significantly predict Alliteration in Molteno et al.'s sample either. Nonetheless, the current findings suggest that deficits in Alliteration may present in children at the more severe end of the FASD continuum.

The PhAB Spoonerisms subtest is a more challenging measure of phonological processing that required children to segment single-syllable words and to then build new words, or word combinations, by combining those segments. It involves executive functioning (EF) skills beyond basic phonological awareness, such as monitoring and inhibitory processes, as well as WM (Varvara et al., 2014). Children in the FAS/PFAS group performed significantly more poorly on the Spoonerisms subtest than those in both the HE and control groups, even after controlling for potential confounders. (Note that when methaqualone users were excluded, the difference in performance between the FAS/PFAS and control group fell just short of the conventional level of statistical significance, $p = .051$). Molteno et al. (2011) reported that average oz AA/day was significantly related to poorer performance on the Spoonerisms subtest in their sample. Together, these results suggest that the Spoonerisms subtest may be a particularly sensitive measure of PAE-related effects on phonological processing, especially in cases of heavier PAE or where there are PAE-related physical features. PAE has repeatedly been linked to deficits in EF (e.g., Kodituwakku, 2007; Mattson et al., 2011; Mattson et al., 1999; Rasmussen, 2005), which may help explain why this more challenging phonological processing task was so sensitive to alcohol effects.

Regarding the PhAB Non-Word Reading subtest, neither FASD diagnosis nor continuous PAE measures significantly predicted performance after control for potential confounders. This finding is consistent with some previous studies in the field, but inconsistent with others. For instance, Carmichael Olson et al. (1998) reported similar results, finding no deficits on Non-

Word Reading among adolescents with FAS (n = 9) compared to a minimally- or non-exposed cohort group (n = 174) at 14-16 years of age.

The findings reported here and by Carmichael Olson et al. (1998) stand in contrast to those reported by Streissguth et al. (1994), who investigated Non-Word Reading in a cohort of 462 adolescents with PAE at 14 years of age. They included various measures of alcohol consumption both at the time prior to pregnancy recognition and during pregnancy: average oz AA/day, average monthly occasions of drinking, a quantity-frequency-variability index (QFV), average drinks/occasion, maximum drinks/occasion, and ever drinking > 5 drinks/occasion. All of the measures related to alcohol consumption prior to pregnancy recognition significantly predicted Non-Word Reading performance, and the following measures of alcohol consumption during pregnancy significantly predicted Non-Word Reading performance: QFV, average drinks/occasion, maximum drinks/occasion, and ever drinking > 5 drinks/occasion. PAE-related effects on Non-Word Reading remained significant after adjustment for sociodemographic predictors such as child race and child sex, familial SES, and maternal weight gain during pregnancy.

An obvious advantage for the Streissguth et al. study is its relatively large sample size. That study had much more statistical power to detect significant effects of PAE on Non-Word Reading than did the current study or the study by Carmichael Olson et al. (1998). Another cross-study methodological difference that may account for the discrepancy in results is the nature of the task used. As Rack, Snowling, and Olson (1992) argue, not all Non-Word Reading tests are created equal; they vary in their level of difficulty as a function of how closely the non-words resemble real words. The Non-Word Reading test used in the current sample may, therefore, not have been challenging enough to detect PAE-effects at this age.

Regarding the PhAB Picture Naming and Digit Naming subtests, neither FASD diagnosis nor continuous PAE measures significantly predicted performance after control for potential confounders. These findings stand in contrast to those of Glass et al. (2015), who also included a naming speed task in their research involving children aged 8 to 16 years (M = 12.5) with heavy PAE (n = 49) or with minimal or no PAE (n = 47). Their task involved various semantic categories (i.e., letters, numbers, colors, shapes, and sizes), similar to the Picture Naming and Digit Naming subtests used in the current study, yet they found significant PAE-related effects on their participants' performance. Similarly, Molteno et al. (2011) reported PAE-related effects on naming speed tasks, even after controlling for confounders such as child sex and mother's marital status.

An important consideration in the interpretation of results regarding naming speed tests in FASD samples is that, despite their overlap with phonological processes and despite being significant predictors of reading ability, performance on naming speed tasks involve cognitive processes beyond phonology, with a heavy focus on processing speed (Wolf et al., 2000). Given the robust findings regarding PAE-related processing speed deficits (Burden et al., 2005; Jacobson et al., 1994; Jacobson et al., 1993; Kable & Coles, 2004), it was surprising to find no PAE-related deficits on either naming speed tasks in the current sample. However, these results are consistent with the reading rate results in this sample. Recall that no PAE-related deficits in reading rate were present after controlling for potential confounders in the current sample, and that reading rate is also impacted by processing speed deficits. It may, then, be the case that PAE-related processing speed deficits were not pronounced enough in the current sample to detect effects on either reading rate or naming speed tasks.

Regarding the PhAB fluency measures (viz., the Alliteration Fluency, Rhyme Fluency, and Semantic Fluency subtests), none of the continuous PAE measures significantly predicted performance after inclusion of potential confounders in the regression model. However, ANCOVAs detected significant between-group differences, even after confounder inclusion, on the Alliteration Fluency and Rhyme Fluency subtests. Specifically, the HE group significantly outperformed those in the FAS/PFAS group on both of those subtests, whereas the control group significantly outperformed the FAS/PFAS group on the Rhyme Fluency subtest. Hence, performance on the latter subtest appears to be somewhat more sensitive to the effects of PAE than does performance on the other fluency subtests.

These findings provide partial replication of those reported by Schonfeld, Mattson, Lang, Delis, and Riley (2001). They found PAE-related effects on Verbal Fluency (a combination of scores on measures similar to the PhAB Alliteration Fluency and Semantic Fluency subtests) at 8 to 15 years of age, after control for confounders. Kodituwakku et al. (2006) also found deficits in both Letter Fluency (similar to PhAB Alliteration Fluency) and Category Fluency (similar to PhAB Semantic Fluency) in 62 children with FAS (*M* age = 7.6 years) compared to 61 controls (*M* age = 7.6 years). Furthermore, they found a group x fluency type interaction, indicating that their FAS group performed more poorly on both Letter Fluency and Category Fluency, compared to controls, but had relatively greater difficulty with Letter Fluency than with Category Fluency. A similar pattern of performance was seen in the current sample (i.e., poorer performance on Alliteration Fluency than Semantic Fluency), but PAE-related findings for the Semantic Fluency task merely tended towards significance before the inclusion of potential confounders. Performance deficits on the Semantic Fluency subtest may have been more pronounced if the current sample included more heavily affected children (i.e., those with FAS).

The inclusion of the Semantic Fluency subtest in the current study was, however, merely for comparison with tests of phonological fluency (Alliteration Fluency and Rhyme Fluency), and results from the current study indicate that phonological fluency appears to be more sensitive to the effects of PAE than semantic fluency. It is tempting, then, to interpret these results as suggestive of specific PAE-related deficits in phonology, beyond basic fluency. However, although deficits in phonology may contribute, Ho et al. (2002) argue that tasks similar to the Alliteration Fluency subtest appear to be more challenging than tasks of semantic fluency due to a more difficult search strategy, which loads more heavily on EF (Riva, Nichelli, & Devoti, 2000).

In sum, PAE was related to performance deficits on a number of phonological processing outcomes in the current sample. However, some aspects of these performance deficits could be accounted for by deficits in other higher-order cognitive processes. The following section discusses the possible mediating role of one such cognitive process in PAE-related reading and phonological processing outcomes.

WM Mediation of PAE Effects on Reading Ability and Phonological Processing

My second hypothesis stated that PAE-related deficits in reading ability and phonological processing would be mediated by deficits in WM. I tested this hypothesis using both simple and multiple regression analyses (as suggested by Baron & Kenny, 1986), and assessed the statistical significance of mediation effects using the Sobel test (Sobel, 1982). Given that FASD diagnosis was a stronger predictor of reading and phonological processing outcomes than continuous measures of PAE, I used group status (exposed versus non-exposed) as a dichotomous categorical predictor in these analyses. Only the FAS/PFAS and Control groups were included, so that I could contrast the performances of children whose reading and phonological processing

abilities appeared to be impacted by heavy PAE with children who did not have such exposure. I tested mediation only for those reading and phonological processing outcomes that were previously identified as showing FASD-related effects even after consideration of potential confounding variables: NARA Comprehension and PhAB Alliteration, Spoonerisms, Alliteration Fluency, and Rhyme Fluency. This hypothesis was at least partially confirmed for all five outcomes.

The ultimate aim of reading is comprehension, but the attainment of this goal involves a complex interplay of multiple cognitive processes, only one of which is WM (Verhoeven et al., 2011). WM allows the reader to: (1) rehearse phonological information, necessary for word decoding and reading comprehension, using the phonological loop component; (2) maintain visual representations of the text layout, using the visuospatial sketchpad component; and (3) switch between the processing and storing aspects of information processing, using the central executive system that allows for attentional control of WM. Unsurprisingly, then, WM capacity has proven to be a robust predictor of reading comprehension in previous studies (Cain et al., 2004; Carretti et al., 2009). Consistent with such findings, WM was a significant predictor of reading comprehension (as measured by performance on the NARA Comprehension subtest) in the current sample. Furthermore, when WM scores were entered into the regression model predicting comprehension, FASD diagnosis went from a significant to a marginally significant predictor of comprehension. The result of a subsequent Sobel test revealed that WM partially mediated the effects of FASD diagnosis on comprehension.

Research on reading deficits in individuals with dyslexia have often focused on underlying phonological processing deficits (Bruck, 1992; Kirby et al., 2003). The current study therefore included tasks of phonological processing to determine whether children with PAE also

exhibit such deficits. However, as I have repeatedly argued throughout this paper, tasks of phonological processing also involve other cognitive processes that may be affected by PAE, such as mental set shifting, attention, and WM, to name a few (Ho et al., 2002; Riva et al., 2000; Varvara et al., 2014). The current research focused only on WM and found that it accounted for significant variance in performance on four measures of phonological processing: PhAB Alliteration, Spoonerisms, Alliteration Fluency, and Rhyme Fluency.

Regarding the model predicting performance on the PhAB Alliteration subtest, FASD diagnosis did not remain a significant predictor after WM scores were entered. Results from a subsequent Sobel test revealed that WM fully mediated the effects of FASD diagnosis on PhAB Alliteration performance. This task required children to hold three words in mind, segment those words, compare the initial three sounds, make a decision about which two sounds were same, and then recall which two words those sounds belonged to before repeating them back to the examiner. Even though the task appears to be a fairly simple measure of phonological awareness, at face value it also appears to rely quite heavily on WM capacity. This perspective on the test is borne out by these regression results.

Regarding the model predicting performance on the PhAB Spoonerisms subtest, FASD diagnosis remained a significant predictor after WM scores were entered, although the magnitude of its significance decreased. Results from a subsequent Sobel test revealed that WM partially mediated the effects of FASD diagnosis on PhAB Spoonerisms performance. As mentioned before, this subtest involves EF skills beyond basic phonological awareness, such as monitoring and inhibitory processes, as well as WM (Varvara et al., 2014) Thus, the remaining variance explained by FASD diagnosis could, at least partially, be accounted for by other EF deficits.

Regarding the model predicting performance on the PhAB Alliteration Fluency subtest, FASD diagnosis did not remain a significant predictor after WM scores were entered. Results from a subsequent Sobel test revealed that WM fully mediated the effects of FASD diagnosis on PhAB Alliteration Fluency performance.

Regarding the model predicting performance on the PhAB Rhyme Fluency subtest, FASD diagnosis remained a significant predictor after WM scores were entered, although the magnitude of its significance decreased. Results from a subsequent Sobel test revealed that WM partially mediated the effects of FASD diagnosis on PhAB Alliteration Fluency performance.

Fluency tasks are typically used as tests of EF and involve at least strategic search and mental set shifting, in addition to WM (Kodituwakku et al., 2006; Rende, Ramsberger, & Miyake, 2002; Riva et al., 2000; Schonfeld et al., 2001). As mentioned earlier, Alliteration Fluency appears to involve a search strategy that places heavier demands on EF than that of Semantic Fluency (Ho et al., 2002; Riva et al., 2000). The search strategy involved in Rhyme Fluency may, then, place even heavier demands on EF processes (beyond WM), which could account for some of the remaining variability in the Rhyme Fluency performance of exposed children, but this is purely speculation.

The results discussed here highlight the importance of considering WM deficits in relation to PAE-related performance deficits on tests of reading and phonological processing. The importance of WM in reading has been well-established by prior research (Cain et al., 2004; Carretti et al., 2009) but, to my knowledge, only one other study has investigated the contribution of WM to PAE-related reading deficits. Glass et al. (2015) found that phonological processing, speeded naming, and WM significantly predicted word reading their sample. Furthermore, there was an interaction effect such that WM was a much stronger predictor of

word reading in children with heavy PAE than controls. When phonological processing and speeded naming were controlled for in subsequent analyses, WM still accounted for significant word reading variance in children with heavy PAE but not in controls.

The findings of Glass et al. (2015) and of the current study can help guide future interventions designed to address PAE-related reading deficits. A local language and literacy intervention study showed improvements in syllable manipulation, letter-sound knowledge, word reading, and non-word reading in children with FASD who received language and literacy training compared to children with FASD who did not receive such training (Adnams et al., 2007). However, the intervention group did not show any significant gains on a general scholastic test of reading. Although the authors noted that this lack of improvement in reading might have been due to the test not being sensitive enough to reflect gains in weaker readers, it might also be an indication that reading interventions for this population need to focus on additional cognitive processes, such as WM, that are involved in reading. Rehearsal training resulted in WM span gains in children with FASD (Loomes, Rasmussen, Pei, Manji, & Andrew, 2008) and a WM intervention for children with special needs appeared to benefit their reading comprehension (Dahlin, 2011). Thus, careful consideration of the contributions of WM deficits to reading difficulties could help researchers design interventions with more far-reaching impact on reading outcomes for children with PAE.

Limitations and Future Directions

This study had several limitations that should be addressed by future researchers investigating the relations between PAE and reading and phonological processing. The first of these limitations concerns the measures used to assess various aspects of reading and phonological processing. Regarding reading comprehension, different types of comprehension

questions (e.g., literal, inference, prediction, or personal response) can be assessed in various ways (e.g., true/false, who/what/where/why, or multiple choice; Day & Park, 2005). The reading test used in the current study did not distinguish between those different types of comprehension questions. Therefore, it was not possible to drill down to the specific components of reading comprehension that may have been affected by PAE.

Furthermore, regarding this instrument-related limitation, due to a lack of normed Afrikaans reading and phonological processing tests, this study employed translated and adapted versions of English-language tests. Despite best efforts, the Afrikaans and English versions of these tests may, therefore, have differed in certain aspects.

A second major limitation of the current study concerns the violation of assumptions underlying parametric testing. However, non-parametric equivalents might have underestimated the subtle, yet clinically significant, effects of PAE on reading and phonological processing. Nevertheless, the results of the current research should, therefore, be interpreted with caution and require replication in other samples by future research.

A third major limitation of the current study, that is also common to all epidemiological studies, was that it likely did not include all of the potential confounding variables that may be influential in reading and phonological processing research. For example, bilingualism has important influences on phonological awareness and executive functioning (Bialystok, 2001) but was not considered in the present study. The inclusion of potential confounding variables such as these would serve to further elucidate the impacts on reading and phonological processing that are specific to PAE.

Lastly, the current study presents a purely cross-sectional perspective of PAE-related reading and phonological processing deficits. Given that the multiple cognitive processes

involved in reading and phonological processing tasks reach maturity at different developmental stages (Wolf et al., 2000), an important direction for future research would be to determine how performances on reading and phonological processing test might be differentially affected by PAE at different ages.

Summary and Conclusion

The current study is the first, to my knowledge, to demonstrate the mediating role of working memory in phonological processing and reading comprehension deficits in children with heavy prenatal alcohol exposure. In addition, it confirmed findings from previously published research showing the detrimental impacts that prenatal alcohol exposure can have on children's later reading and phonological processing abilities. However, the deficits observed in the current sample appear to be restricted to children who were more severely impacted by heavy prenatal alcohol exposure, namely those who meet the requirements for FAS or PFAS diagnoses. Given the possible adverse impact of reading deficits on children's social and academic development, as well as their later employment opportunities, the absence of differences in reading and phonological processing performance between nonsyndromal children with heavy prenatal alcohol exposure and demographically similar children without such exposure warrants further investigation.

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APPENDIX A

Test Items from Original PhAB and Translated and Adapted Afrikaans Subtests

Table A1
Alliteration Subtests

	English				Afrikaans			
Part 1 Practice Items								
A.	shop	mat	shell	(sh)	son	mat	seun	(s)
B.	lot	mess	mud	(m)	les	mes	man	(m)
C.	pick	pat	run	(p)	pak	pot	red	(p)
Part 1 Test Items								
1.	ship	fat	fox	(f)	net	nie	sak	(n)
2.	mug	zip	men	(m)	dag	pot	duif	(d)
3.	bike	name	nose	(n)	hok	tak	tyd	(t)
4.	dig	dot	pen	(d)	kop	kam	bul	(k)
5.	tin	sack	top	(t)	bed	man	mat	(m)
Part 2 Practice Items								
D.	plum	crane	cloud	(c)	blaf	klaar	bruin	(b)
E.	brain	bleed	school	(b)	krag	staat	krap	(k)
Part 2 Test Items								
6.	snake	clap	crawl	(c)	skoen	brood	brand	(b)
7.	plate	pram	draw	(p)	skip	plaas	staan	(s)
8.	sleep	clown	snail	(s)	trap	koud	troon	(t)
9.	cross	twig	truck	(t)	plaat	pret	staan	(p)
10.	drip	skirt	dwarf	(d)	skool	klomp	kraan	(k)

Table A2
Rhyme Subtests

	English			Afrikaans		
Practice Items						
A.	sail	boot	nail	red	kop	net
B.	red	fed	leg	sag	bel	sel
C.	big	hiss	miss	pen	wen	rug
Part 1 Test Items						
1.	made	hide	fade	pot	straf	laf
2.	wig	fig	pin	eet	sak	meet
3.	bus	harm	farm	sit	net	wit
4.	pack	lack	sag	dag	lag	dit
5.	sap	hop	top	tas	ken	pen
6.	nut	cut	pet	rek	byt	bek
7.	sand	hand	cup	min	sin	tol
8.	cat	fan	mat	bad	kos	los
9.	dot	mop	top	het	vat	met
10.	tub	mud	cub	pop	sop	byl
11.	dog	man	fog	af	bul	laf
12.	sip	win	bin	om	by	sy
Part 2 Test Items						
13.	badge	match	catch	koud	foon	sout
14.	fate	late	made	klaar	daar	deur
15.	tease	geese	piece	nooit	soort	ooit
16.	lip	sip	rib	seer	smaak	raak

17.	dog	sock	log	sien	poot	tien
18.	had	sad	mat	soen	doen	maat
19.	lick	big	tick	meer	teer	taak
20.	bead	wheat	seat	staal	heel	haal
21.	cob	hop	sob	duur	kook	rook

Table A3

Spoonerisms Subtests

	English					Afrikaans				
Part 1 Practice Items										
A.	cat	with a	/f/	gives	(fat)	kat	met ‘n	/v/	gee	(vat)
B.	lip	with a	/t/	gives	(tip)	sop	met ‘n	/p/	gee	(pop)
C.	dog	with a	/l/	gives	(log)	pot	met ‘n	/r/	gee	(rot)
Part 1 Test Items										
1.	cot	with a	/g/	gives	(got)	sak	met ‘n	/t/	gee	(tak)
2.	fun	with a	/b/	gives	(bun)	sit	met ‘n	/d/	gee	(dit)
3.	red	with a	/b/	gives	(bed)	rol	met ‘n	/k/	gee	(kol)
4.	go	with a	/s/	gives	(so)	man	met ‘n	/k/	gee	(kan)
5.	might	with a	/f/	gives	(fight)	pen	met ‘n	/w/	gee	(wen)
6.	make	with a	/t/	gives	(take)	pak	met ‘n	/s/	gee	(sak)
7.	need	with a	/st/	gives	(steed)	lag	met ‘n	/s/	gee	(sag)
8.	gaze	with a	/cr/	gives	(craze)	pad	met ‘n	/b/	gee	(bad)
9.	stoke	with a	/br/	gives	(broke)	sug	met ‘n	/l/	gee	(lug)
10.	crime	with a	/ch/	gives	(chime)	sin	met ‘n	/m/	gee	(min)
Part 2 Practice Items										
D.	King John	gives	(Jing Kon)			vet man	gee	(met van)		
E.	lazy dog	gives	(daisy log)			koel dag	gee	(doel kag)		
F.	snow black	gives	(blow snack)			wit huis	gee	(hit wuis)		
Part 2 Test Items										
11.	sad cat	gives	(cad sat)			veel meer	gee	(meel veer)		
12.	big pip	gives	(pig bip)			donker kamer	gee	(konker damer)		
13.	fed man	gives	(med fan)			meer kos	gee	(keer mos)		
14.	boast core	gives	(coast bore)			gaan loop	gee	(laan goop)		
15.	riding boot	gives	(biding root)			sonder hulp	gee	(honder sulp)		
16.	float down	gives	(dote flown)			my kat	gee	(ky mat)		
17.	prickly man	gives	(mickly pran)			goed koop	gee	(koed goop)		
18.	which brute	gives	(britch woot)			koue drankie	gee	(doue krankie)		
19.	crowded ship	gives	(shouded crip)			bitter koffie	gee	(kitter boffie)		
20.	plane crash	gives	(crane plash)			dom seun	gee	(som deun)		

Table A4

Non-word Reading Subtests

	English	Afrikaans
Card 1 Practice Items		
A.	tib	tim
B.	lom	lom
C.	rad	wam
Card 2 One-Syllable Items		
1.	pim	tov
2.	gat	sen
3.	fot	bot
4.	lub	gaam

5.	hin	gens
6.	chog	glaar
7.	trum	duis
8.	pran	wer
9.	nabe	sil
10.	leaze	laap
Card 3 Two-Syllable Items		
11.	haplut	resig
12.	yutmip	sele
13.	musnate	meker
14.	pootfeg	mogter
15.	shendom	bierso
16.	ligtade	sigter
17.	cromgat	sinter
18.	ropsatch	tomer
19.	rissbick	kater
20.	plutskril	loomte

Table A5
Fluency Subtests

	English	Afrikaans
Semantic Fluency		
Practice Item	things in your school	dinge in jou skool
1.	things to eat	dinge om te eet
2.	animals	diere
Alliteration Fluency		
Practice Item	/k/	/k/
1.	/b/	/b/
2.	/m/	/m/
Rhyme Fluency		
Practice Item	bat	bad
1.	more	meer
2.	whip	skip

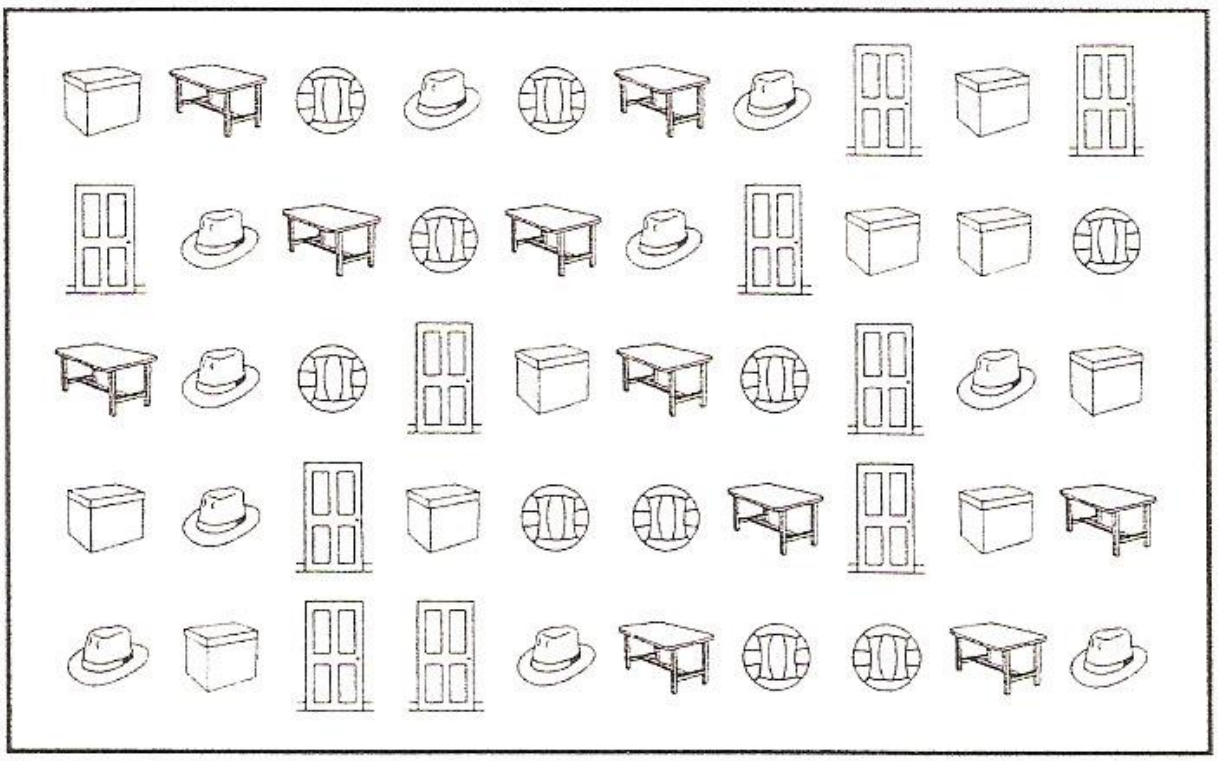

Figure A1. Picture Naming subtest sequence example.

23929 54635 55852 91549 12856 85811 45932 48431 83659 28896

Figure A2. Digit Naming subtest sequence example.

APPENDIX B

Wayne State University Ethics Approval

WAYNE STATE UNIVERSITY

IRB Administration Office
87 East Canfield, Second Floor
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
http://irb.wayne.edu

NOTICE OF EXPEDITED AMENDMENT APPROVAL

To: Sandra Jacobson
Psychiatry
University Square Office Plaza

From: Dr. Scott Millis _____
Chairperson, Behavioral Institutional Review Board (B3)

Date: May 25, 2012

RE: IRB #: 026708B3F
Protocol Title: Neural Bases of Eyeblink Conditioning in FASD
Funding Source: Sponsor: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM
Sponsor: NATIONAL INSTITUTES OF HEALTH
Protocol #: 0802005726

Expiration Date: March 14, 2013

Risk Level / Category: 45 CFR 46.404 - Research not involving greater than minimal risk

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The above-referenced protocol amendment, as itemized below, was reviewed by the Chairperson/designee of the Wayne
State University Institutional Review Board (B3) and is APPROVED effective immediately.

- Protocol – Change in treatment which includes collecting the blood draw at 1-3 weeks instead of 6 weeks. The earlier blood draw provides a more accurate reflection of iron transport across the placenta during pregnancy. This change does not affect risks to participants.
- Consent Form (dated 05/21/2012) – Parental Permission/Research Informed Consent (English and Afrikaans Versions) updated to reflect protocol changes.

WAYNE STATE UNIVERSITY

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NOTICE OF FULL BOARD AMENDMENT APPROVAL

To:	Sandra Jacobson Psychiatry Department of Psychiatry and B	
From:	Dr. Scott Millis or designee Chairperson, Behavioral Institutional Review Board (B3)	
Date:	July 18, 2013	
RE:	IRB #:	026708B3F
	Protocol Title:	Neural Bases of Eyeblink Conditioning in FASD
	Funding Source:	Sponsor: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM Sponsor: NATIONAL INSTITUTES OF HEALTH
	Protocol #:	0802005726
Expiration Date:		February 20, 2014
Risk Level / Category:		45 CFR 46.404 - Research not involving greater than minimal riskResearch not involving greater than minimal risk

The above-referenced protocol amendment, as itemized below, was reviewed by the Wayne State University Institutional Review Board (B3) and is **APPROVED** effective immediately.

- Protocol – Change in enrollment criteria includes the addition of children ages 13-14 to complete the 2r phase of the longitudinal study. This change does not affect risks to participants.
- Oral Assent Script – Resubmission of Oral Assent Script for Ages 7-12 (English Version and Afrikaans Version).
- Assent Form (dated 6/4/2013) – Addition of Documentation of Adolescent Assent Form for Ages 13-14 (English Version and Afrikaans Version).
- Consent Form (dated 4/18/2013, Protocol Version #2r) - Parental Permission/Research Informed Consent (English Version and Afrikaans Version) updated to reflect change in age range and telephone number.
- Consent Form (dated 4/18/2013, Protocol Version #2rr Alternate) - Parental Permission/Research Informed Consent (English Version and Afrikaans Version) updated to reflect change in telephone number.

WAYNE STATE UNIVERSITY

IRB Administration Office
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NOTICE OF EXPEDITED AMENDMENT APPROVAL

To: Sandra Jacobson
Psychiatry
Department of Psychiatry and B

From: Dr. Deborah Ellis or designee _____
Chairperson, Behavioral Institutional Review Board (B3)

Date: June 11, 2014

RE:

IRB #:	026708B3F
Protocol Title:	Neural Bases of Eyeblink Conditioning in FASD
Funding Source:	Sponsor: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM Sponsor: NATIONAL INSTITUTES OF HEALTH
Protocol #:	0802005726
Expiration Date:	February 19, 2015
Risk Level / Category:	45 CFR 46.404 - Research not involving greater than minimal riskResearch not involving greater than minimal risk

The above-referenced protocol amendment, as itemized below, was reviewed by the Chairperson/designee of the Wayne State University Institutional Review Board (B3) and is APPROVED effective immediately.

- Protocol - Enrollment criteria modified to reflect change in participants to be seen between ages of 8 to 13 years to ages of 8 to 17 years.
- Protocol - Other - Compensation modified to reflect change to Rand/Dollar conversion update. The compensation remains R150 regardless of USD.
- Consent Form - Parental Permission/Research Informed Consent - English and Afrikaans versions (revision dated 5/27/2014) - Consent Form modified to reflect change in enrollment criteria (increased age range to 8-17 years of age) and compensation amount of R150 due to conversion update between Rand and USD.

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NOTICE OF FULL BOARD CONTINUATION APPROVAL

To: Sandra Jacobson
Psychiatry
Department of Psychiatry and B

From: Dr. Deborah Ellis or designee D Ellis, PhD Signed
Chairperson, Behavioral Institutional Review Board (B3)

Date: December 21, 2015

RE: IRB #: 026708B3F

Protocol Title: Neural Bases of Eyeblink Conditioning in FASD

Funding Source: Sponsor: NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM
Sponsor: NATIONAL INSTITUTES OF HEALTH
Institute Proposal: 15111866

Protocol #: 0802005726

Expiration Date: December 16, 2016

Risk Level / Category: 45 CFR 46.404 - Research not involving greater than minimal riskResearch not involving greater than minimal risk

Continuation for the above-referenced protocol and items listed below (if applicable) were **APPROVED** following Full Board review by the Wayne State University Institutional Review Board (B3) for the period of 12/21/2015 through 12/16/2016. This approval does not replace any departmental or other approvals that may be required.

- Actively accruing participants.
- Infant Pilot Study Prescreening consent (#4r), dated 8/4/10, in English and Afrikaan
- Infant Study Consent (#4.1r), dated 11/14/14, in English and Afrikaan
- Infant MRI Pilot Study Consent (#4.2), dated 1/6/12, in English and Afrikaan

- Federal regulations require that all research be reviewed at least annually. You *may* receive a *"Continuation Renewal Reminder"* approximately two months prior to the expiration date; however, it is the Principal Investigator's responsibility to obtain review and continued approval ***before*** the expiration date. Data collected during a period of lapsed approval is unapproved research and can *never* be reported or published as research data.
- All changes or amendments to the above-referenced protocol require review and approval by the IRB **BEFORE** implementation.
- Adverse Reactions/Unexpected Events (AR/UE) must be submitted on the appropriate form within the timeframe specified in the IRB Administration Office Policy (http://www.irb.wayne.edu/policies-human-research.php).

NOTE:

1. Upon notification of an impending regulatory site visit, hold notification, and/or external audit the IRB Administration Office must be contacted immediately.
2. Forms should be downloaded from the IRB website at **each** use.

WAYNE STATE UNIVERSITY

IRB Administration Office
87 East Canfield, Second Floor
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
http://irb.wayne.edu

NOTICE OF EXPEDITED AMENDMENT APPROVAL

To: Sandra Jacobson
Psychiatry
Department of Psychiatry and B

From: Dr. Deborah Ellis or designee D. Ellis, PhD / Signed
Chairperson, Behavioral Institutional Review Board (B3)

Date: October 11, 2016

RE:

IRB #:	026708B3F
Protocol Title:	Neural Bases of Eyeblink Conditioning in FASD
Funding Source:	Sponsor: National Institute on Alcohol Abuse and Alcoholism Sponsor: National Institutes of Health Institute Proposal: 15111866
Protocol #:	0802005726
Expiration Date:	December 16, 2016
Risk Level / Category:	45 CFR 46.404 - Research not involving greater than minimal riskResearch not involving greater than minimal risk

The above-referenced protocol amendment, as itemized below, was reviewed by the Chairperson/designee of the Wayne State University Institutional Review Board (B3) and is APPROVED effective immediately.

- Study Closed to Accrual - The last participant was consented by research staff on 10/10/2015. Accrual of new pregnant women has ended, but researchers continue to study the infants born to these women in the follow-ups, at birth, and at 6 and 12 months postpartum.

Notify the IRB of any changes to the funding status of the above-referenced protocol.

University of Cape Town Ethics Approval

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Annual Progress Report

REC REF Number	187/2008
Title	Neural Bases of Eyeblink Conditioning in FASD
Principal Investigator	A/Prof E M Meintjes

List of documentation

RESEARCH ETHICS COMMITTEE
2011 -05- 19
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

HREC office use only (FWA00001637; IRB00001938)			
☐ Approved ✓	This serves as notification of annual approval, including all documentation described above.		
☐ Not approved	See attached comments.		
Type of review	☐ Expedited ✓	☐ Full committee	
Expiry date	30 MAY 2012		
Signature Chairperson of the HREC	Signed	Date	20/5/11

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30/5/2013
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	Signed	Date Signed	9/10/12

Principal Investigator to complete the following:

1. Protocol information

Date form submitted	October 3, 2012		
HREC REF Number	187/2008	Current Ethics Approval was granted until	30/05/2012
Protocol title	Neural Bases of Eyeblink Conditioning in FASD		
Protocol number (if applicable)			
Principal Investigator	A/Prof EM Meintjes		
Department / Office Internal Mail Address	Department of Human Biology, Room 5.14 Anatomy Building, Faculty of Health Sciences, Anzio Road, Observatory		

1.1 Does this protocol receive US Federal funding?	X☐ Yes	☐ No
1.2 Has sponsorship of this study changed? If yes, please attach a revised summary of the budget.	☐ Yes	☐X No

2. List of documentation

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

UNIVERSITY OF CAPE TOWN

HUMAN RESEARCH ETHICS COMMITTEE
24 JUL 2013
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) **This serves as notification of annual approval, including any documentation described below.**			
☑ Approved	Annual progress report	Approved until/next renewal date	30.5.2014
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	Signed	Date Signed	26/07/2013

Comments to PI from the HREC

Principal Investigator to complete the following:

1. Protocol information

Date form submitted	18 July 2013		
HREC REF Number	187/2008	Current Ethics Approval was granted until	30/5/2013
Protocol title	Neural Bases of Eyeblink Conditioning in FASD		
Protocol number (if applicable)			
Are there any sub-studies linked to this study?	☐ Yes X No		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	A/Prof EM Meintjes		
Department / Office Internal Mail Address	Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, 7925		

1.1 Does this protocol receive US Federal funding?	X Yes	☐ No
1.2 Does this study require full committee approval?	☐ Yes	X No

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES

Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)			
☑ Approved	☐ Type of review: Expedited	☐ Full committee	
This serves as notification that all changes and documentation described below are approved.			
Signature Chairperson of the HREC	Signed	Date	19/6/2014

Note: All amendments should include a Synopsis justifying the changes for the amendment (please see notice dated 23 April 2012)

Principal Investigator to complete the following:

1. Protocol information

Date form submitted	19 June 2014		
HREC REF Number	187/2008		
Protocol title	Neural Bases of Eyeblink Conditioning in FASD		
Protocol number (if applicable)			
Principal Investigator	A/Prof EM Meintjes		
Department / Office Internal Mail Address	Human Biology		
1.1 Is this a major or a minor amendment? (see FHS006hlp)		☐ Major	X Minor
1.2 Does this protocol receive US Federal funding?		X Yes	☐ No
1.3 If the amendment is a major amendment and receives US Federal Funding, does the amendment require full committee approval?		☐ Yes	X No

2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary.

FHS006 – Protocol Amendment – Neural Bases of Eyeblink Conditioning in FASD – **Addendum to perform an ERP Study of Number Processing and Error Detection in FAS and ADHD**

New English and Afrikaans maternal consent forms attached
English and Afrikaans Assent forms attached
Amended Synopsis Attached

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
Email: nosi.tsama@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

24 August 2015

HREC REF: 471/2015

Prof E Meintjes
Biomedical Engineering
Human Biology
Anatomy Building

Dear Prof Meintjes

PROJECT TITLE: NEURAL BASES OF COGNITIVE AND BEHAVIOURAL EFFECTS OF FASD

Thank you for your response to the Faculty of Health Sciences Human Research Ethics Committee dated 21 August 2015.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th August 2016.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

Signed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI),and Declaration of Helsinki guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC 471/2015

APPENDIX C

Informed Consent – ENGLISH

Parental Permission/Research Informed Consent
Title of Study: Neural Bases of Eyeblink Conditioning in FASD

We are pleased to invite you and your child _____ to continue to take part in the study that you have been in since you were pregnant and your baby was born. Please read this form and ask us any questions you have before agreeing to be in the study. The people conducting this study are doctors and scientists from the Faculty of Health Sciences of the University of Cape Town School in South Africa and Wayne State University School of Medicine in the United States: Ernesta Meintjes, Ph.D., and Christopher Molteno, M.D., from University of Cape Town, and Sandra W. Jacobson, Ph.D., and Joseph L. Jacobson, Ph.D., from Wayne State University in the United States. It is being paid for by the National Institute on Alcohol Abuse and Alcoholism in the United States and the Department of Science and Technology and the National Research Foundation of South Africa.

Study Purpose: In this study we want to learn whether some aspects of a child's thinking and behavior are different when a mother drinks or and smokes during pregnancy, and whether genes (characteristics that you inherit from your parents) make it more or less likely that the child will show these differences. Other purposes of the study are to see whether your child's abilities when s/he was a baby and 5 years old predict how he or she is doing at 8-17 years of age. To help decide whether or not to agree to take part with your child in this study, a project staff member has talked with you about the risks and benefits of the study. This consent form summarizes the information given to you by the project staff member during this informed consent process.

The study will use new methods for studying the brain called MRI neuroimaging to better understand how drinking alcohol and smoking during pregnancy can affect a child's development. In neuroimaging, the child lies in a scanner that uses magnets to take pictures of the brain. In this part of the study, we will take pictures on the new scanner at Tygerberg Hospital while your child lies still and watches a video and does some simple finger tapping, attention, and memory tasks.

Study Procedures: If you agree to have your child take part in this study, we will bring you and your child to the our laboratory at the University of Cape Town (UCT) for 2-3 visits that will each take about 4 hours and to Tygerberg Hospital for 1-2 visits that should take about 3-4 hours in total.

- During the visits to University of Cape Town, your child will do simple tasks involving finger tapping, attention, learning and memory, arithmetic, word meanings, puzzles, circle drawing, and mazes (Wechsler Intelligence Scale for Children; paced/unpaced finger tapping; Circle Drawing task; timing and pitch perception tasks; California Verbal Learning Test).
- We will test your child's vision.
- In one task, your child will put on a special helmet. While your child is watching a video, a puff of air from the helmet will cause him/her to blink while hearing a tone. We will ask your child questions about the video afterwards.
- We will weigh and measure your child and take a photograph to look for facial features that often relate to alcohol exposure during pregnancy.
- During this visit, we will ask you some questions about your child's behavior and attention (Disruptive Behavior Disorders assessment), daily activities (Child Behavior Checklist), school and health history, and any medications that s/he is taking.
- We will ask you to update us about stressful experiences in your daily life during the past year (Life Events Scale), your current drinking, smoking, and drug use, attention problems you may have had as a child (Barkley-Murphy ADHD Scale), and stressful feelings that you experience,

including sadness, anxiety, and distress (Beck Depression Inventory; Structured Clinical Interview for DSM-IV).

- At the end of the first visit, our research driver and nurse will take you and your child to a nearby clinic, where a technician/nurse will take a 5 cc blood sample (approximately 1 teaspoon) from your child's vein to test for lead and iron deficiency anemia. About 10 cc of blood (about 2 teaspoons) will be obtained from your child and yourself to study genetic differences that you and your child inherited from your family and have been found to be related to differences in alcohol use, depression, attachment, or child attention/behavior and development. These samples will be stored and used for future genetic analyses.
- During the first visit to Tygerberg, your child will first practice the finger tapping, and attention and memory tasks s/he will be doing on a computer while lying in the scanner. During the neuroimaging, your child will lie on a padded plastic bed that slides into the scanner. We will ask him/her to lie as still as possible while the pictures are being taken. Taking these pictures of the brain does not hurt and is used every day by many people in the hospital. During the second visit to Tygerberg, our assistant will again practice the finger tapping and attention/memory tasks with your child and review with him/her the airpuff learning task that s/he has done in our laboratory at UCT. Your child will be shown special goggles that s/he will wear in the scanner and told that s/he will feel the airpuff and hear some tones while watching a video and that we will be asking him/her some questions about the video at the end of the scan. During some of the time in the scanner, your child will watch videos and during some of the time s/he will do the finger tapping and other tasks that were practiced before entering the scanner. There will be two sessions in the scanner at each visit to Tygerberg—both on the same day—one in the morning and one after lunch, which we will give you and your child while you are at Tygerberg. Each session in the scanner will last no longer than 45-60 minutes. Children with the following may not have an MRI but will take part in the rest of the visits: implanted medical devices, such as aneurysm clips in the brain, heart pacemakers, and cochlear (inner ear) implants; lead-based tattoos; or pieces of metal close to or in an important organ (such as, the eye); claustrophobia or fear of being in a small space.

Benefits: There may be no direct benefits for you; however, information from this study may help other people now or in the future. We will give you information about your child's development at this age. We will use the findings from this study for research purposes only. However, if a serious problem is found, we will tell you and refer your child to a doctor and/or someone who can help, if you would like us to do so. If your child is suffering from any major illness, we will send you Red Cross Children's Hospital. No information about your child will be given to any doctors, hospitals, or schools unless you ask us and allow us to do so in writing.

Risks: None of the procedures we use at UCT or Tygerberg are dangerous for you or your child. The risks of drawing blood include some temporary discomfort or swelling, and rarely, infection. These risks that will be minimized because the procedure will be done by a trained phlebotomist (nurse/technician who has been specially trained to draw blood). We will begin by introducing you and your child to the research staff and will give you both breakfast each day before the assessment begins. You will be present in a room nearby during all of your child's assessments and will be present with your child during the physical examination and blood draw. During the MRI neuroimaging assessments, certain metal objects, such as, watches, credit cards, hairpins, and writing pens, may be damaged by the MRI scanner or pulled away from the body by the magnet. For these reasons, we will ask your child to remove these before going into the scanner. When the scanner makes the pictures, the bed may shake, and your child will hear loud banging noises. S/he will be given earplugs or headphones to protect the ears. Also, some people feel nervous in a small closed space, such as when they are in the scanner. Your child will be able to see out of the scanner at all times, and we will not start until s/he tells us that s/he is comfortable. S/he will be able to stop the scanning at any time by squeezing a ball that s/he will hold in one hand and can talk to us using an intercom that is built into the scanner. There are no known harmful long-term effects of the magnetic fields used in this study. There is little risk that anything you tell us will be told to people outside the study and we will do everything we can to keep this information secret, as described

below, except that evidence of child abuse or neglect will be reported to the appropriate authorities, as required by law, and may report other illegal activities that are reported to us during the visit.

Research Related Injuries: If you or your child is injured during the study, you will get treatment including first aid, emergency treatment and follow-up care, as needed. No reimbursement, compensation, or free medical care is offered by Wayne State University or the University of Cape Town. If you think that your child has suffered a research related injury, let the investigator know right away.

Study Costs: There will be no cost to you or your child for taking part in this research study, and you and your child will be transported to the laboratory at University of Cape Town and Tygerberg Hospital by our driver.

Compensation: For taking part in this research study, we will give you R180 for each visit and a photo of your child, and we will give your child a small gift. You and your child will also be given breakfast and lunch each time you and your child come to University of Cape Town or Tygerberg Hospital.

Confidentiality: We will keep all information collected about you and your child during the study secret to the extent permitted by law. This information will not be used in any way that can allow anyone else to know what you or your child has told us, except that evidence of child abuse or neglect will be reported to the appropriate authorities, as required by law. You and your child's names will not be in the research records, only your code number. We will not give out any information that names you or your child unless you give us written permission, but your records may be reviewed by the study sponsor, the Human Investigation Committee at Wayne State University, the University of Cape Town Research Ethics Committee, or governmental agencies with appropriate regulatory oversight. The list linking names and code numbers will be stored in locked file cabinets in the research laboratory. Only project staff members who need to contact you by telephone or in person will be allowed to look in these files. Information from this study, including photos may be presented in scientific meetings or journals or for teaching purposes, but your and your child's names will be kept secret.

Voluntary Participation/Withdrawal: Taking part in this study is voluntary. You may decide to have your child take part and later change your mind and quit the study. You and your child are also free not to answer any questions or to stop any task before it is finished. Withdrawal from the study would not lead to any problems for you or your child. The researcher or the sponsor may also stop your child's taking part in this study without your agreeing to it.

Questions: If you have any questions now or in the future, you may contact Drs. Ernesta Meintjes or Christopher Molteno at 021-406-6291 or Dr. Sandra W. Jacobson at 001-313-993-5454. If you have questions or concerns about you or your child's rights as a research participant, you can contact the Chairs of either the University of Cape Town Research Ethics Committee (021 406-6338) or the Wayne State University Human Investigation Committee (001-313-577-1628).

Consent to Participate in a Research Study: To voluntarily agree to have your child take part in this study, you must sign on the line below. If you decide to take part with your child, you or your child may quit at any time. You are not giving up any of your or your child's legal rights by signing this form. Your signature shows that you have read, or had read to you, this whole consent form, including the risks and benefits, and that we have answered all your questions. We will give you a copy of this consent form to take home.

_____ _____

Signature of Parent or Legally Authorized Guardian Date

Printed Name of Parent or Authorized Guardian Time

Oral Assent (children age 7-12 years) Date

**Signature of Witness (When applicable) Date

Printed Name of Witness Time

Signature of Person Obtaining Consent Date

Printed Name of Person Obtaining Consent Time

** Use when parent has had consent form read to them (i.e. illiterate, legally blind, translated into foreign language).

Informed Assent – ENGLISH

Documentation of Adolescent Assent Form
(ages 13-17)
Title: Neural Bases of Eyeblink Conditioning in FASD
Study Investigator: Sandra W. Jacobson, Joseph L. Jacobson,
Christopher D. Molteno, Ernesta M. Meintjes

Why am I here?
This is a research study. Only people who choose to take part are included in research studies. You are being asked to take part in this study because you are one of a large group of children who have been taking part in this study since you were born and have taken part in visits as an infant and at 5 years of age. We are inviting you to take part in the next phase of this study. Please take time to make your decision. Talk to your family about it and be sure to ask questions about anything you don't understand.

Why are they doing this study?
This study is being done to find out how children learn and remember things and solve simple problems. We are trying to understand whether and how diet, alcohol, smoking, and drug exposure during pregnancy may affect development. We study children at different ages using different tasks to see how they grow and develop.

What will happen to me?
Here at University of Cape Town, we will be studying what happens when you feel a puff of air in your eye. You will sit in a chair wearing a special helmet and will watch a video. From time to time, you will feel a puff of air from the helmet and sometimes you will hear a tone. You will also do simple tasks involving tapping your finger, naming pictures, learning lists of words, reading and arithmetic, puzzles, mazes, memory and computer tasks, and tasks about how other people feel and understand another person's point of view. We will also weigh you, measure how tall you are, take a photo, and check how well you can see. You will spend this morning here and will come back to University of Cape Town another day to do the air puff task and the other tasks that I mentioned.

The second part of the study involves neuroimaging, which is a new way to learn about the brain by taking pictures of the brain. These pictures can help us better understand how the brain works. For this part of the study we will drive you and your mother to Tygerberg Hospital. During the neuroimaging, you will lie on a plastic bed that slides into a large machine called a scanner. We will ask you to lie as still as possible while the pictures are being taken. Taking these pictures of the brain does not hurt and is used everyday by many people in the hospital. During some of the time in the scanner, you will watch videos and during some of the time you will do simple tasks involving tapping your finger or doing simple puzzles, or reading and arithmetic, or learning and memory, or looking at pictures and figuring out if two people seem to have the same feeling. There will be one session in the scanner.

We will also ask you to give us a sample of your spit (saliva) and have a nurse take a small amount of blood from your arm to study how your genes (family characteristics that you get from your parents) affect how you do these tasks and how you act.

How long will I be in the study?

You will be in the study for this phase two days for about 3-4 hours at our laboratory at University of Cape Town (including breakfast, a snack, and lunch) and one visit involving about 45-50 minutes in the scanner and 1 hour of training and assessment outside the scanner at Tygerberg Hospital.

Will the study help me?

You will not benefit from being in this study; however information from this study may help other people in the future better understand how the brain performs different tasks and whether diet, alcohol, smoking, or drug exposure during pregnancy affects how the brain performs.

While taking part in this phase of the research study, we will give you a small gift and a photo taken of your brain at the end of the scanning. We will provide breakfast, a snack, and lunch each time you come to our laboratory at University of Cape Town or Tygerberg Hospital.

Will anything bad happen to me?

There are no risks from being in the scanner at Tygerberg Hospital or from any of the tasks we do with you in our laboratory at University of Cape Town. The risk of drawing blood include some temporary discomfort swelling and rarely infection. These risks will be small because the blood will be taken by a trained person (nurse/technician). Some people feel nervous in a small closed space, such as when they are in the scanner. You will practice what it is like in a pretend scanner beforehand. We will give you earplugs or headphones so that the loud banging of the scanner will not bother you. There is a button you can press to ask questions or stop the scan at anytime. You can see out of the scanner at all times, and we will not start until you are comfortable with the set-up.

Do my parents or guardians know about this? (If applicable)

This study information has been given to your parents/guardian and they said that you could take part in the study. You can talk this over with them before you decide.

Research Related Injuries

In the event that this research related activity results in an injury, treatment will be made available including first aid, emergency treatment, and follow-up care as needed. Care for such will be billed in the ordinary manner to you or your insurance company/South African public assistance. No reimbursement, compensation, or free medical care is offered by Wayne State University or the University of Cape Town. If you think that you have suffered a research related injury, please contact the Cape Town PI (Dr. Christopher Molteno) right away at 021-406-6291.

What about confidentiality?

Every reasonable effort will be made to keep your records (medical or other) and/or your information confidential, however we do have to let some people look at your study records.

We will keep your records private unless we are required by law to share any information. The law says we have to tell someone if you might hurt yourself or someone else. The study doctor can use the study results as long as you cannot be identified.

The following information must be released/reported to the appropriate authorities if at any time during the study there is concern that:

- child abuse or elder abuse has possibly occurred,
- you disclose illegal criminal activities, illegal substance abuse or violence

What if I have any questions?

For questions about the study please call Dr. Christopher Molteno at 021-406-6291. If you have questions or concerns about your rights as a research participant, the Chair of the Institutional Review Board can be contacted at 001-313-577-1628 or you can contact the Chair of the University of Cape Town Research Ethics Committee at 021-406-6338.

Do I have to be in the study?

You don't have to be in this study if you don't want to or you can stop being in the study at any time. Please discuss your decision with your parents and researcher. No one will be angry if you decide to stop being in the study.

AGREEMENT TO BE IN THE STUDY

Your signature below means that you have read the above information about the study and have had a chance to ask questions to help you understand what you will do in this study. Your signature also means that you have been told that you can change your mind later and withdraw if you want to. By signing this assent form you are not giving up any of your legal rights. You will be given a copy of this form.

_____ _____

Signature of Participant (13 yrs & older) Date

_____

Printed name of Participant (13 yrs & older)

_____ _____

**Signature of Witness (When applicable) Date

_____

Printed Name of Witness

_____ _____ _____

Signature of Person who explained this form Date

_____

Printed Name of Person who explained form

** Use when participant has had consent form read to them (i.e., illiterate, legally blind, translated into foreign language).

Informed Consent – AFRIKAANS

Toestemming deur Ouer/Ingeligte Toestemming tot Navorsing
Titel van Studie: Neurale Basis van Oogknip Kondisionering in FASD

Jy en u kind _____ word uitgenooi om deel te neem aan ons navorsingstudie. Lees asseblief hierdie vorm deur en vra vir ons enige vrae wat u het voordat u instem om in die studie te wees. Die mense wat hierdie studie doen is dokters en wetenskaplikes aan die Universiteit van Kaapstad se Fakulteit Gesondheidswetenskappe in Suid-Afrika en Wayne State Universiteit Mediese Skool in die Verenigde State: Ernesta Meintjes, Ph.D., en Christopher Molteno, M.D., van die Universiteit van Kaapstad, en Sandra W. Jacobson, PhD., en Joseph L. Jacobson, Ph.D., van Wayne State Universiteit in die Verenigde State. Die studie word geborg deur die Nasionale Instituut oor Alkohol Misbruik en Alkoholisme in die Verenigde State en die Departement van Wetenskap en Tegnologie en die Nasionale Navorsingsraad van Suid-Afrika.

Doel van die Studie: In hierdie studie wil ons leer hoe sommige aspekte van hoe ‘n kind dink en optree verskillend is wanneer ‘n ma drink en/of rook tydens swangerskap, en of gene (eienskappe wat jy van u ouers erf) dit meer of minder waarskynlik maak dat die kind hierdie verskille sal wys. Bykomende doelwitte van die studie is om te ondersoek die mate waartoe toetse wat gedoen is tydens die babajare en tydens 5-jarige ouderdom die kind se prestasie op 8-14-jarige ouderdom voorspel. Om u te help met u besluit om aan die studie deel te neem of nie, het ‘n projek personeellid die risiko’s en voordele met u bespreek. Hierdie toestemmingsvorm is ‘n opsomming van die inligting wat aan u gegee is deur die projek personeellid tydens hierdie ingligte toestemmingsproses.

Hierdie studie sal nuwe metodes wat MRI neurobeelding genoem word, gebruik om beter te verstaan hoe die drink van alkohol en rook tydens swangerskap ‘n kind se ontwikkeling kan affekteer. In neurobeelding lê die kind in ‘n skandeerder wat magnete gebruik om prentjies van die brein te neem. In hierdie deel van die studie sal ons prentjies neem met die nuwe skandeerder by Tygerberg Hospitaal terwyl u kind stil lê en na ‘n video kyk, en sekere eenvoudige take doen waartydens hy/sy sy/haar vingers moet tik, moet aandag gee, en sekere goed moet onthou.

Studie Prosedures: Indien jy instem om u kind aan hierdie studie te laat deelneem, sal ons u en u kind na ons laboratorium bring by die Universiteit van Kaapstad (UK) vir 2-3 besoeke wat elk ongeveer 4 ure sal duur, en na Tygerberg Hospitaal vir 1 - 2 besoeke wat elk omtrent 3-4 ure in totaal behoort te duur.

- Tydens die besoeke aan die Universiteit van Kaapstad sal u kind eenvoudige take doen waartydens hy/sy sy/haar vingers moet tik, moet aandag gee, dinge probeer onthou, somme doen, betekenis van woorde moet gee, legkaarte doen, doolhowe doen, en sirkels teken (Wechsler Intelligensie Skaal vir Kinders; vingertik taak; Sirkel Teken Taak, tyd en frekwensie persepsie take; Californieë Verbale Leer Toets).
- Ons sal u kind se visie toets / toets hoe goed u kind kan sien.
- In een taak sal u kind ‘n spesiale helm opsit. Terwyl u kind na ‘n video kyk, sal ‘n blasie lug uit die helm kom wat sal maak dat u kind sy/haar oog knip terwyl hy/sy ‘n geluid hoor.
- Ons sal u kind weeg en meet en ‘n foto neem om te kyk vir gesigskenmerke wat dikwels verbandhou met alkohol blootstelling tydens swangerskap.
- Tydens hierdie besoek sal ons u ook 'n paar vrae vra oor u kind se gedrag, vermoë om aandag te gee (Steurende Gedragsteuring Toets), daaglikse aktiwiteite (Kindergedrag Vraelys), skool en gesondheidsgeskiedenis, sowel as enige medikasie wat hy/sy neem.
- Ons sal u vra om ons op hoogte te bring oor stresvolle ervarings in u daaglikse lewe gedurende die afgelope jaar (Lewensgebeurtenis Skaal), u huidige drank- en dwelmgebruik en rookpatrone, probleme wat jy as ‘n kind mag gehad het om aandag te gee (Barkley-Murphy AAHV Skaal), en

stresvolle gevoelens wat jy ervaar, insluitend hartseer, angs, en bekommernis (Beck Depressie Vraelys, Gestruktureerde Kliniese Onderhoud vir DSM-IV).

- Aan die einde van die eerste besoek sal ons navorsingsbestuurder en verpleegster u en u kind neem na 'n nabye kliniek, waar 'n tegnikus/verpleegster ‘n 5cc bloedmonster (ongeveer 1 teelepel) van u kind se aar sal neem om te toets vir lood en ystertekort anemie. Omtrent 10 cc bloed (ongeveer 2 teelepels) sal geneem word van u en u kind om genetiese verskille te bestudeer wat verband hou met verskille in alkohol metabolisme, depressie, gehegtheid, of die kind se aandag en ontwikkeling. Hierdie monsters sal gestoor word en gebruik word vir toekomstige genetiese analises.
- Tydens die eerste besoek aan Tygerberg, sal u kind eers die vingertik- en aandag en geheuetake oefen wat hy/sy op ‘n rekenaar sal doen terwyl hy/sy in die skandeerder lê. Gedurende die neurobeelding sal u kind op ‘n sagte plastiek bed lê wat in die skandeerder inskuif. Ons sal hom/haar vra om so stil as moontlik te lê terwyl die prentjies geneem word. Die afneem van hierdie prentjies (foto’s) van die brein maak nie seer nie en word elke dag deur baie mense in die hospitaal gebruik. Tydens die tweede besoek aan Tygerberg sal ons assistent weer die vingertik- en aandag/geheuetake met u kind oefen en met hom/haar hersien die lugblasie leertaak wat hy/sy in ons laboratorium by UK gedoen het. Tydens die skandeerbesoeke sal ons vir u kind spesiale brille wys wat hy/sy sal dra in die skandeerder. Ons sal vir u kind sê dat hy/sy die lugblasie sal voel en ‘n soort geluid sal hoor terwyl hy/sy na ‘n video kyk en dat ons vir hom/haar ‘n paar vrae oor die video sal vra aan die einde van die skandering. Vir 'n gedeelte van die tyd in die skandeerder sal u kind na videos kyk, en vir 'n gedeelte van die tyd sal hy of sy die vingertik en ander take doen wat ons geoefen het voordat hy/sy die skandeerder binnegegaan het. Daar sal gedurende elk van die besoeke aan Tygerberg twee sessies in die skandeerder wees – albei op dieselfde dag - een in die oggend en een na middagete. Ons sal vir u en u kind middagete gee terwyl julle by Tygerberg is. Elke sessie in die skandeerder sal niks langer as 45-60 minute duur nie. Kinders met enige van die volgende toestande mag nie 'n MRI onderneem nie: ingeplante mediese toestelle soos aneurisme knippies in die brein, hart pasaangeërs, en binne-oor inplantings; loodgebasseerde tattoeërmerke, of stukkies metaal naby aan of binne-in 'n belangrike orgaan (soos die oog); engtevrees of die vrees om binne 'n klein ruimte beperk te wees.

Voordele: Daar mag dalk geen direkte voordele vir u wees nie, maar inligting van hierdie studie mag ander mense help, nou of in die toekoms. Jy sal inligting ontvang oor u kind se huidige ontwikkeling op hierdie ouderdom. Ons sal die bevindings van hierdie studie slegs gebruik vir navorsingsdoeleindes. Indien 'n ernstige probleem egter gevind word, sal ons vir u sê en u kind verwys na 'n dokter en/of iemand wat kan help, indien jy dit wil hê. Indien u kind aan enige ernstige siekte ly, sal ons u na die Rooikruis Kinderhospitaal stuur. Geen inligting oor u kind sal uitgegee word aan enige dokters, hospitale, of skole tensy jy dit skriftelik versoek en toelaat nie.

Risiko’s: Geen prosedures wat ons by UK of Tygerberg sal gebruik is gevaarlik vir u of u kind nie. Die risiko’s van bloedtrek sluit soms ‘n bietjie tydelike ongemak of swelling in, en by uitsondering, infeksie. Hierdie risiko’s sal verminder word omdat die prosedure deur ‘n opgeleide flebotomis (verpleegster/tegnikus wat spesiaal opgelei is om bloed te trek) gedoen sal word. Ons sal begin deur u en u kind aan die projekpersoneel bekend te stel en sal vir julle albei ontbyt gee elke dag voordat die toetse begin. Terwyl al u kind se toetse gedoen word sal jy in ‘n vertrek naby u kind wees en jy sal saam met u kind wees tydens die fisiese ondersoek en wanneer die bloed getrek word. Tydens die MRI neurobeelding mag sekere voorwerpe soos horlosies, kredietkaarte, haarknippies en skryfpenne beskadig word deur die MRI skandeerder of deur die magnet weggetrek word van die liggaam. Om hierdie redes sal ons u kind vra om hierdie voorwerpe af te haal voordat hy/sy die skandeerder binnegaan. Wanneer die skandeerder die prentjies neem, mag die bed skud, en u kind sal harde kapgeluide hoor. Hy/sy sal oorpluisies en oorfone gegee word om sy/haar ore te beskerm. Sommige mense voel ook senuweeagtig in ‘n klein beperkte spasie soos wanneer hulle in die skandeerder is. U kind sal te alle tye by die skandeerder kan uitsien, en ons sal nie begin voordat hy/sy nie vir ons sê dat hy/sy gemaklik is nie. Hy/sy sal ook enige tyd kan stop deur ‘n bal te druk wat hy/sy in een hand sal vashou en hy/sy sal met ons kan praat deur ‘n interkom wat in die skandeerder ingebou is. Sover almal

weet is daar geen skadelike langtermyn effekte as gevolg van die magnetise velde wat in hierdie studie gebruik word nie. Daar is baie min kans dat enigiets wat jy vir ons vertel vir ander mense buite die studie gesê sal word en ons sal alles doen wat ons kan om hierdie inligting geheim te hou behalwe, soos hieronder beskryf, indien daar tekens is van kindermishandeling of –verwaarlosing sal dit egter aan die toepaslike owerhede gerapporteer word, soos deur die wet vereis. Ons mag ook ander onwettige aktiwiteite rapporteer wat aan ons tydens die besoek bekend gemaak word.

Navorsingsverwante Beserings: Indien jy of u kind tydens die studie beseer word sal jy behandeling ontvang wat insluit eerstehulp, noodbehandeling en opvolg-sorg soos benodig. Geen vergoeding, terugbetaling, of gratis mediese sorg word verskaf deur Wayne State Universiteit of die Universiteit van Kaapstad nie. Laat die navorser onmiddelik weet as jy dink dat u kind ‘n navorsingsverwante besering opgedoen het.

Studiekostes: Daar sal geen koste wees vir u of u kind om aan hierdie navorsing deel te neem nie, en jy en u kind sal deur ons bestuurder vervoer word na die laboratorium by UK en Tygerberg Hospitaal.

Vergoeding: Vir u deelname aan hierdie navorsingstudie sal ons u R150 ($25) gee vir elke besoek en ‘n foto van u kind, en vir u kind sal ons ‘n klein geskenkie gee. Ons sal ook vir u en u kind ontbyt en middagete gee elke keer as julle na UK of Tygerberg Hospitaal toe kom.

Vertroulikheid: Ons sal alle inligting wat ons tydens die studie versamel oor u en u kind geheim hou tot die mate waartoe die wet dit toelaat. Hierdie inligting sal nie gebruik word op enige manier wat enigiemand anders sal toelaat om te weet wat jy of u kind vir ons vertel het nie, behalwe dat tekens van kindermishandeling of –verwaarlosing aan die toepaslike owerhede gerapporteer sal word, soos deur die wet vereis. Jy en u kind sal in ons navorsingsrekords slegs deur ‘n kodenommer geïdentifiseer word en julle name sal nie op die rekords verskyn nie. Ons sal nie inligting uitgee wat u of u kind by name noem nie tensy jy ons skriftelik toestemming gee, maar u rekords mag hersien word deur die studie borg, die Menslike Navorsings Komitee by Wayne State Universiteit, of regeringsliggame met toepaslike regulatoriese oorsig. Die lys wat deelnemers se identifikasienommers met hul name verbind sal gestoor word in geslote kabinette in die navorsingslaboratorium. Slegs personeellede wat nodig het om u telefonies of persoonlik te kontak sal toegelaat word om na hierdie leêrs te kyk. Inligting vanaf hierdie studie, insluitend foto’s en videos mag aangebied word by wetenskaplike vergaderings of joernale of vir opleidingsdoeleindes gebruik word, maar u en u kind se name sal geheim gehou word.

Vrywillige Deelname/Onttrekking: Deelname aan hierdie studie is vrywillig. Jy mag besluit om u kind aan die studie te laat deelneem en later van besluit verander en die studie los. Jy en u kind is ook vry om enige vrae nie te beantwoord nie, of om enige taak te stop voordat dit klaar is. Onttrekking aan die studie sal geen probleme vir u of u kind veroorsaak nie. Die navorser of die borg mag u kind se deelname aan hierdie studie stop sonder dat jy daartoe instem.

Vrae: Indien jy enige vrae het nou of in die toekoms, kan jy Drs. Ernesta Meintjes of Christopher Molteno kontak by 021-406-6291 of Dr. Sandra W. Jacobson by 091-313-993-5454. Indien jy enige vrae of bekommernisse het oor u of u kind se regte as ‘n deelnemer aan die navorsing, kan jy die voorsitters kontak van die Universiteit van Kaapstad Navorsings-Etiek Komitee (021 406-6338) of die Wayne State Universiteit se Menslike Navorsings Komitees (001-313-577-1628).

Toestemming om aan ‘n Navorsingstudie deel te neem: Om vrywilliglik in te stem om u kind te laat deelneem aan hierdie studie, moet jy op die lyn hieronder teken. Indien jy besluit om met u kind deel te neem, mag jy of u kind enige tyd stop. Jy gee nie enige van u of u kind se regte op deur hierdie vorm te teken nie. U handtekening wys dat jy hierdie hele toestemmingsvorm gelees het of dat dit aan u voorgelees is, insluitend die risiko’s en voordele, en dat ons al u vrae beantwoord het. Ons sal vir u ‘n kopie van hierdie toestemmingsvorm gee om huis toe te neem.

_____ _____
Handtekening van Ouer of Wetlik Gemagtigde Voog Datum

_____ _____
Naam in drukskrif van Ouer of Wetlik Gemagtigde Voog Tyd

_____ _____
Mondelinge Instemming (kinders van ouderdom 7-12) Datum

_____ _____
**Handtekening van Getuie (wanneer van toepassing) Datum

_____ _____
Naam van Getuie in drukskrif Tyd

_____ _____
Handtekening van Persoon wat Toestemming neem Datum

_____ _____
Naam in drukskrif van Persoon wat Toestemming neem Tyd

**Gebruik wanneer toestemmingsvorm aan ouer voorgelees is (bv. wanneer ongeletterd, wetlik blind, vertaal in 'n vreemde taal).

Informed Assent – AFRIKAANS

Dokumentasie van Adolessente Instemming Form
(Ouderdomme 13-17)
Titel: Neurale Basis van Oogknip Kondisionering in FASD
Studie Navorsers: Sandra W. Jacobson, Joseph L. Jacobson,
Christopher D. Molteno, Ernesta M. Meintjes

Hoekom is ek hier?
Hierdie is 'n navorsingstudie. Slegs mense wat kies om deel te neem word ingesluit by navorsingstudies. Jy word gevra om deel te neem aan hierdie studie omdat jy een van 'n groot groep kinders is wat al aan hierdie studie deelneem vandat jy gebore is en het deel geneem aan besoeke toe jy 'n baba was en toe jy 5 jaar oud was. Ons nooi jou uit om deel te neem aan die volgende fase van hierdie studie. Vat asseblief jou tyd om 'n besluit te neem. Gesels met jou familie daaroor en maak seker om vrae te vra oor enige iets wat jy nie verstaan nie.

Hoekom doen hulle hierdie studie?
Hierdie studie word gedoen om uit te vind hoe kinders dinge leer en onthou en hoe hulle eenvoudige probleme oplos. Ons probeer om te verstaan hoe en of dieet, alkohol, rook, en blootstelling aan dwelms gedurende swangerskap ontwikkeling kan beïnvloed. Ons bestudeer kinders op verskillende ouderdomme met verskillende take om te sien hoe hulle groei en ontwikkel.

Wat sal met my gebeur?
Hier by die Universiteit van Kaapstad, sal ons bestudeer wat gebeur wanneer jy 'n blasie lug in jou oog voel. Jy sal in 'n stoel sit met 'n spesiale helm op jou kop en jy sal 'n video kyk. Elke nou en dan, sal jy 'n lugblasie uit die helm voel kom en soms sal jy 'n geluid hoor. Jy sal ook eenvoudige take doen waartydens jy jou vinger moet tik, prentjies benoem, lyste met woorde leer, lees en somme doen, legkaarte doen, doolhowe doen, geheue en rekenaar take doen en take oor hoe ander mense voel en 'n

ander persoon se oogpunt insien. Ons sal jou ook weeg, meet hoe lank jy is, 'n foto neem en kyk hoe goed jy kan sien. Jy sal vanoggend hier spandeer en sal terug kom na die Universiteit van Kaapstad toe op 'n ander dag om die lugblasie taak en die ander take wat ek genoem het te doen.

Die tweede deel van die studie behels neurobeelding, wat ‘n nuwe manier is om van die brein te leer deur prentjies te neem van die brein. Hierdie prentjies kan ons help om beter te verstaan hoe die brein werk. Vir hierdie deel van die studie sal ons jou en jou ma na Tygerberg Hospitaal toe vervoer. Gedurende die neurobeelding, sal jy op ‘n plastiek bed lê wat in ‘n groot masjien inskuif wat ‘n skandeerder genoem word. Ons sal jou vra om so stil as moontlik te lê terwyl die prentjies geneem word. Die afneem van hierdie prentjies (foto’s) van die brein maak nie seer nie en word elke dag deur baie mense in die hospitaal gebruik. Vir 'n gedeelte van die tyd in die skandeerder sal jy na videos kyk, en vir ‘n gedeelte van die tyd sal jy eenvoudige take doen waartydens jy jou vinger moet tik of eenvoudige legkaarte doen, of lees en somme doen, of dinge probeer onthou, of na prentjies kyk en probeer uitwerk of twee mense dieselfde gevoelens voel. Daar sal een sessie in die skandeerder wees.

Ons sal jou ook vra om vir ons ‘n bietjie van jou spoeg (speeksel) te gee en 'n verpleegster sal 'n klein hoeveelheid bloed van jou arm neem om te bestudeer hoe jou gene (familie eienskappe wat jy van jou ouers af kry) beïnvloed hoe jy hierdie take doen en hoe jy optree.

Hoe lank sal ek in die studie wees?
Jy sal twee dae in die studie wees vir hierdie fase, vir ongeveer 3-4 ure by ons laboratorium by die Universiteit van Kaapstad (insluitend ontbyt, 'n peuselhappie, en middagete) en een besoek van sowat 45-50 minute in die skandeerder en 1 uur van opleiding en assessering buite die skandeerder by Tygerberg Hospitaal.

Sal die studie my help?
Jy sal nie daarby baat om in hierdie studie te wees nie, maar inligting uit hierdie studie kan ander mense in die toekoms help om beter te verstaan hoe die brein verskillende take verrig en of dieet, alkohol, rook, of blootstelling aan dwelms gedurende swangerskap beïnvloed hoe die brein werk.

Terwyl jy in hierdie fase van die navorsing deel neem, sal ons vir jou 'n klein geskenkie gee en 'n foto wat van jou brein geneem is aan die einde van die skandering. Ons sal ontbyt, 'n peuselhappie, en middagete voorsien elke keer as jy na ons laboratorium toe kom by die Universiteit van Kaapstad of Tygerberg Hospitaal.

Sal enige iets sleg met my gebeur?
Daar is geen risiko's verbonde aan om in die skandeerder by Tygerberg Hospitaal te wees nie, of enige van die take wat ons met jou doen in ons laboratorium aan die Universiteit van Kaapstad nie. Die risiko van bloed trek sluit in 'n bietjie tydelike ongemak, swelling en selde infeksie. Hierdie risiko's sal klein wees, want die bloed sal geneem word deur 'n opgeleide persoon (verpleegster/tegnikus).

Sommige mense voel senuweeagtig in ‘n klein beperkte spasie, soos wanneer hulle in die skandeerder is. Jy sal voor die tyd oefen hoe dit gaan voel in 'n oefen skandeerder. Ons sal vir jou oorpluisies of oorfone gee sodat die harde geraas van die skandeerder jou nie pla nie. Daar is 'n knoppie wat jy kan druk om vrae te vra of die skandering te stop op enige tyd. Jy kan te alle tye by die skandeerder uitsien, en ons sal nie begin voordat jy gemaklik is nie.

Weet my ouers of voogde hiervan? (Indien van toepassing)
Hierdie studie inligting is aan jou ouers/voogde gegee en hulle het gesê dat jy kan deel neem aan die studie. Jy kan met hulle hieroor praat voordat jy besluit.

Navorsingsverwante Beserings
Indien hierdie navorsingsverwante aktiwiteite lei tot 'n besering, sal behandeling beskikbaar gemaak word, insluitend eerstehulp, noodbehandeling, en opvolg-sorg soos benodig. Sulke sorg sal betaalbaar wees in die gewone manier deur jou of jou versekerings maatskappy/Suid-Afrikaanse openbare hulp. Geen terugbetaling, vergoeding, of gratis mediese sorg word verskaf deur Wayne State Universiteit of die

Universiteit van Kaapstad nie. As jy dink dat jy 'n navorsingsverwante besering opgedoen het, kontak asseblief dadelik die Kaapstad hoofnavorser (Dr Christopher Molteno) by 021-406-6291.

Wat van vertroulikheid?

Elke redelike poging sal aangewend word om jou rekords (mediese of ander) en/of jou inligting konfidensieel te hou, maar ons moet sommige mense na jou studie rekords laat kyk.
Ons sal jou rekords geheim hou tensy ons deur die wet vereis word om enige inligting te deel. Die wet sê dat ons iemand moet vertel as jy dalk jouself of iemand anders mag seer maak. Die studie dokter kan die studie resultate gebruik so lank as wat jy nie geïdentifiseer kan word nie.

Die volgende inligting moet vrygelaat word/gerapporteer word aan die toepaslike owerhede indien daar te eniger tyd gedurende die studie kommer is dat:

- kindermisbruik of mishandeling van bejaardes moontlik plaasgevind het,
- jy onwettige kriminele aktiwiteite openbaar, onwettige drank-en dwelmmisbruik, of geweld

Wat as ek enige vrae het?

Vir vrae oor die studie kontak asseblief vir Dr Christopher Molteno by 021-406-6291. Indien jy enige vrae of bekommernisse het oor jou regte as 'n deelnemer aan die navorsing, kan die voorsitter van die Wayne State Universiteit se Menslike Navorsings Komitee gekontak word by 001-313-577-1628 of jy kan die voorsitter van die Universiteit van Kaapstad Navorsings-Etiek Komitee kontak by 021-406-6338.

Moet ek in die studie wees?

Jy hoef nie in hierdie studie te wees as jy nie wil nie of jy kan ophou om in die studie te wees op enige stadium. Bespreek asseblief jou besluit met jou ouers en navorser. Niemand sal kwaad wees as jy besluit om op te hou om in die studie te wees nie.

INSTEMMING OM IN DIE STUDIE TE WEES

Jou handtekening hieronder beteken dat jy die bogenoemde inligting oor die studie gelees het, en dat jy kans gekry het om vrae te vra om jou te help verstaan wat jy in hierdie studie gaan doen. Jou handtekening beteken ook dat daar aan jou verduidelik is dat jy later van besluit mag verander en onttrek as jy wil. Jy gee nie enige van jou regte op deur hierdie vorm te teken nie. Ons sal vir jou 'n kopie van hierdie toestemmingsvorm gee.

_____ _____

Handtekening van Deelnemer (13 j. & ouer) Datum

_____

Naam van Deelnemer in drukskrif (13 j. & ouer)

_____ _____

**Handtekening van Getuie (Wanneer van toepassing) Datum

_____

Naam van Getuie in drukskrif

_____ _____

Handtekening van Persoon wat vorm verduidelik het Datum

_____

Naam van Persoon wat vorm verduidelik het

**Gebruik wanneer toestemmingsvorm aan deelnemer voorgelees is (bv. wanneer ongeletterd, wetlik blind, vertaal in 'n vreemde taal).

APPENDIX D

Correlations Between Continuous PAE Measures and Outcome Variables

Table D1

Pearson Correlation Matrix for Continuous Prenatal Alcohol Exposure and Neale Analysis of Reading Ability Variables

Variable	1[a]	2[a]	3[a]	4	5	6
1. AA/day (oz)[a]	1.00					
2. AA/occasion (oz)[a]	.76***	1.00				
3. Drinking days/week[a]	.91***	.58***	1.00			
4. Reading Rate	-.11†	-.07	-.15*	1.00		
5. Reading Accuracy	-.07	.03	-.10†	.75***	1.00	
6. Comprehension	-.17*	-.06	-.20**	.75***	.88***	1.00

Note. AA = absolute alcohol. Statistics presented are Pearson correlation coefficients (*r*). All tests were 1-tailed. [a]Non-normally distributed variables.
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D2

Pearson Correlation Matrix for Continuous Prenatal Alcohol Exposure and Phonological Assessment Battery Variables

Variable	1[a]	2[a]	3[a]	4[a]	5[a]	6	7[a]	8	9	10	11	12
1. AA/day (oz)[a]	1.00											
2. AA/occasion (oz)[a]	.76***	1.00										
3. Drinking days/week[a]	.91***	.58***	1.00									
4. Alliteration[a]	-.17*	-.05	-.14*	1.00								
5. Rhyme[a]	-.09	-.01	-.12†	.70***	1.00							
6. Spoonerisms	-.16*	-.05	-.19**	.52***	.71***	1.00						
7. Non-word Reading[a]	-.08	.02	-.10†	.58***	.73***	.69***	1.00					
8. Picture Naming	.06	.03	.14*	-.34***	-.43***	-.52***	-.41***	1.00				
9. Digit Naming	.14*	.01	.18*	-.58***	-.57***	-.61***	-.64***	.62***	1.00			
10. Alliteration Fluency	-.14*	-.05	-.17*	.57***	.64***	.67***	.63***	-.45***	-.61***	1.00		
11. Rhyme Fluency	-.05	-.01	-.12†	.44***	.61***	.60***	.52***	-.46***	-.47***	.54***	1.00	
12. Semantic Fluency	-.06	-.06	-.14*	.14*	.19**	.35***	.18*	-.41***	-.34***	.37***	.33***	1.00

Note. AA = absolute alcohol. Statistics presented are Pearson correlation coefficients (*r*). All tests were 1-tailed. [a]Non-normally distributed variables.
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D3

Spearman Correlation Matrix for Continuous Prenatal Alcohol Exposure and Neale Analysis of Reading Ability Variables

Variable	1[a]	2[a]	3[a]	4	5	6
1. AA/day (oz)[a]	1.00					
2. AA/occasion (oz)[a]	.92***	1.00				
3. Drinking days/week[a]	.96***	.84***	1.00			
4. Reading Rate	-.16*	-.14*	-.17*	1.00		
5. Reading Accuracy	-.06	-.01	-.07	.74***	1.00	
6. Comprehension	-.16*	-.10	-.16*	.71***	.89***	1.00

Note. AA = absolute alcohol. Statistics presented are Spearman correlation coefficients (ρ). All tests were 1-tailed. [a]Non-normally distributed variables.
*$p < .05$. ***$p < .001$.

Table D4

Spearman Correlation Matrix for Continuous Prenatal Alcohol Exposure and Phonological Assessment Battery Variables

Variable	1[a]	2[a]	3[a]	4[a]	5[a]	6	7[a]	8	9	10	11	12
1. AA/day (oz)[a]	1.00											
2. AA/occasion (oz)[a]	.92***	1.00										
3. Drinking days/week[a]	.96***	.84***	1.00									
4. Alliteration[a]	-.11†	-.08	-.10	1.00								
5. Rhyme[a]	-.05	-.01	-.06	.64***	1.00							
6. Spoonerisms	-.18*	-.12†	-.20**	.59***	.74***	1.00						
7. Non-word Reading[a]	-.02	.02	-.03	.53***	.69***	.71***	1.00					
8. Picture Naming	.15*	.11†	.20**	-.41***	-.41***	-.54***	-.40***	1.00				
9. Digit Naming	.13†	.08	.14*	-.57***	-.50***	-.65***	-.61***	.63***	1.00			
10. Alliteration Fluency	-.16*	-.13†	-.17*	.52***	.60***	.64***	.57***	-.44***	-.60***	1.00		
11. Rhyme Fluency	-.11†	-.08	-.15*	.45***	.60***	.59***	.48***	-.44***	-.45***	.48***	1.00	
12. Semantic Fluency	-.12†	-.13*	-.16*	.23**	.20**	.33***	.21**	-.44***	-.38***	.32***	.32***	1.00

Note. AA = absolute alcohol. Statistics presented are Spearman correlation coefficients (ρ). All tests were 1-tailed. [a]Non-normally distributed variables.
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D5

Kendall Correlation Matrix for Continuous Prenatal Alcohol Exposure and Neale Analysis of Reading Ability Variables

Variable	1[a]	2[a]	3[a]	4	5	6
1. AA/day (oz)[a]	1.00					
2. AA/occasion (oz)[a]	.78***	1.00				
3. Drinking days/week[a]	.85***	.66***	1.00			
4. Reading Rate	-.11*	-.11*	-.12*	1.00		
5. Reading Accuracy	-.04	-.01	-.05	.58***	1.00	
6. Comprehension	-.12*	-.07	-.12*	.55***	.73***	1.00

Note. AA = absolute alcohol. Statistics presented are Kendall correlation coefficients (τ). All tests were 1-tailed. [a]Non-normally distributed variables.
*$p < .05$. ***$p < .001$.

Table D6

Kendall Correlation Matrix for Continuous Prenatal Alcohol Exposure and Phonological Assessment Battery Variables

Variable	1[a]	2[a]	3[a]	4[a]	5[a]	6	7[a]	8	9	10	11	12
1. AA/day (oz)[a]	1.00											
2. AA/occasion (oz)[a]	.78***	1.00										
3. Drinking days/week[a]	.85***	.66***	1.00									
4. Alliteration[a]	-.09†	-.07	-.08†	1.00								
5. Rhyme[a]	-.04	-.01	-.05	.52***	1.00							
6. Spoonerisms	-.14**	-.10*	-.15**	.46***	.58***	1.00						
7. Non-word Reading[a]	-.01	.01	-.02	.41***	.53***	.53***	1.00					
8. Picture Naming	.12*	.08†	.14**	-.31***	-.30***	-.38***	-.29***	1.00				
9. Digit Naming	.10*	.07	.10*	-.44***	-.37***	-.48***	-.45***	.47***	1.00			
10. Alliteration Fluency	-.12*	-.10*	-.12*	.41***	.46***	.49***	.44***	-.32***	-.45***	1.00		
11. Rhyme Fluency	-.08†	-.06	-.11*	.35***	.46***	.45***	.36***	-.32***	-.34***	.36***	1.00	
12. Semantic Fluency	-.09†	-.10*	-.12*	.17**	.14**	.24***	.15**	-.31***	-.27***	.23***	.23***	1.00

Note. AA = absolute alcohol. Statistics presented are Kendall correlation coefficients (τ). All tests were 1-tailed. [a]Non-normally distributed variables.
†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Correlations Between Outcome and Potential Confounding Variables

Table D7

Pearson Correlation Matrix for Neale Analysis of Reading Ability and Potential Confounding Variables

Variable	1	2	3	4	5[b]	6	7
1. Reading Rate	1.00						
2. Reading Accuracy	.75***	1.00					
3. Comprehension	.75***	.88***	1.00				
4. Education (years)[a]	.25**	.22**	.30***	1.00			
5. Prenatal smoking[b]	-.10	-.07	-.13	-.24**	1.00		
6. Sex of child	.23**	.10	.12	.02	.01	1.00	
7. Child's age at testing	.28***	.29***	.29***	.03	-.07	.03	1.00

Note. Statistics presented are Pearson correlation coefficients (*r*). All tests were 2-tailed. [a]Primary caregiver's years of education. [b]Non-normally distributed variables.

**$p < .01$. ***$p < .001$.

Table D8

Pearson Correlation Matrix for Phonological Assessment Battery and Potential Confounding Variables

Variable	1[a]	2[a]	3	4[a]	5	6	7	8	9	10	11[a]	12	13
1. Alliteration[a]	1.00												
2. Rhyme[a]	.70***	1.00											
3. Spoonerisms	.52***	.71***	1.00										
4. Non-word Reading[a]	.58***	.73***	.69***	1.00									
5. Picture Naming	-.34***	-.43***	-.52***	-.41***	1.00								
6. Digit Naming	-.58***	-.57***	-.61***	-.64***	.62***	1.00							
7. Alliteration Fluency	.57***	.64***	.67***	.63***	-.45***	-.61***	1.00						
8. Rhyme Fluency	.44***	.61***	.60***	.52***	-.46***	-.47***	.54***	1.00					
9. Semantic Fluency	.14†	.19*	.35***	.18*	-.41***	-.34***	.37***	.33***	1.00				
10. Education (years)[b]	.26**	.35***	.29***	.20*	-.21**	-.32***	.26**	.28***	.17*	1.00			
11. Prenatal smoking[a]	-.08	-.12	-.12	-.04	.13	.13	-.15†	-.09	-.10	-.24**	1.00		
12. Sex of child	.16*	.05	.02	.10	-.17*	-.30***	.19*	.05	.19*	.02	.01	1.00	
13. Child's age at testing	.20*	.14†	.35***	.16*	-.41***	-.40***	.25**	.16†	.45***	.03	-.07	.03	1.00

Note. Statistics presented are Pearson correlation coefficients (*r*). All tests were 2-tailed. [a]Non-normally distributed variables. [b]Primary caregiver's years of education.

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D9

Spearman Correlation Matrix for Neale Analysis of Reading Ability and Potential Confounding Variables

Variable	1	2	3	4	5[b]	6	7
1. Reading Rate	1.00						
2. Reading Accuracy	.74***	1.00					
3. Comprehension	.71***	.89***	1.00				
4. Education (years)[a]	.22**	.18*	.28***	1.00			
5. Prenatal smoking[b]	-.16†	-.10	-.13	-.24**	1.00		
6. Sex of child	.21**	.08	.12	-.03	-.07	1.00	
7. Child's age at testing	.25**	.30***	.29***	-.03	-.05	.01	1.00

Note. Statistics presented are Spearman correlation coefficients (ρ). All tests were 2-tailed. [a]Primary caregiver's years of education. [b]Non-normally distributed variables.

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D10

Spearman Correlation Matrix for Phonological Assessment Battery and Potential Confounding Variables

Variable	1[a]	2[a]	3	4[a]	5	6	7	8	9	10	11[a]	12	13
1. Alliteration[a]	1.00												
2. Rhyme[a]	.64***	1.00											
3. Spoonerisms	.59***	.74***	1.00										
4. Non-word Reading[a]	.53***	.69***	.71***	1.00									
5. Picture Naming	-.41***	-.41***	-.54***	-.40***	1.00								
6. Digit Naming	-.57***	-.50***	-.65***	-.61***	.63***	1.00							
7. Alliteration Fluency	.52***	.60***	.64***	.57***	-.44***	-.60***	1.00						
8. Rhyme Fluency	.45***	.60***	.59***	.48***	-.44***	-.45***	.48***	1.00					
9. Semantic Fluency	.23**	.20*	.33***	.21**	-.44***	-.38***	.32***	.32***	1.00				
10. Education (years)[b]	.22**	.30***	.29***	.17*	-.20*	-.24**	.18*	.27**	.11	1.00			
11. Prenatal smoking[a]	-.07	-.14†	-.14†	-.06	.22**	.15†	-.15†	-.13	-.11	-.24**	1.00		
12. Sex of child	.17*	.03	.03	.07	-.16*	-.30***	.18*	.06	.16*	-.03	-.07	1.00	
13. Child's age at testing	.28***	.18*	.34***	.21**	-.41***	-.44***	.26**	.13†	.44***	-.03	-.05	.01	1.00

Note. Statistics presented are Spearman correlation coefficients (ρ). All tests were 2-tailed. [a]Non-normally distributed variables. [b]Primary caregiver's years of education.

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D11

Kendall Correlation Matrix for Neale Analysis of Reading Ability and Potential Confounding Variables

Variable	1	2	3	4	5[b]	6	7
1. Reading Rate	1.00						
2. Reading Accuracy	.58***	1.00					
3. Comprehension	.55***	.73***	1.00				
4. Education (years)[a]	.16**	.13*	.20***	1.00			
5. Prenatal smoking[b]	-.12*	-.08	-.10†	-.18**	1.00		
6. Sex of child	.18**	.07	.10	-.02	-.06	1.00	
7. Child's age at testing	.18**	.21***	.20***	-.02	-.04	.01	1.00

Note. Statistics presented are Kendall correlation coefficients (τ). All tests were 2-tailed. [a]Primary caregiver's years of education. [b]Non-normally distributed variables.

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table D12

Kendall Correlation Matrix for Phonological Assessment Battery and Potential Confounding Variables

Variable	1[a]	2[a]	3	4[a]	5	6	7	8	9	10	11[a]	12	13
1. Alliteration[a]	1.00												
2. Rhyme[a]	.52***	1.00											
3. Spoonerisms	.46***	.58***	1.00										
4. Non-word Reading[a]	.41***	.53***	.53***	1.00									
5. Picture Naming	-.31***	-.30***	-.38***	-.29***	1.00								
6. Digit Naming	-.44***	-.37***	-.48***	-.45***	.47***	1.00							
7. Alliteration Fluency	.41***	.46***	.49***	.44***	-.32***	-.45***	1.00						
8. Rhyme Fluency	.35***	.46***	.45***	.36***	-.32***	-.34***	.36***	1.00					
9. Semantic Fluency	.17**	.14*	.24***	.15*	-.31***	-.27***	.23***	.23***	1.00				
10. Education (years)[b]	.18**	.23***	.22***	.12*	-.15**	-.17**	.13*	.20**	.09	1.00			
11. Prenatal smoking[a]	-.06	-.10†	-.10†	-.05	.16**	.11†	-.11†	-.10	-.08	-.18**	1.00		
12. Sex of child	.15*	.03	.02	.06	-.13*	-.25***	.16*	.05	.13*	-.02	-.06	1.00	
13. Child's age at testing	.21***	.13*	.23***	.15**	-.29***	-.30***	.18**	.09†	.30***	-.02	-.04	.01	1.00

Note. Statistics presented are Kendall correlation coefficients (τ). All tests were 2-tailed. [a]Non-normally distributed variables. [b]Primary caregiver's years of education.

†$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

APPENDIX E

Assumption Checks

Outliers. The distributions of all variables were investigated for outliers > 3 *SDs* above the mean. The following outliers were identified: one outlier in the distribution of primary caregiver's years of education, two in Picture Naming, three in Digit Naming, one in Semantic Fluency, and two in Digit Span Backwards. However, most of these outliers fell very close to the next scores within the distributions and were therefore left unchanged. The three Digit Naming outliers were recoded to 1 point above the next highest observed value to prevent them from exerting undue influence on statistical analyses (Winder, 1971).

Normality. Due to the sensitivity of normality tests to large sample sizes (Field, 2006), normality was inspected visually. Among the potential confounding and mediator variables, primary caregiver's years of education, child's age at testing, and Digit Span Backwards were normally distributed, whereas the distribution for prenatal smoking was positively skewed. When split according to diagnostic category (for the purposes of ANOVA and ANCOVA analyses), primary caregiver's years of education, and child's age at testing were normally distributed within all three diagnostic categories, whereas prenatal smoking was positively skewed within all three diagnostic categories.

With regards to the continuous PAE measures, the distributions of oz AA/day, oz AA/occasion, and drinking days/week were all positively skewed. When split according to diagnostic category, oz AA/day, oz AA/occasion, and drinking days/week were fairly normally distributed for the FAS/PFAS group but positively skewed for the HE and Control groups.

The reading outcome variables, NARA Reading Accuracy, Reading Rate, and Comprehension, were all fairly normally distributed. When split according to diagnostic

category, Reading Accuracy and Reading Rate were normally distributed within all three diagnostic categories, whereas comprehension was normally distributed within the HE and Control groups but slightly positively skewed within the FAS/PFAS group.

As for the phonological processing variables, Spoonerisms, Picture Naming, Digit Naming, Alliteration Fluency, Rhyme Fluency, and Semantic Fluency were more or less normally distributed, whereas the distributions of the Alliteration, Rhyming, and Non-Word Reading variables were negatively skewed. When split according to diagnostic category, Alliteration and Rhyming were negatively skewed within all three diagnostic groups. Spoonerisms was normally distributed within the HE and Control groups but positively skewed within the FAS/PFAS group. Non-Word Reading was fairly normally distributed in the FAS/PFAS group but negatively skewed within the HE and Control groups. Picture Naming, Digit Naming, and Alliteration Fluency were normally distributed within all three diagnostic categories. Rhyme Fluency and Semantic Fluency were normally distributed within the HE and Control groups but slightly positively skewed within the FAS/PFAS groups.

Independence. The assumption of independence was upheld for all variables.

Assumption Checks Specific to ANCOVA

Homogeneity of variance. Table E1 shows the results from Levene's homogeneity of variance tests related to ANCOVA analyses. The assumption of homogeneity of variance was upheld for NARA Reading Accuracy and Reading Rate, but not for Comprehension. As for the PhAB variables, the assumption was upheld for Spoonerisms, Non-Word Reading, Picture Naming, Digit Naming, Alliteration Fluency, Rhyme Fluency, and Semantic Fluency, but not for Alliteration or Rhyme.

Table E1
Levene's Tests of Equality of Error Variances for ANCOVA Variables

Variable	*F*	df_1	df_2	*p*
Outcome variable				
Neale Analysis of Reading Ability				
Reading Accuracy	1.02	2	156	.363
Reading Rate	1.77	2	156	.173
Comprehension	5.01	2	156	.008**
Phonological Assessment Battery				
Alliteration	8.58	2	156	<.001***
Rhyme	3.27	2	156	.041*
Spoonerisms	0.35	2	155	.708
Non-Word Reading	1.13	2	156	.327
Picture Naming (Completion time)	1.26	2	156	.288
Digit Naming (Completion time)	1.88	2	155	.157
Alliteration Fluency	1.08	2	155	.342
Rhyme Fluency	2.04	2	156	.134
Semantic Fluency	2.68	2	156	.072†

Note. †$p < .10$. *$p < .05$. **$p < .01$. ***$p < .001$.

Independence of covariates and independent variable. In order for this assumption to be upheld, the diagnostic groups should not differ on the covariates. The results of between-group analyses in Table 3 show that this assumption was upheld for sex of child and child's age at testing, but not for primary caregiver's years of education or for prenatal smoking.

Homogeneity of regression slopes. For this assumption to be upheld, the relationships between outcome variables and covariates must not differ across diagnostic groups. Table E2 shows that this assumption was upheld for NARA Reading Accuracy and primary caregiver's years of education, but not for Reading Accuracy and child's age at testing. The assumption was upheld for the relationships between NARA Reading Rate and: primary caregiver's years of education, prenatal smoking, and sex of child; but not for Reading Rate and child's age at testing. The assumption was upheld for NARA Comprehension and primary caregiver's years of education, but not for Comprehension and child's age at testing. The assumption was upheld for PhAB Alliteration and: caregiver's years of education, sex of child, and child's age at testing.

The assumption was upheld for PhAB Rhyme and: primary caregiver's years of education, as well as child's age at testing; but not for Rhyme and prenatal smoking. The assumption was upheld for PhAB Spoonerisms and: primary caregiver's years of education, as well as prenatal smoking; but not for Spoonerisms and child's age at testing. The assumption was upheld for PhAB Non-Word Reading and: primary caregiver's years of education, as well as child's age at testing. The assumption was upheld for PhAB Picture Naming and: primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. The assumption was upheld for PhAB Digit Naming and: primary caregiver's years of education, prenatal smoking, sex of child, and child's age at testing. The assumption was upheld for PhAB Alliteration Fluency and: primary caregiver's years of education, prenatal smoking, and sex of child; but not for Alliteration Fluency and child's age at testing. The assumption was upheld for PhAB Rhyme Fluency and primary caregiver's years of education, but not for Rhyme Fluency and child's age at testing. The assumption was upheld for PhAB Semantic Fluency and: primary caregiver's years of education, sex of child, and child's age at testing

Assumption Checks and Model Diagnostics Specific to Regression Analyses

No multicollinearity. Model 1: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.16), indicating that this assumption was upheld. Model 2: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.05), indicating that this assumption was upheld. Model 3: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.07), indicating that this assumption was upheld. Model 4: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.04), indicating that this assumption was upheld. Model 5: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} =

Table E2
ANCOVA Interaction Effects to Test Homogeneity of Regression Slopes Assumption

	FASD x edu[a]		FASD x cig[b]		FASD x sex[c]		FASD x age[d]	
Outcome variable	*F*	*p*	*F*	*p*	*F*	*p*	*F*	*P*
Neale Analysis of Reading Ability								
Reading Accuracy	0.70	.498	-	-	-	-	5.04	.008**
Reading Rate	1.79	.171	1.28	.281	0.35	.703	6.46	.002**
Comprehension	0.10	.902	-	-	-	-	3.29	.040*
Phonological Assessment Battery								
Alliteration	1.66	.195	-	-	3.05	.051†	0.30	.744
Rhyme	0.67	.514	3.07	.049*	-	-	0.26	.775
Spoonerisms	0.76	.468	1.10	.337	-	-	3.60	.030*
Non-Word Reading	1.20	.305	-	-	-	-	2.65	.074†
Picture Naming	0.42	.655	0.37	.691	0.95	.391	2.98	.054†
Digit Naming	0.92	.402	1.18	.311	0.74	.480	2.33	.101
Alliteration Fluency	0.11	.899	0.92	.399	0.57	.567	3.31	.039*
Rhyme Fluency	1.92	.151	-	-	-	-	5.72	.004**
Semantic Fluency	0.48	.622	-	-	0.86	.427	1.12	.331

Note. FASD = fetal alcohol spectrum disorder. [a]ANCOVA interaction term for IV (FASD diagnosis) and the covariate primary caregiver's years of education. [b]ANCOVA interaction term for IV and the covariate prenatal smoking. [c]ANCOVA interaction term for IV and the covariate sex of child. [d]ANCOVA interaction term for IV and the covariate child's age at testing.
†$p < .10$. *$p < .05$. **$p < .01$.

1.06), indicating that this assumption was upheld. Model 6: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.18), indicating that this assumption was upheld. Model 7: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.20), indicating that this assumption was upheld. Model 8: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.16), indicating that this assumption was upheld. Model 9: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.14), indicating that this assumption was upheld. Model 10: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.16), indicating that this assumption was upheld. Model 11: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.16), indicating that this assumption was upheld. Model 12: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.18), indicating that this

assumption was upheld. Model 13: None of the VIF scores were > 10 and the average VIF score was not substantially > 1 (M_{VIF} = 1.06), indicating that this assumption was upheld.

Homoscedasticity. Model 1: Figure E1 shows that this assumption was upheld. Model 2: Figure E2 shows that this assumption was upheld. Model 3: Figure E3 shows that this assumption was upheld. Model 4: Figure E4 shows that this assumption was not upheld. Model 5: Figure E5 shows that this assumption was not upheld. Model 6: Figure E6 shows that this assumption was upheld. Model 7: Figure E7 shows that this assumption was upheld. Model 8: Figure E8 shows that this assumption was not upheld. Model 9: Figure E9 shows that this assumption was not upheld. Model 10: Figure E10 shows that this assumption was not upheld. Model 11: Figure E11 shows that this assumption was upheld. Model 12: Figure E12 shows that this assumption was upheld. Model 13: Figure E13 shows that this assumption was not upheld.

Linearity: Model 1: Figure E1 shows that this assumption was upheld. Model 2: Figure E2 shows that this assumption was upheld. Model 3: Figure E3 shows that this assumption was upheld. Model 4: Figure E4 shows that this assumption was upheld. Model 5: Figure E5 shows that this assumption was upheld. Model 6: Figure E6 shows that this assumption was upheld. Model 7: Figure E7 shows that this assumption was upheld. Model 8: Figure E8 shows that this assumption was upheld. Model 9: Figure E9 shows that this assumption was upheld. Model 10: Figure E10 shows that this assumption was upheld. Model 11: Figure E11 shows that this assumption was upheld. Model 12: Figure E12 shows that this assumption was upheld. Model 13: Figure E13 shows that this assumption was upheld.

Independent errors. Model 1: The Durbin-Watson statistic was 2.06, indicating that this assumption was upheld. Model 2: The Durbin-Watson statistic was 1.99, indicating that this assumption was upheld. Model 3: The Durbin-Watson statistic was 2.00, indicating that this

assumption was upheld. Model 4: The Durbin-Watson statistic was 1.85, indicating that this assumption was upheld. Model 5: The Durbin-Watson statistic was 1.86, indicating that this assumption was upheld. Model 6: The Durbin-Watson statistic was 1.91, indicating that this assumption was upheld. Model 7: The Durbin-Watson statistic was 1.90, indicating that this assumption was upheld. Model 8: The Durbin-Watson statistic was 2.10, indicating that this assumption was upheld. Model 9: The Durbin-Watson statistic was 2.16, indicating that this assumption was upheld. Model 10: The Durbin-Watson statistic was 2.16, indicating that this assumption was upheld. Model 11: The Durbin-Watson statistic was 2.01, indicating that this assumption was upheld. Model 12: The Durbin-Watson statistic was 2.02, indicating that this assumption was upheld. Model 13: The Durbin-Watson statistic was 1.81, indicating that this assumption was upheld.

Normally distributed errors. Model 1: Normally distributed. Model 2: Normally distributed. Model 3: Normally distributed. Model 4: Non-normal; negatively skewed. Model 5: Non-normal; negatively skewed. Model 6: Normally distributed. Model 7: Normally distributed. Model 8: Non-normal; slightly positively skewed. Model 9: Normally distributed. Model 10: Normally distributed. Model 11: Normally distributed. Model 12: Normally distributed. Model 13: Normally distributed.

Model diagnostics. Model 1: Only 5% of cases fell outside of 2 *SD*, indicating that the model was a fairly good fit of the sample data (given the conventional 5% cut-off; Field, 2009). There were five cases with Mahalanobis distances beyond the conventional cut-off of 15 (15.02, 15.86, 20.97, 22.25, & 29.42; Fields, 2009), indicating possible influential cases in the data. However, no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 2: Only 4% of cases fell outside of 2 *SD*, indicating that the model was a

good fit of the sample data. There were four cases with Mahalanobis distances > 15 (15.29, 18.32, 18.81, & 20.15), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 3: Only 4% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were three cases with Mahalanobis distances > 15 (18.28, 20.25, & 28.20), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 4: Nine percent of cases fell outside of 2 *SD*, indicating that the model was not a very good fit of the sample data. There were four cases with Mahalanobis distances > 15 (16.02, 19.05, 19.64, & 21.06), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 5: Ten percent of cases fell outside of 2 *SD*, indicating that the model was not a very good fit of the sample data. There were three cases with Mahalanobis distances > 15 (19.26, 20.99, & 29.42), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 6: Only 2% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were four cases with Mahalanobis distances > 15 (15.69, 19.54, 20.09, & 20.29), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 7: Only 2% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were three cases with Mahalanobis distances > 15 (19.92, 21.44, & 28.02), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 8: Only 5% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were five cases with Mahalanobis distances > 15 (15.02, 15.86, 20.97, 22.25, & 29.42), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 9: Six percent of cases fell outside of 2 *SD*, indicating that the model was not a very good fit of the sample data.

There were four cases with Mahalanobis distances > 15 (16.60, 20.80, 21.58, & 21.68), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 10: Six percent of cases fell outside of 2 *SD*, indicating that the model was not a very good fit of the sample data. There were six cases with Mahalanobis distances > 15 (15.07, 15.11, 15.77, 20.88, 23.10, & 29.33), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 11: Only 4% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were six cases with Mahalanobis distances > 15 (15.46, 15.59, 16.53, 20.40, 20.81, & 21.19), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 12: Only 4% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were eight cases with Mahalanobis distances > 15 (15.02, 15.03, 15.37, 15.82, 16.44, 20.85, 22.23, & 29.32), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model. Model 13: Only 5% of cases fell outside of 2 *SD*, indicating that the model was a good fit of the sample data. There were three cases with Mahalanobis distances > 15 (19.26, 20.99, & 29.42), but no Cook's distances were > 1, suggesting that these cases did not exert undue influence on the model.

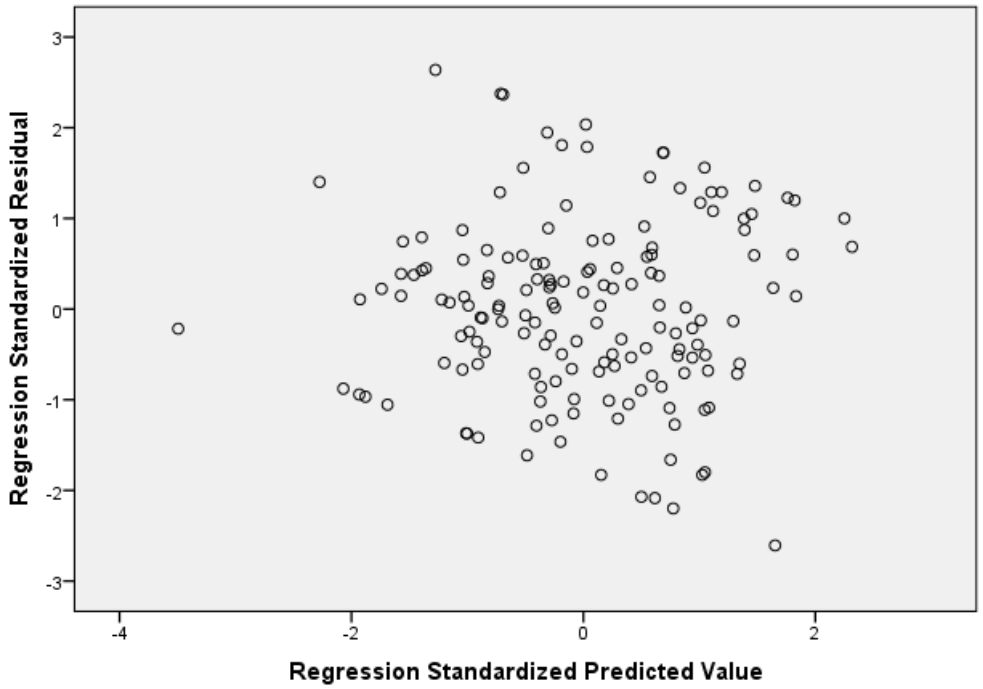

Figure E1. Scatterplot showing homoscedasticity and linearity within residuals of Model 1.

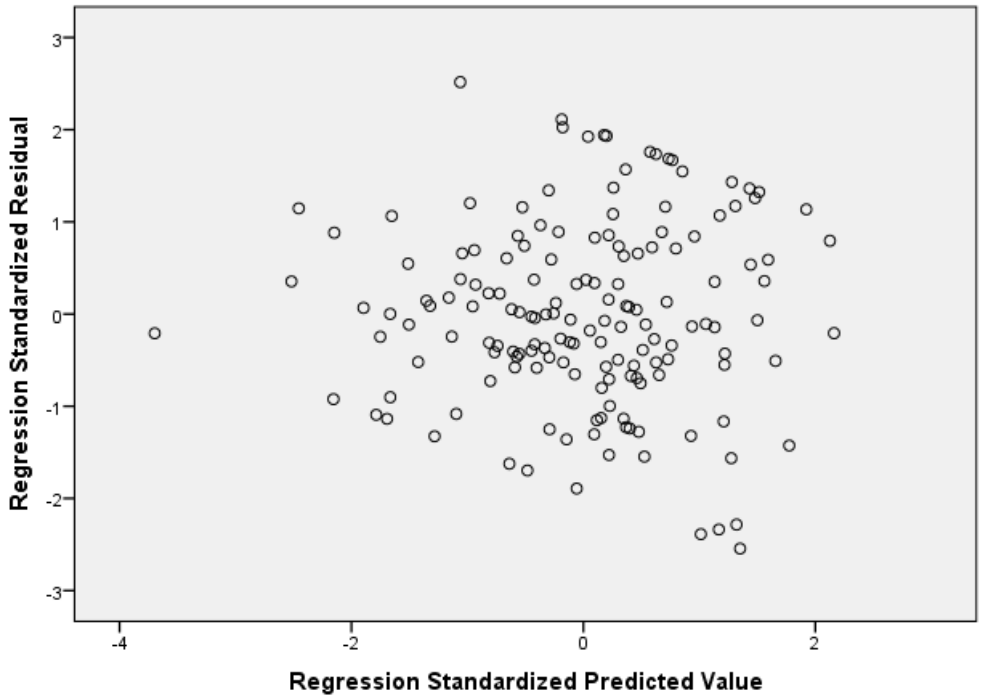

Figure E2. Scatterplot showing homoscedasticity and linearity within residuals of Model 2.

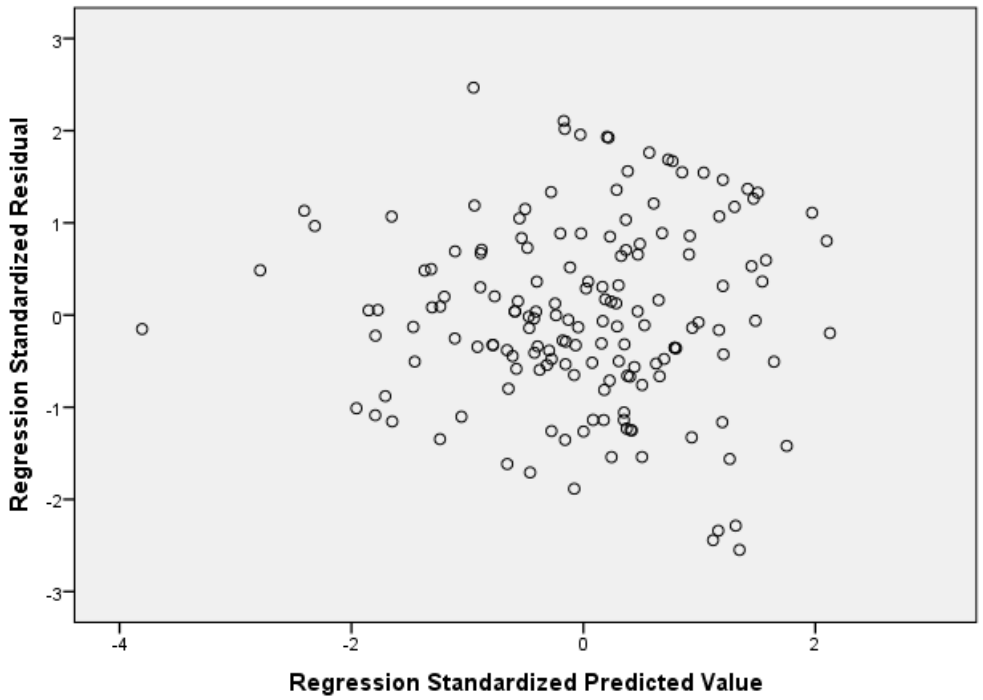

Figure E3. Scatterplot showing homoscedasticity and linearity within residuals of Model 3.

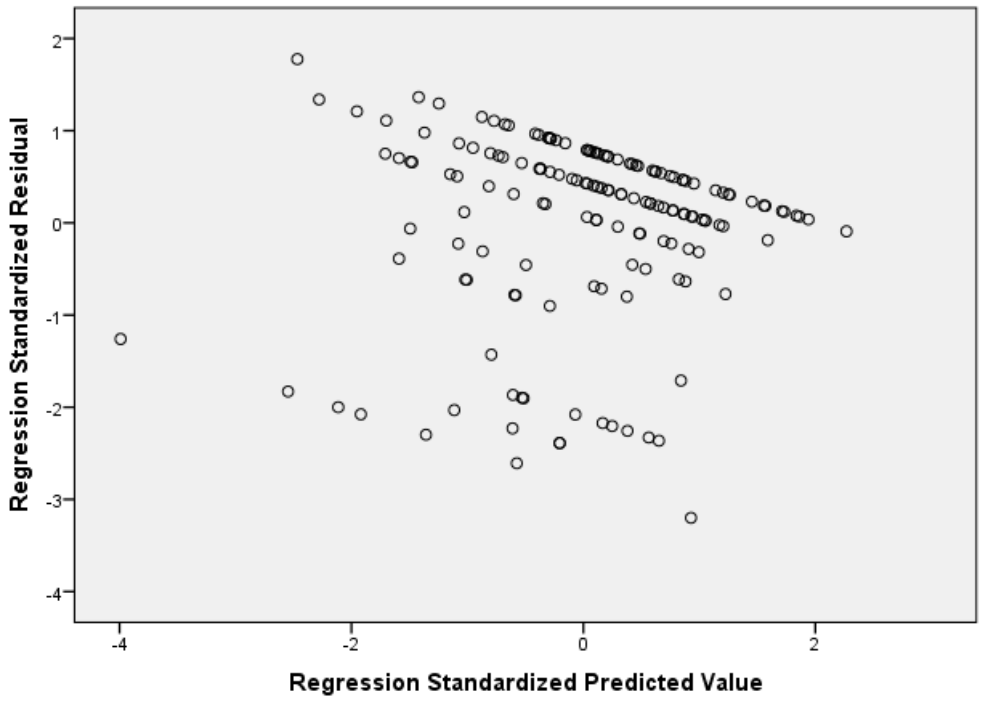

Figure E4. Scatterplot showing heteroscedasticity and linearity within residuals of Model 4.

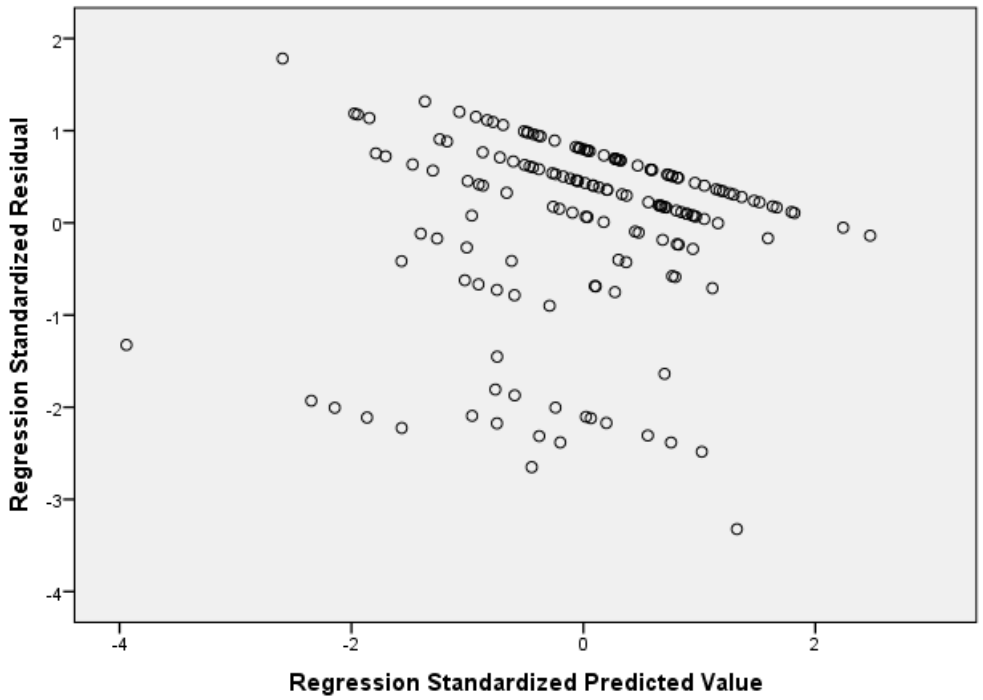

Figure E5. Scatterplot showing heteroscedasticity and linearity within residuals of Model 5.

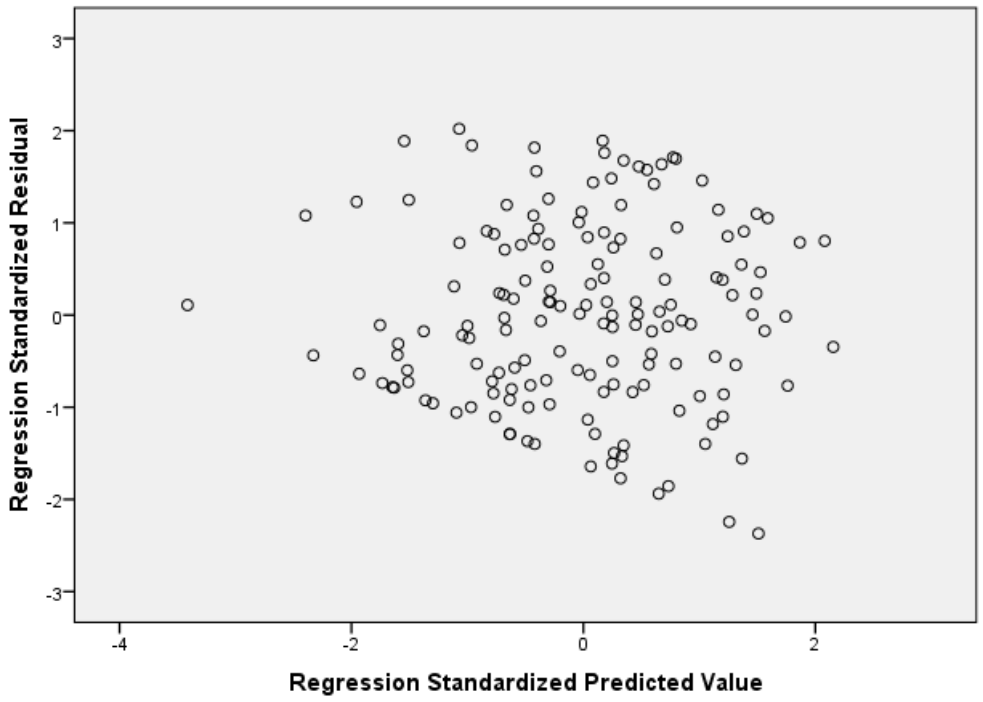

Figure E6. Scatterplot showing homoscedasticity and linearity within residuals of Model 6.

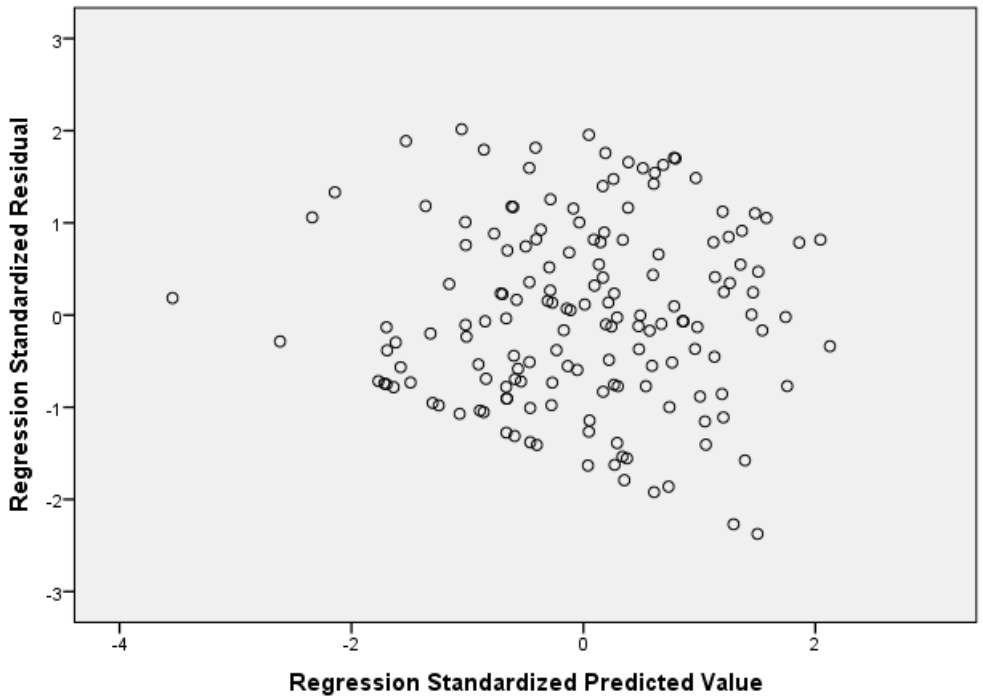

Figure E7. Scatterplot showing homoscedasticity and linearity within residuals of Model 7.

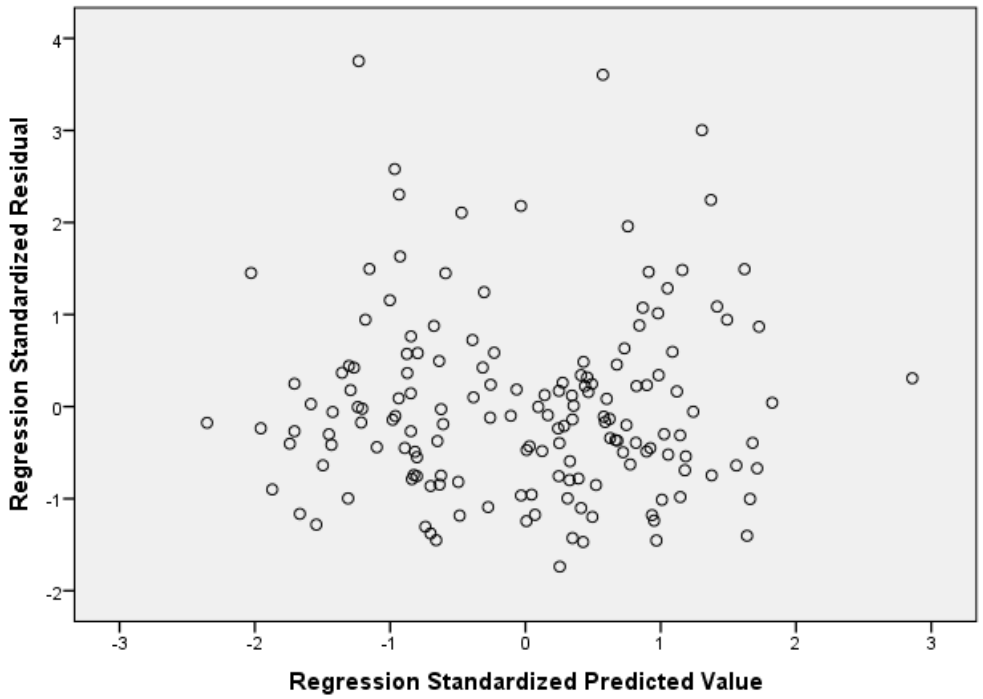

Figure E8. Scatterplot showing heteroscedasticity and linearity within residuals of Model 8.

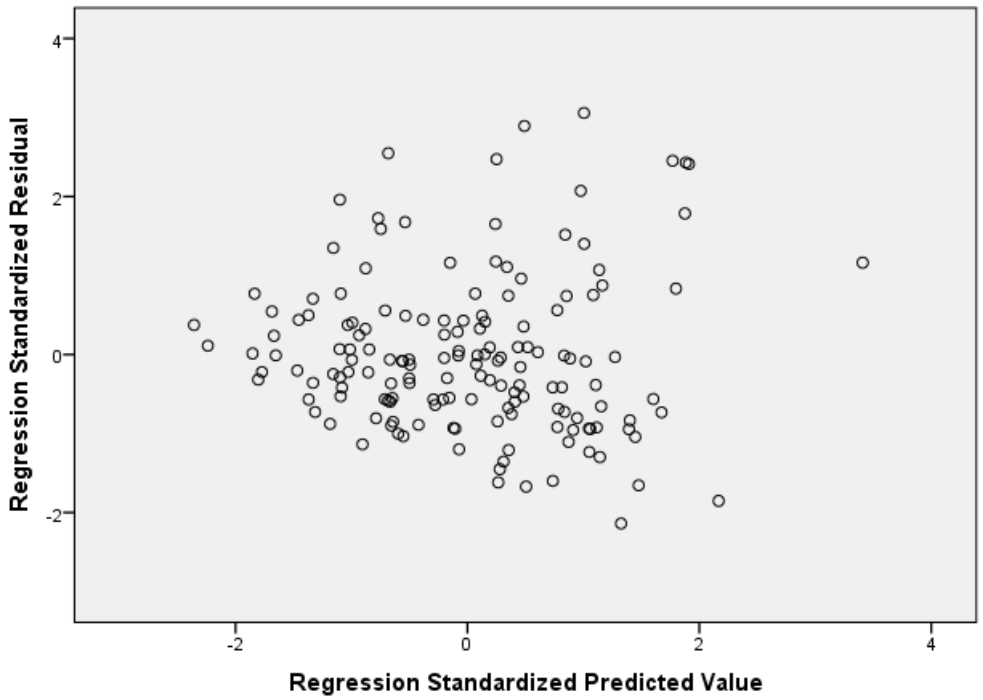

Figure E9. Scatterplot showing heteroscedasticity and linearity within residuals of Model 9.

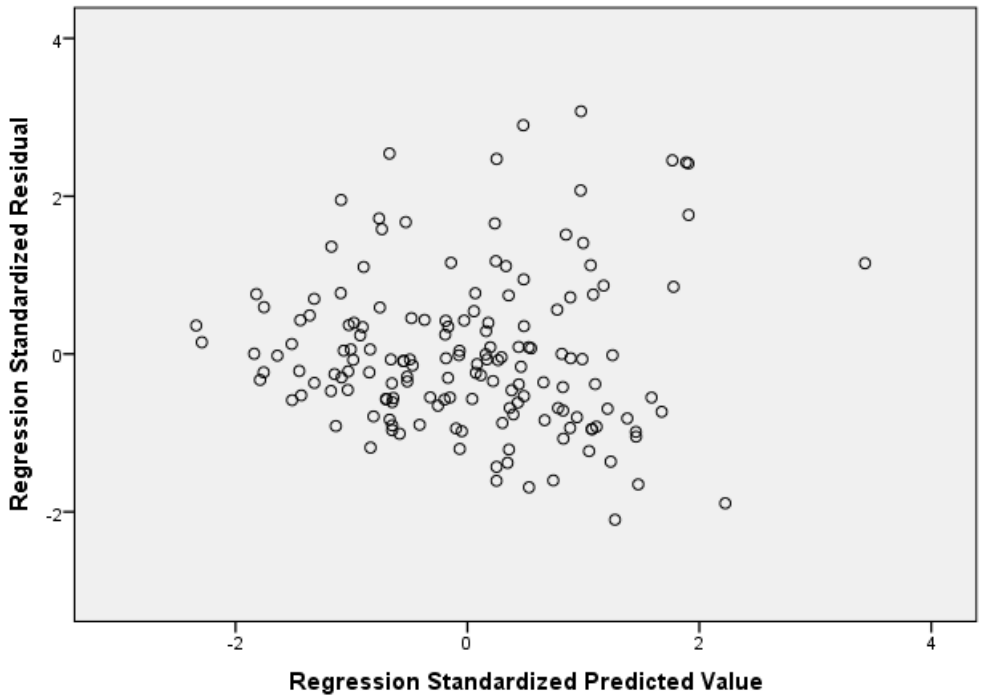

Figure E10. Scatterplot showing heteroscedasticity and linearity in residuals of Model 10.

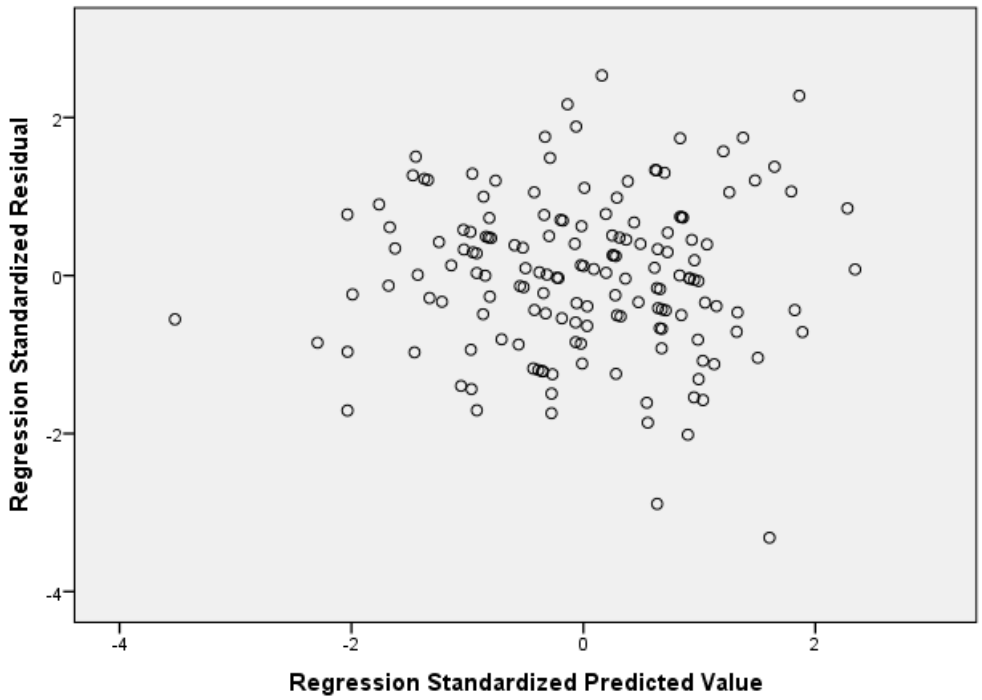

Figure E11. Scatterplot showing homoscedasticity and linearity in residuals of Model 11.

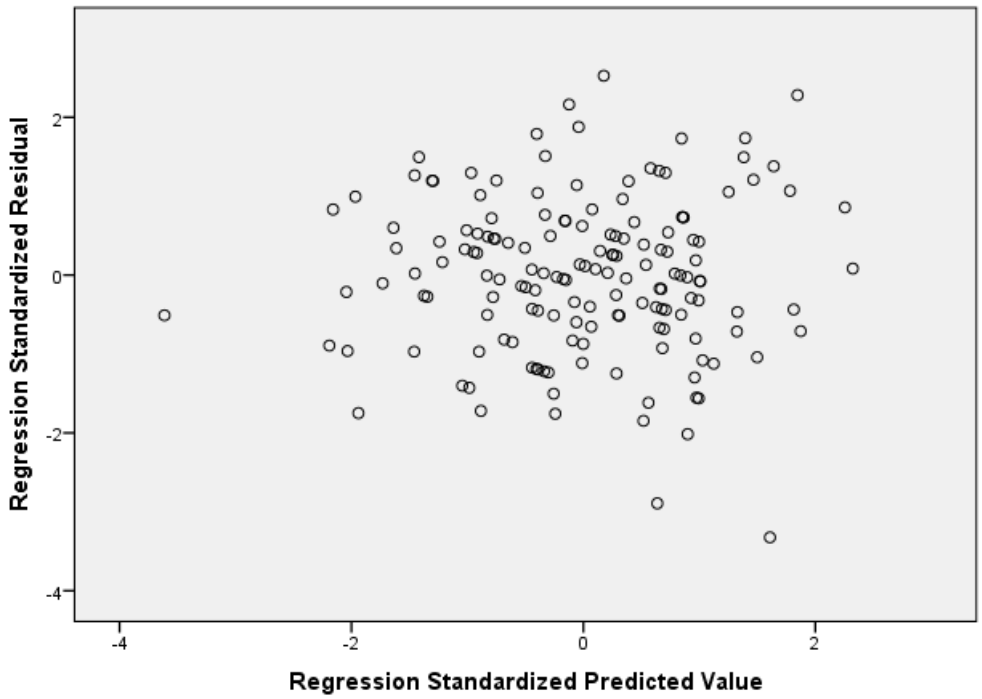

Figure E12. Scatterplot showing homoscedasticity and linearity in residuals of Model 12.

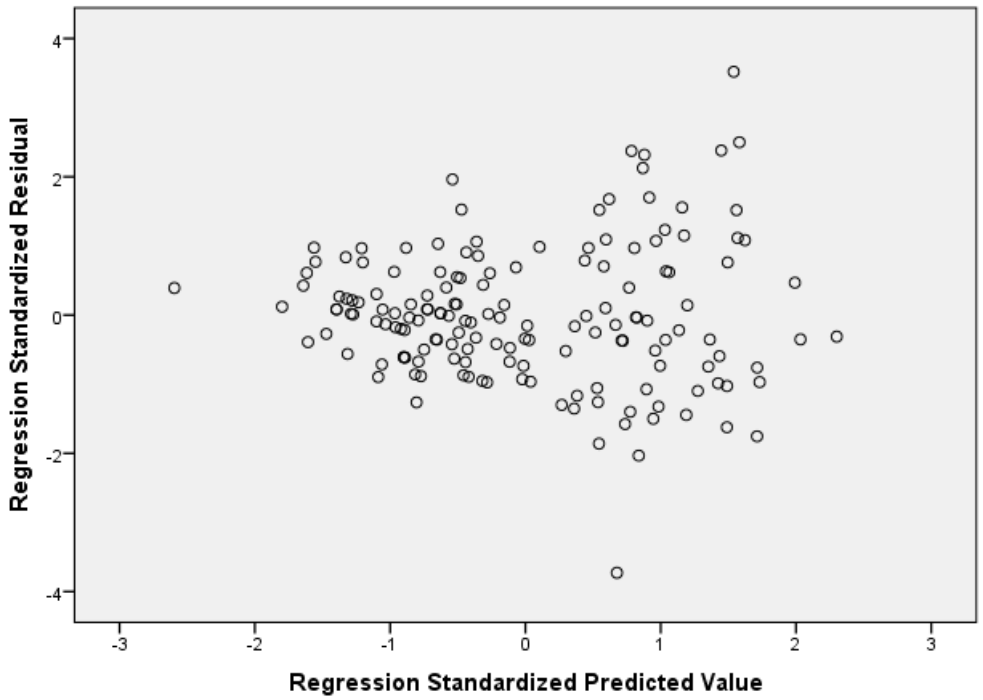

Figure E13. Scatterplot showing heteroscedasticity and linearity in residuals of Model 13.

APPENDIX F

Table F1
LSD Pairwise Comparisons for Neale Analysis of Reading Ability ANCOVAs

Outcome variable	Comparisons	*M* difference	*SE*	*p*	95% Confidence interval	
					Lower bound	Upper bound
Reading Accuracy	Control – HE	-0.48	0.40	.233	-1.27	0.31
	HE – FAS/PFAS	0.81	0.47	.087†	-0.12	1.73
	Control – FAS/PFAS	0.33	0.48	.490	-0.61	1.27
Reading Rate	Control – HE	-0.06	0.39	.883	-0.82	0.70
	HE – FAS/PFAS	0.91	0.44	**.041***	0.04	1.78
	Control – FAS/PFAS	0.85	0.46	.063†	-0.05	1.76
Comprehension	Control – HE	-0.16	0.37	.658	-0.89	0.56
	HE – FAS/PFAS	1.14	0.43	**.009****	0.29	1.99
	Control – FAS/PFAS	0.98	0.44	**.027***	0.11	1.85

Note. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed nonsyndromal.
$^{\dagger}p < .10$. $^{*}p < .05$. $^{**}p < .01$.

Table F2
LSD Pairwise Comparisons for Phonological Assessment Battery ANCOVAs

Outcome variable	Comparisons	*M* difference	*SE*	*P*	95% Confidence interval	
					Lower bound	Upper bound
Alliteration	Control – HE	-0.63	0.50	.208	-1.62	0.36
	HE – FAS/PFAS	1.48	0.59	**.013***	0.32	2.64
	Control – FAS/PFAS	0.85	0.60	.161	-0.34	2.03
Rhyme	Control – HE	-1.70	1.02	.097†	-3.70	0.31
	HE – FAS/PFAS	1.90	1.16	.104	-0.40	4.19
	Control – FAS/PFAS	0.20	1.20	.866	-2.17	2.57
Spoonerisms	Control – HE	-0.69	1.51	.647	-3.67	2.29
	HE – FAS/PFAS	4.60	1.72	**.008****	1.20	8.01
	Control – FAS/PFAS	3.91	1.77	**.029***	0.42	7.41
Non-Word Reading	Control – HE	-2.12	1.06	**.048***	-4.21	-0.02
	HE – FAS/PFAS	2.43	1.25	.053†	-0.04	4.89
	Control – FAS/PFAS	0.31	1.27	.805	-2.20	2.82
Picture Naming	Control – HE	-0.28	3.65	.940	-7.49	6.94
	HE – FAS/PFAS	-6.49	4.18	.122	-14.74	1.76
	Control – FAS/PFAS	-6.76	4.32	.119	-15.30	1.77
Digit Naming	Control – HE	4.19	3.18	.190	-2.10	10.47
	HE – FAS/PFAS	-6.28	3.65	.087†	-13.49	0.93
	Control – FAS/PFAS	-2.09	3.77	.579	-9.53	5.35
Alliteration Fluency	Control – HE	-0.83	0.76	.275	-2.33	0.67
	HE – FAS/PFAS	2.30	0.86	**.008****	0.61	3.99
	Control – FAS/PFAS	1.47	0.89	.102	-0.30	3.23
Rhyme Fluency	Control – HE	-0.56	0.55	.317	-1.65	0.54
	HE – FAS/PFAS	2.41	0.65	**<.001*****	1.12	3.69
	Control – FAS/PFAS	1.85	0.66	**.006****	0.54	3.16
Semantic Fluency	Control – HE	0.36	0.92	.698	-1.46	2.18
	HE – FAS/PFAS	1.61	1.08	.140	-0.53	3.74
	Control – FAS/PFAS	1.96	1.10	.078†	-0.22	4.14

Note. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed nonsyndromal.
$^{\dagger}p < .10$; $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$.