Verbal Learning and Memory in Fetal Alcohol Spectrum Disorders: Findings from Cape Town and Detroit

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ABSTRACT

Prenatal alcohol exposure is associated with a range of negative cognitive outcomes in children, including, frequently, impaired verbal learning and memory. The aim if the current research was to replicate previous findings on the effects of heavy prenatal alcohol exposure on verbal learning and memory, as well as elaborate on previous research including children with moderate prenatal alcohol exposure. A continuous measurement of alcohol consumption was included to better assess dose-response relationships. Data from two independent prospective longitudinal cohorts were analysed. The Cape Town Cohort included 29 children with a history of heavy prenatal alcohol exposure, as well as 18 demographically matched controls. The Detroit Cohort included 40 children with a history of moderate-to-heavy prenatal alcohol exposure, as well as 251 light-to non-exposed demographically matched controls. Verbal learning and memory were assessed using the California Verbal Learning Test-Children's Version. Results showed that, in the Cape Town Cohort, the primary impairment in the heavily-exposed children occurred at the level of encoding; in the Detroit Cohort, in contrast, the primary impairment in moderately-exposed children was at the level of retrieval. Recognition memory was vulnerable to the effects of prenatal alcohol exposure in both cohorts. Taken together these results indicated that impairments in executive functioning may be the primary cognitive mechanism underlying verbal learning and memory deficits in fetal alcohol spectrum disorders.

The effects of prenatal alcohol exposure on cognitive development are widespread (Mattson, Schoenfeld, & Riley, 2001). As a result, there is a growing body of literature that is working towards defining a cognitive and behavioural phenotype for FASD. Verbal learning and memory deficits are widely reported in children with FASD (Mattson and Roebuck, 2002; Rasmussen, Horne & Witol, 2006; Willford, Richardson, Leech & Day, 2004). Previous research has, however, yielded inconclusive results about the nature of the cognitive mechanisms underlying verbal learning and memory impairments in children with moderate to heavy prenatal alcohol exposure. Considering the educational implications of deficits in verbal learning and memory, it is imperative that confirmatory research be conducted.

Fetal Alcohol Spectrum Disorders (FASD): Diagnosis and classification

The adverse effects of prenatal alcohol exposure have physical, social, and cognitive manifestations in the development of exposed individuals. Fetal alcohol syndrome (FAS) represents the most severe end of the spectrum of outcomes. The three main diagnostic criteria for FAS are the presence of deficits in central nervous system (CNS) development and functioning, deficient physical growth patterns, and craniofacial irregularities (e.g., short palpebral fissures, thin upper lip, and a broad nasal bridge; Hoyme et al., 2005; Kodituwakku, 2007; Mattson, Schoenfeld, & Riley, 2001; Mattson et al., 1998).

Variability in the timing and amount of prenatal alcohol exposure, and presence of maternal risk factors (e.g., maternal smoking during pregnancy), produce a range of manifestations in the presentation of facial, CNS, and growth dysmorphology. As a result, children who have a history of prenatal alcohol exposure may not present with all of the features necessary for a diagnosis of FAS, but there may be sufficient cognitive-behavioural deficits (e.g., generally lowered IQ scores, attention and verbal learning impairments) to indicate that the teratogenic effects of alcohol have affected CNS development (Mattson et al., 1998; Hoyme et al., 2005).

The aforementioned variability in the timing and amount of prenatal alcohol exposure has led to the inclusion of a range of diagnostic criteria under the umbrella term fetal alcohol spectrum disorders (FASD; Kodituwakku, 2007; Rasmussen, 2005). Partial FAS (PFAS) is diagnosed where a history of prenatal alcohol exposure has been confirmed; some of the characteristic facial features are present; and either the CNS, cognitive-behavioural, or physical growth symptoms are present. The category alcohol-related birth defects (ARBD) relates more

specifically to a diagnosis based on the confirmation of maternal drinking, as well as the presence of congenital physical abnormalities (e.g. cardiac, skeletal, and renal anomalies) but not to the associated CNS development deficits (Hoyme et al., 2005; Rasmussen, 2005). Alcohol-related neurodevelopmental disorder (ARND), on the other hand, is diagnosed where there are deficits in CNS development, or there are impairments in cognitive and behavioural functioning, in the presence of a history of prenatal alcohol exposure (Jacobson & Jacobson, 2002).

FASD: Cognitive and behavioural deficits

Neuropsychological studies have shown that children with prenatal alcohol exposure present with deficits in general intellectual functioning (i.e., their IQ scores are lower than those of typically developing demographically matched controls), as well as with deficits in information processing speed, verbal and non-verbal learning and memory, attention, executive functioning, and visual-spatial perception (Jacobson, Jacobson, Sokol, Martier, & Ager, 1993; Mattson et al., 1998; Rasmussen, 2005; Rasmussen et al., 2006; for a review see, Kodituwakku, 2007). Mattson et al. (1998) compared neuropsychological functioning in children with and without the physical features associated with prenatal alcohol exposure. In terms of overall functioning, they found that a consistent pattern of neuropsychological deficits was displayed not only in children with FAS, but also in those children not displaying growth dysmorphology. Impairments on verbal and nonverbal learning and memory tasks were present for both diagnostic groups; however, participants in the FAS group performed worse than those in the alcohol-exposed, non-dysmorphic group. These findings, and similar data from other studies (e.g. Mattson et al., 2001), suggest that neuropsychological impairments need to be investigated in each of the categories along the FASD diagnostic spectrum.

Consistent with the findings of neuropsychological studies, structural neuroimaging studies have shown that children with prenatal alcohol exposure have structural abnormalities specific to the cerebellum, corpus callosum, basal ganglia, frontal lobes, and hippocampus (for a review, see Spandoni, McGee, Fryer, & Riley, 2007). The development of the cerebellum is particularly vulnerable to the effects of prenatal alcohol exposure and is generally smaller in individuals with FAS (Archibald et al., 2001). O'Hare et al. (2005) measured the cerebellar vermis using high-resolution magnetic resonance imaging (MRI) in 21 children prenatally exposed to alcohol and 21 typically developing children. They found significant displacement and size reduction in the anterior vermis of the cerebellum for participants in the alcohol-exposed

group compared to participants in the non-exposed control group. Consistent with previously reported deficits in verbal memory associated with FASD, these structural anomalies and size reductions were inversely related to word-recall performance on list-learning tasks.

Verbal Learning in FASD

Memory and learning impairments are frequently reported in cases where there has been moderate to heavy prenatal alcohol exposure. Of particular interest here are the reported deficits in verbal learning and memory. Mattson et al. (1998) compared verbal learning abilities in children diagnosed with FAS, children who had prenatal exposure to alcohol (PEA), and a typically developing demographically matched control group (NC). They found that participants in the FAS and PEA groups displayed significant impairments compared to NC participants in the *learning* of verbal information, but were not impaired on tasks measuring the *retention* of verbal information. The process of the acquisition (i.e., deficits at the encoding, or learning, stage of memory processing) of verbal information was therefore highlighted as a particularly vulnerable cognitive process in children with heavy prenatal alcohol exposure, regardless of whether they present with the physical features of FAS. The results of this study suggest that deficits in verbal learning and memory need to be delineated according to the specific underlying cognitive processes that might be impaired.

Following this line of inquiry, Mattson and Roebuck (2002) investigated the verbal learning and memory performance of children aged 8-16 years in both a heavily-exposed group (ALC) and non-exposed demographically matched control group (CON). Results indicated that the overall learning of new verbal information was impaired: CON group participants learned faster than their ALC group counterparts. This pattern of data confirms that heavy prenatal alcohol exposure has a negative impact on the acquisition of verbal information. Furthermore, consistent with the findings of Mattson et al. (1998), verbal memory for information over a delay (i.e., retention) was similar across the ALC and CON groups when the initial rate of information learning was taken into consideration. Mattson and Roebuck (2002) suggest that this pattern of data was observed because the CON participants may have utilized an "implicit learning strategy" (p. 881) to aid the retention of verbal information learnt during the repeated trials of the list learning task. In contrast, children with heavy alcohol exposure may not have employed such learning strategies (e.g., semantic clustering). The absence of such learning strategies over

repeated learning trials may account for the impairments in the acquisition and, ultimately, recall of verbal information for children with heavy prenatal alcohol exposure.

Willford et al.'s (2004) research on the effects of moderate prenatal alcohol exposure in a longitudinal cohort study provide further support for the importance of learning strategies in verbal memory. Children with moderate prenatal alcohol exposure were assessed at 14 years of age. Moderately exposed participants were impaired in the immediate and delayed recall of word pairs, but their recall for a story was spared. This finding suggests that when FASD children are given a structure for recalling information, as in free recall of a story, they can perform at a normal level. However, when such a structure is absent, as in free recall of a word list, performance is impaired. The results from this study further suggested that the participants' impaired acquisition of initial verbal information was underlying the larger verbal learning and memory deficits associated with prenatal alcohol exposure. Together the findings of Mattson et al. (1998), Mattson and Roebuck (2002), and Willford et al. (2004) suggest that the absence of learning strategies during the encoding stages of memory processing may be the primary cognitive mechanism underlying verbal memory deficits for children with moderate to heavy alcohol exposure.

Rationale, Specific Aims, and Hypotheses

Confirmatory research is necessary to define verbal learning and memory impairments in children with moderate to heavy alcohol exposure. Furthermore, confirmatory research, will allow for exploration of the proposed cognitive mechanisms underlying verbal learning and memory impairments in children with a history of moderate to heavy prenatal alcohol exposure.

The aim of the current research was, therefore, aimed to assess verbal learning and memory in children with a history of moderate and heavy prenatal alcohol exposure. In doing so, the research sought to replicate previous research findings regarding verbal learning and memory impairments in FASD. A second aim of the research was to elaborate on the limited research into verbal learning and memory in participants with moderate prenatal exposure by extending the study to include light and moderately exposed participants. Furthermore, a continuous measure of alcohol exposure, obtained using the timeline follow-back interview schedule (Sokol, Martier, & Ernhart, 1983), was included such that dose-response relationships between verbal learning and memory and prenatal alcohol exposure could be assessed.

The proposed hypotheses were:

(1) Children with moderate and heavy prenatal alcohol exposure would be impaired in verbal learning and memory performance when compared to typically developing controls.

(2) Deficits in verbal learning and memory would be due primarily to the effects of prenatal alcohol exposure and not confounding variables (e.g., prenatal cocaine exposure).

(3) Children with heavy prenatal alcohol exposure would be more impaired on tests of verbal learning and memory than children with moderate exposure.

(4) Children with moderate to heavy prenatal alcohol exposure would display impairment at the level of encoding new verbal information, as opposed to impaired retention and recall.

(5) There would be a dose-response relationship between amount of prenatal alcohol exposure and degree of verbal learning and memory impairment.

METHODS

Design and Setting

The current research is quasi-experimental and cross-sectional in design. It is partly nested within an ongoing cohort study that has been running in Cape Town since 1999. Data collected as part of a prospective longitudinal study, based in Detroit, Michigan, were also used in this study.

Data were obtained from the Cape Town cohort when participants were 9 years of age and from the Detroit cohort when participants were 14 years of age. The current research therefore features analyses of two independent cohorts: The Cape Town longitudinal cohort and the Detroit longitudinal cohort. The current research provides a comparison of alcohol-exposed participants and non-exposed, demographically matched, control participants on a standardized measure of verbal learning and memory.

Testing of participants from the Cape Town cohort took place in the Child Development Research Laboratory on the University of Cape Town's Health Sciences Campus. Testing of participants from the Detroit cohort took place in the Child Development Research Laboratory at Wayne State University.

Participants

Participant Recruitment and Demographic Information

Cape Town cohort. The pregnant mothers of the 47 children in this cohort were recruited between July 1999 and January 2002 for a prospective longitudinal study investigating neurobehavioral development and the outcomes of prenatal alcohol exposure. The children were born to women residing in a low socioeconomic status (SES), predominantly Coloured, area of the Western Cape. This study site was chosen as a result of the high prevalence of alcohol abuse amongst women (Jacobson, Jacobson, Molteno, & Odendal, 2006). Prospective interviews assessing levels of prenatal alcohol consumption were conducted at a local antenatal clinic. Mothers were invited to participate in the research if they met the eligibility criteria outlined below (see Inclusion Criteria section).

Children were assessed in September 2005 by two expert dysmorphologists (H. Eugene Hoyme and Luther K. Robinson) according to standard diagnostic protocol (Hoyme, 2005; see Jacobson et al., 2008). Dysmorphic features, particularly palpebral fissure length, philtrum and vermilion ratings, were assessed according a standardized rating scale. There was substantial agreement about Fetal Alcohol Syndrome (FAS) diagnosis, with heavily exposed children being divided into three diagnostic groups: FAS, Partial FAS (PFAS), and Heavily Exposed (HE).

Table 1 summarizes the sample characteristics of the diagnostic groups in the Cape Town cohort. The 47, primarily Afrikaans-speaking, participants were between the ages of 6.9 and 9.7, with a mean age of 9.17. There were no statistically significant differences between diagnostic groups for SES, age, and gender (see Table 1). Participants were, therefore, considered to be matched on those three demographic variables. The mean SES scores for the FAS, PFAS, HE, and Control Groups fell between the third and fourth levels of Hollingshead's (1975) five level SES index. All of the participants in the current research are, therefore, of a low-SES background.

In terms of maternal drug use, cocaine was used by one mother during pregnancy. Marijuana was used by three mothers during pregnancy. Furthermore, maternal characteristics differed significantly for primary caregiver's years of education and maternal cigarette smoking during pregnancy (see Table 1).

Detroit cohort. The pregnant mothers of the 291 children in this cohort were recruited between September 1986 and April 1989 as part of a longitudinal study investigating the developmental effects of moderate to heavy prenatal alcohol exposure. The children were born to

women residing in a low-SES area of Detroit. All of the participants were African-American. Prospective interviews were conducted with women during pregnancy, and they were invited to participate in the research according to the inclusion criteria outlined below (see Inclusion Criteria section). To reduce the risks that alcohol effects would be confounded by prenatal cocaine exposure, a group of heavy cocaine, but light alcohol users were also recruited.

Table 2 summarizes the sample characteristics in the Detroit cohort. The 291, primarily English-speaking, participants were aged between 13.26 and 16.5 years, with a mean age of 14.42. As in the Cape Town cohort, there were no statistically significant differences between exposure groups for SES, age, and gender (see Table 2). Participants were therefore considered to be matched on the three demographic variables. Mean SES scores across the alcohol exposure groups fell into the third and fourth levels of the Hollingshead (1975) 5 factor SES index. Participants in the Detroit cohort were therefore all from low-SES backgrounds.

In terms of maternal drug use, 101 of the 291 recruited mothers used cocaine during pregnancy. 86 of the 291 recruited mothers used marijuana during pregnancy. Furthermore, maternal characteristics differed significantly for mother's age at delivery and maternal cigarette smoking during pregnancy (see Table 2).

Inclusion Criteria

Mothers were invited to participate in the study if their average consumption level of absolute alcohol (AA) per day was equal to or above 1.0 oz, which is classified as heavy exposure, or if binge drinking (4 standard drinks per session) during pregnancy was reported. In the Detroit cohort, all women drinking 0.5 AA/day were invited to participate, and 5% of women who abstained or drank < 0.5 AA/day were also included. Women consuming 0.5 to 0.99 oz AA/day were considered moderate drinkers.

Materials

Although there are no published norms for South Africa, the standardized measures included in the current research are widely used within clinical research in South Africa. In both Cape Town and Detroit cohorts, test scores for participants with a history of prenatal alcohol exposure were compared to those of the non-exposed control participants, and not to the published normative data.

General intellectual functioning and maternal characteristics were assessed as part of the neuropsychological batteries administered in both the Cape Town and Detroit cohorts. Although these variables were included in the sample characteristics, the measures were not key to the current study.

Verbal Learning

The *California Verbal Learning Test – Children's Version* (CVLT-C; Delis, Kramer, Kaplan, & Ober, 1994) is a measure of verbal learning and memory. The test provides an indication of the stage at which any disruption in verbal memory might occur (e.g., at encoding or retrieval). The CVLT-C has been used previously in research into the effects of prenatal alcohol exposure (Mattson & Roebuck, 2002), and has good reliability and validity (Delis et al., 1994). The test is structured around a series of recall trials designed to measure the various stages of, or processes underlying, verbal learning and memory for a shopping list. Participants are required to complete a series of immediate recall trials, a set of short- and long-delay recall trials, and a recognition memory trial. The CVLT-C was administered according to the conventional procedure as described in the administration manual (see the Procedure section below for a summary description).

For the purposes of the Cape Town cohort, the test items were translated into Afrikaans by a linguistics specialist (see Appendix A). Items were then back-translated to ensure the efficacy of the initial translation.

Maternal Drug and Alcohol Consumption Data

A timeline follow-back interview protocol (Sokol, Martier, & Ernhart, 1983) was used at recruitment to obtain maternal alcohol consumption data (Jacobson, Chiodo, Sokol, & Jacobson, 2002). The use of the timeline follow-back interview yields reliable estimates of maternal alcohol and drug consumption during pregnancy. The interview consists of a series of questions that aim to reconstruct an average week during the mother's pregnancy. Questions pertaining to drug and alcohol use are integrated into the interviewing process such that a reliable measure of maternal cigarette and drug use, as well as a reliable calculation of the alcohol exposure measure (average oz AA/day), might be obtained. The maternal alcohol consumption data provide a continuous measurement of alcohol exposure, which allows for the assessment of dose-response relationships between alcohol exposure and cognitive/behavioural outcome. The continuous

measurement of alcohol consumption was calculated using multipliers developed by Bowman, Stein, and Newton (1975).

Procedure

Ethical approval was obtained from the University of Cape Town's Faculty of Health Science Research Ethics Committee (REC REF: 187/2008; see Appendix B) for data collection on the Cape Town cohort. Ethical approval was granted from Wayne State University's Human Investigation Committee for data collection on the Detroit cohort (HIC number: 099504B3F; see Appendix C). Informed consent and assent were obtained from the mothers and children at recruitment for both cohorts. Renewal of the initial informed consent and assent were obtained at 9 years old in the Cape Town cohort, and at 14 years old in the Detroit cohort (see Appendix D; E and F). In the Cape Town cohort testing occurred during 2009 and 2010. Depending on when mothers and children were recruited this renewal of consent and assent occurred 8 to 11 years after initial consent and assent were obtained. In the Detroit cohort testing occurred during 2003. This renewal of consent and assent occurred between 14 and 17 years after the initial recruitment of mothers and children.

In Cape Town, appointments for testing were scheduled by the project secretary, with participants being transported by the project driver to and from the testing site. In Detroit, the research nurse met the participants at their homes and accompanied them to the testing site. The measures of interest for this study are part of a larger neuropsychological battery that is administered over 2 days.

With regard to the CVLT-C, the first part of the test consists of a series of immediate free recall trials: Participants were instructed by the test administrator to "pretend that you are going shopping on Monday". A list of target words, all related to items one might find in a grocery store, was then presented. At the conclusion of the presentation, the participant was instructed to list all the words that he/she could remember, in any order. Six such trials were administered; the first five all pertained to the same list (the "Monday list") and the sixth to a distracter list (the "Tuesday list"). A short-delay free recall trial was administered immediately after the completion of the sixth free recall trial: Participants were instructed to recall the items that were on the Monday list without any prompting. A short-delay cued-recall trial followed immediately thereafter (i.e., the child was asked to list the words on the list that belonged to specific categories, e.g., fruits and clothes).

Table 1
Cape Town Cohort: Demographic characteristics of the diagnostic groups (n = 47)

Demographic Information	FAS (*n* = 6)	PFAS (*n* = 14)	HE (*n* = 9)	Controls (*n* = 18)	Test Statistic	*p*	ESE
Maternal age at delivery	32.27 (8.02)	25.8 (5.87)	26.85 (7.57)	26.12 (3.41)	2.016	.126	.123
Socioeconomic Status	21.67 (9.91)	30.71 (31.63)	29.22 (24.13)	30.67 (16.12)	0.261	.853	.018
Maternal/caregiver education (years)	9.33 (2.42)	6.5 (2.85)	9.33 (2.18)	10.22 (1.24)	8.305	<.0001**	.367
Prenatal cigarettes (cigarettes/day)	7.45 (3.02)	8.36 (6.48)	5.28 (4.57)	1.75 (5.01)	4.639	.007*	.244
Child's age at testing (years)	9.1 (0.26)	9.14 (0.67)	9.28 (0.23)	9.17 (0.41)	0.294	.829	.020
Gender (% Male)	50 (-)	50 (-)	77.8 (-)	44.4 (-)	2.820	.420	.245
IQ	66.69 (7.33)	66.15 (8.33)	70.86 (12.36)	78.06 (11.1)	4.337	.009*	.232

* $p < .01$; ** $p < .0001$
Note. Means are presented with standard deviations in parentheses. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed. Test statistics were either *F* or χ^2 depending on whether the variable under consideration was categorical or continuous. ESE refers to the estimate of effect size. ESE was calculated using either η^2 or Phi depending on whether a one-way ANOVA or Chi-square test was employed.

Table 2
Detroit Cohort: Demographic characteristics of the exposure groups (n = 291)

Demographic Information	Light (*n* = 251)	Moderate (*n*= 21)	Heavy (*n* =19)	Test Statistic	*p*	ESE
Maternal age at delivery	26.54 (6.01)	29.68 (5.04)	30.13 (6.14)	5.503	.005*	.037
Socioeconomic Status	30.06 (10.13)	27.42 (10.09)	26.84 (10.49)	1.438	.239	.010
Maternal/caregiver education (years)	12.53 (1.90)	11.86 (1.66)	12.58 (2.17)	1.251	.288	.009
Prenatal cigarettes (cigarettes/day)	7.91 (10.03)	16 (12.20)	18.74 (13.60)	14.270	<.0001**	.090
Child's age at testing (years)	14.41 (0.61)	14.57 (0.73)	14.34 (0.59)	0.786	.456	.005
Gender (% Male)	56.2 (-)	52.4 (-)	78.9 (-)	3.978	.137	.117
IQ	79.31 (12.77)	78.05 (15.49)	76.26 (13.50)	0.547	.580	.004

*$p < .01$; **$p < .0001$
Note. Means are presented with standard deviations in parentheses. Test statistics were either *F* or χ^2 depending on whether the variable under consideration was categorical or continuous. ESE refers to the estimate of effect size. ESE was calculated using either η^2 or Phi depending on whether a one-way ANOVA or Chi-square test was employed.

After a filled delay of 20 minutes, long-delay free- and cued-recall trials were administered. These were identical to the short-delay free- and cued-recall trials. Finally, the participant's recognition abilities were tested: The examiner read a list of shopping items, and the participant had to identify which items had appeared on the Monday list.

The CVLT-C was administered following the standardised procedures outlined in the testing manual, in a controlled testing environment, with the seating arrangement around a table remaining consistent across participants at both testing sites (see Figure 1). In both Cape Town and Detroit the examiner was blind to the participant's diagnosis and level of prenatal alcohol exposure. All responses were recorded according to standard testing protocol on the forms provided with the relevant testing manuals. Identical procedures were followed for both cohorts.

Compensation

In Cape Town, children were given a small gift (e.g., stationery set) and mothers were given R150 and a photo of her child as compensation for a half day of testing. In Detroit, the adolescent was given a small gift; each mother was given $30 for each half day of interview, and a photograph of her child as compensation at the end of testing. Adolescents were given $40 for a 5-hr day of testing plus time for lunch, which was provided. These compensations were consistent with guidelines from the respective Ethics Committees so that they would constitute reasonable compensation for time devoted to testing without being so high as to constitute coercion.

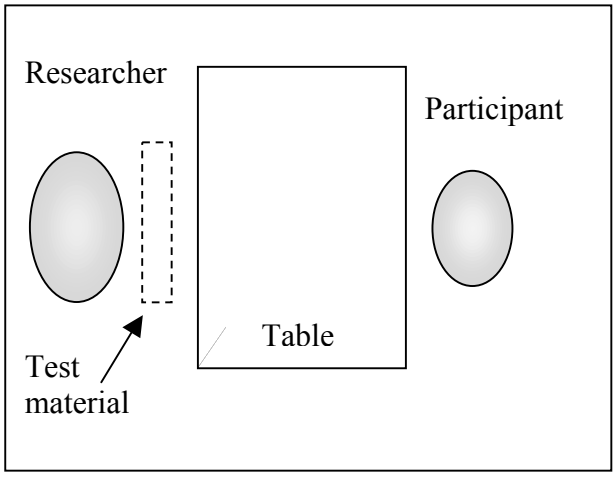

Figure 1. Layout of testing situation

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences version 18.0 (SPSS, 2009). Data from the Cape Town and Detroit cohorts were analysed independently. Statistical analyses were identical in each case and proceeded in four stages.

Stage 1

To explore the data and test the assumptions underlying parametric statistical tests, comprehensive descriptive statistics were calculated for alcohol consumption and for CVLT-C outcome variables. A summary of these CVLT-C outcome variables is provided in Table 3. Specifically, learning trials 1 through 5 and total learning were used as measures of verbal learning, whereas short-delay recall, long-delay recall, short-delay percentage retention, long-delay percentage retention and recognition discrimination accuracy were used as measures of verbal memory. Learning trial 1 was further used as a measure of immediate learning. It is important to note that the short- and long-delay recall and short- and long-delay percentage retention variables measure different things. The short- and long-delay recall outcome variables are raw performance scores. The short- and long-delay percentage retention scores take into account how much information participants learned at the fifth learning trial. It is, therefore, clinically useful to provide a comparison of both variables.

Comprehensive sample characteristic tables were constructed separately for each of the cohorts. Data were checked and cleaned before running any inferential statistical tests. In both cohorts, oz AA/day was normalized using a natural log transformation ($ln[x + 1]$). In the Detroit cohort, skewed maternal marijuana and cocaine use scores were transformed using a natural log function ($ln[x + 1]$), such that the data were normally distributed. Unless otherwise noted, assumptions for parametric tests were upheld.

Stage 2

Dose-response relationships between verbal learning and memory and prenatal alcohol exposure were investigated in both cohorts. In each of the cohorts, one-way analyses of variance (ANOVA) and repeated-measures ANOVAs were used to test for statistically significant relationships between the level of prenatal alcohol exposure and CVLT-C outcomes. In the Cape Town cohort, level of exposure was categorized by diagnosis (FAS, PFAS, HE, or non-exposed).

In the Detroit cohort, level of exposure was categorized according to oz AA/day, with 0.0-0.49 designating none to very low levels (i.e. light) of exposure; 0.5-0.99 moderately exposed; 1.0-1.99 heavily exposed; and greater than 2.0 very heavily exposed. One participant in the Detroit cohort qualified as very heavily exposed. For the purpose of the analyses, therefore, the heavily and very heavily exposed participants were grouped together. In the Detroit cohort, therefore, three alcohol exposure groups were used: light (including both non- and lightly-exposed participants), moderate, and heavy.

Although the research design focused on hypothesis testing, the public health context of prenatal alcohol exposure research results in an increased concern about missing real effects rather than concern for the strict control of alpha values (i.e., Type II vs. Type I errors; Jacobson & Jacobson, 2005). Adjusting alpha values using conservative measures, such as the Bonferroni correction, may result in an underestimation of the subtle effects of prenatal alcohol exposure on verbal learning and memory. Where post-hoc analyses were warranted, Least-Significant Difference (LSD) tests were therefore performed.

Furthermore, research designs that control for the influences of extraneous variables, such as SES, maternal age, and IQ, are necessary for developmental teratology research (Jacobson & Jacobson, 2005; May et al., 2005). Aside from the effects of prenatal alcohol exposure, environmental factors such as prenatal health, socioeconomic status (SES), maternal drinking patterns, maternal age at birth and access to education can all affect cognitive and social development (Jacobson, Jacobson, Sokol, Chiodo, & Corobana, 2004). Although the current research design attempted to account for potential confounding variables, it was beyond the scope of this study to consider the effects of these potential confounding variables in the statistical analyses of the data.

RESULTS

Between-Groups Comparisons

Learning

Cape Town cohort. A series of one-way ANOVAs tested the hypothesis that children with a history of heavy prenatal alcohol exposure would show verbal learning impairments relative to typically developing controls. There were no statistically significant differences in immediate learning across diagnostic groups, $F(3, 43) = 2.114$, $p = .112$, $\eta^2 = .129$. There were, however, statistically significant between-group differences in total learning, $F(3, 43) = 3.153$, p

= .034, η^2 = .180. Post-hoc pairwise comparisons, with alpha set at .05, further indicated that the statistically significant differences were located between the FAS and Control groups, p = .049, and between the PFAS and Control groups, p = .009. This pattern of data suggests that verbal learning impairment occurs at a significantly greater level in the FAS and PFAS groups when compared to typically developing, demographically matched, controls. The results, therefore, confirm the hypothesis that children with heavy prenatal alcohol exposure would display verbal learning impairments when compared to typically developing controls.

Table 3
CVLT-C Outcome Variables Used in the Current Study

Variable name	Description
Trial 1, Trial 2, Trial 3, Trial 4, Trial 5	Number of correctly recalled words on each of the 5 learning trials.
Total learning	Number of words correctly recalled words across the 5 learning trials.
Difference scores	Difference in correct recall between CVLT-C learning trials. Calculated as Trial 2 – Trial 1; Trial 3 – Trial 2; Trial 4 – Trial 3; and Trial 5 – Trial 4 respectively.
Short-delay recall	Number of words correctly recalled after a short delay (i.e., after presentation of the interference list).
Long-delay recall	Number of words correctly recalled after a delay of 20 minutes.
Short-delay % retention	The percentage of information retained from trial 5 to short-delay free recall. Calculated as [short-delay recall/trial 5 recall]*100.
Long-delay % retention	The percentage of information retained from trial 5 to long-delay recall. Calculated as [long-delay recall/trial 5 recall]*100.
Recognition discrimination accuracy	The number of words correctly recognized, when initial learning is accounted for. Calculated as [number of correct hits + correct rejections]/total learning (Delis et al., 1994).

Learning across trials was assessed using a repeated-measure ANOVA. The results indicated that the number of words remembered correctly at each learning trial was significantly affected by diagnostic group, $F(3, 43) = 3.153$, p = .034, η^2 = .180. Post-hoc pairwise comparisons located these between-groups differences as between the FAS and Control group, p = .049, as well as between the PFAS and Control groups, p = .009. There was no statistically significant trial by diagnostic group interaction effect, $F(12, 172) = 3.207$, p = .236, η^2 = .082,

which suggests that the pattern of learning was the same for participants in the FAS, PFAS, HE and Control groups across CVLT-C learning trials. A significant main effect for trials was present, F (4, 172) = 58.718, $p < .0001$, $\eta^2 = .577$. These results indicated that within the diagnostic groups participants correctly recalled a significantly different number of words across the CVLT-C learning trials.

In order to better locate the differences in learning across trials, between-trials difference scores were investigated using one-way ANOVAs. Although none of the comparisons reached statistical significance, a trend towards between-groups significance emerged for the difference score between learning trials 1 and 2 (see Table 4). Mean scores for recall over the learning trials (see Table 5) indicated that this trend towards significance may be explained by a surge in learning for participants in the Control group from Trial 1 to Trial 2. Mean recall scores further suggested that from Trial 2 to Trial 5 participants in the Control group reached a learning plateau. This pattern was also evident in participants with a history of prenatal alcohol exposure (FAS, PFAS, and HE); however, the learning plateau was only reached on Trial 3 and extended to Trial 5 (see Figure 2).

Overall, these data suggest that participants with a history of heavy prenatal alcohol exposure take longer to reach their highest level of performance than typically developing controls. Furthermore, these results suggest that repeated exposure to the to-be-learnt material was not sufficient to enable exposed individuals to reach the same level of overall learning as controls in the Cape Town cohort.

Table 4
Cape Town Cohort: Between-groups comparisons for CVLT-C learning trials difference scores

Difference Score	$F(3, 43)$	p	η^2
Trial 2 – Trial 1	2.390	.082	.143
Trial 3 – Trial 2	1.608	.201	.101
Trial 4 – Trial 3	1.507	.226	.095
Trial 5 – Trial 4	1.702	.181	.106

Table 5
Cape Town Cohort: Descriptive statistics for the CVLT-C learning trials

Diagnostic Group	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
FAS (n = 6)	5.83 (2.14)	7.33 (2.66)	9.33 (2.73)	8.83 (2.32)	10.5 (2.56)
PFAS (n = 14)	5.86 (2.11)	7.86 (2.8)	8.57 (2.82)	9.71 (2.92)	9.64 (2.98)
HE (n = 9)	4.67 (1.41)	8.22 (1.3)	9.78 (2.28)	10.33 (2)	10.44 (2.3)
Control (n = 18)	6.61 (1.85)	10.11 (2.11)	10.33 (2.14)	11.56 (1.5)	11.78 (2.26)

Note. Means are presented with standard deviations in parentheses. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed.

There were too few cases (< 10%) in Cohort 1 to examine effects of prenatal cocaine or marijuana exposure on the outcomes. To assess whether prenatal exposure to marijuana and cocaine had a confounding impact on the effects of prenatal alcohol exposure on verbal learning, the analyses were re-run excluding one case where maternal cocaine use was present, as well as three cases in which maternal marijuana use was present. Across the two sets of analyses the magnitude of effect, assessed using η^2, remained virtually unchanged. Based on these data, maternal marijuana and cocaine use during pregnancy could not be considered responsible for the observed effects.

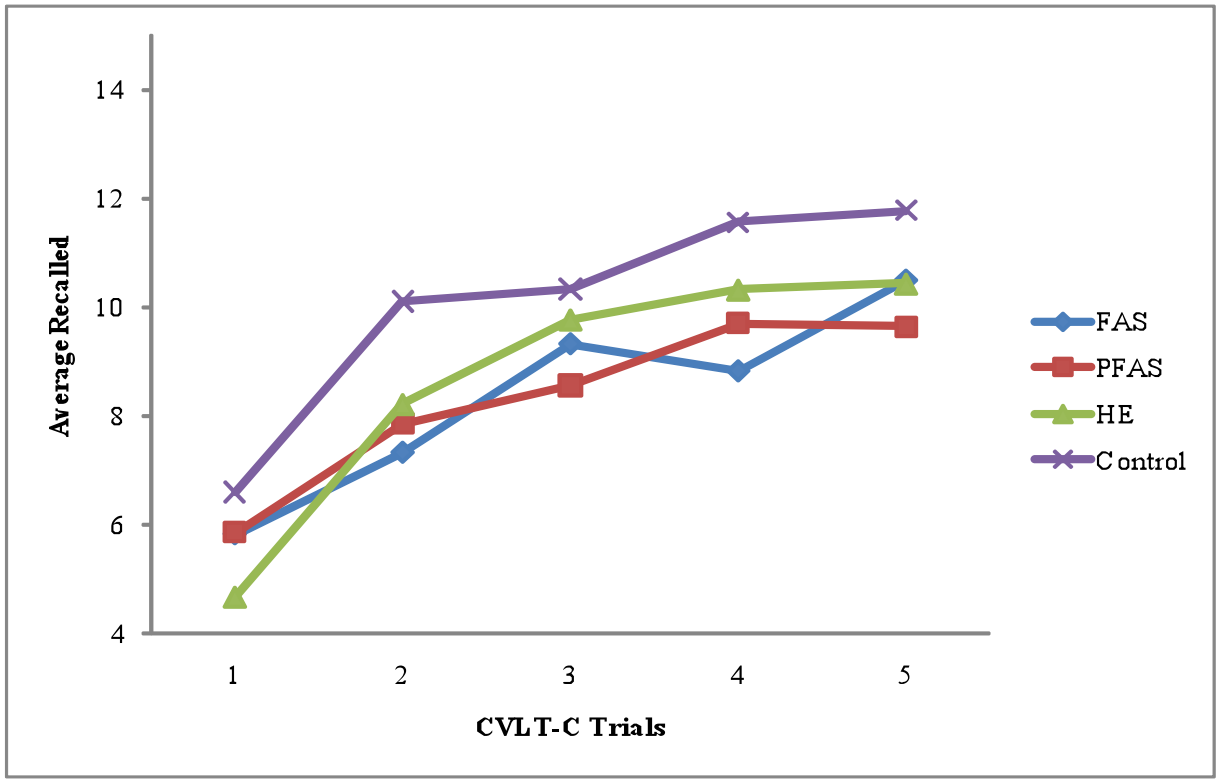

Figure 2. Mean recall of FAS, PFAS, HE, and Control participants across CVLT-C learning trials

Detroit cohort. A series of one-way ANOVAs, similar to those reported above for the Cape Town cohort, tested the hypothesis that participants with moderate to heavy levels of prenatal alcohol exposure would display verbal learning impairments relative to non- or light exposed controls. There were no statistically significant between-group differences in terms of immediate learning, $F(2, 288) = 0.885$, $p = .414$, $\eta^2 = .006$. Furthermore, there were no statistically significant between-group differences in total learning, $F(2, 288) = 1.820$, $p = .164$, $\eta^2 = .012$.

Learning across trials was assessed using a repeated-measure ANOVA. The results indicated that there was no statistically significant main effect of exposure group, and no trial × exposure interaction effect, $F(2, 288) = 1.820$, $p = .164$, $\eta^2 = .012$, and $F(8, 1152) = 0.899$, $p = .516$, $\eta^2 = .006$, respectively. A significant main effect for trials was, however, present, $F(4, 1152) = 142.437$, $p < .0001$, $\eta^2 = .331$. These results indicate that even though there wasn't a significant between groups difference in the number of correct words recalled over the five learning trials, within groups there was a significant difference in the amount of information correctly recalled across trials.

As with the Cape Town cohort, learning over trials was further assessed using between-trials difference scores as the dependent variable in a series of one-way ANOVAs. Again, none of these ANOVAs indicated the presence of statistically significant between-group differences (see Table 6). However, mean scores for recall over the learning trials indicate that, on each of learning trials 3, 4, and 5, participants in the heavy exposure group learned slightly less information than those in the light and moderate exposure groups (see Table 7). This difference is evident in the learning curves of the three exposure groups (see Figure 3).

These results, therefore, do not support the hypothesis that children with a history of moderate to heavy alcohol exposure are impaired in verbal learning when compared to typically developing, demographically matched, control participants.

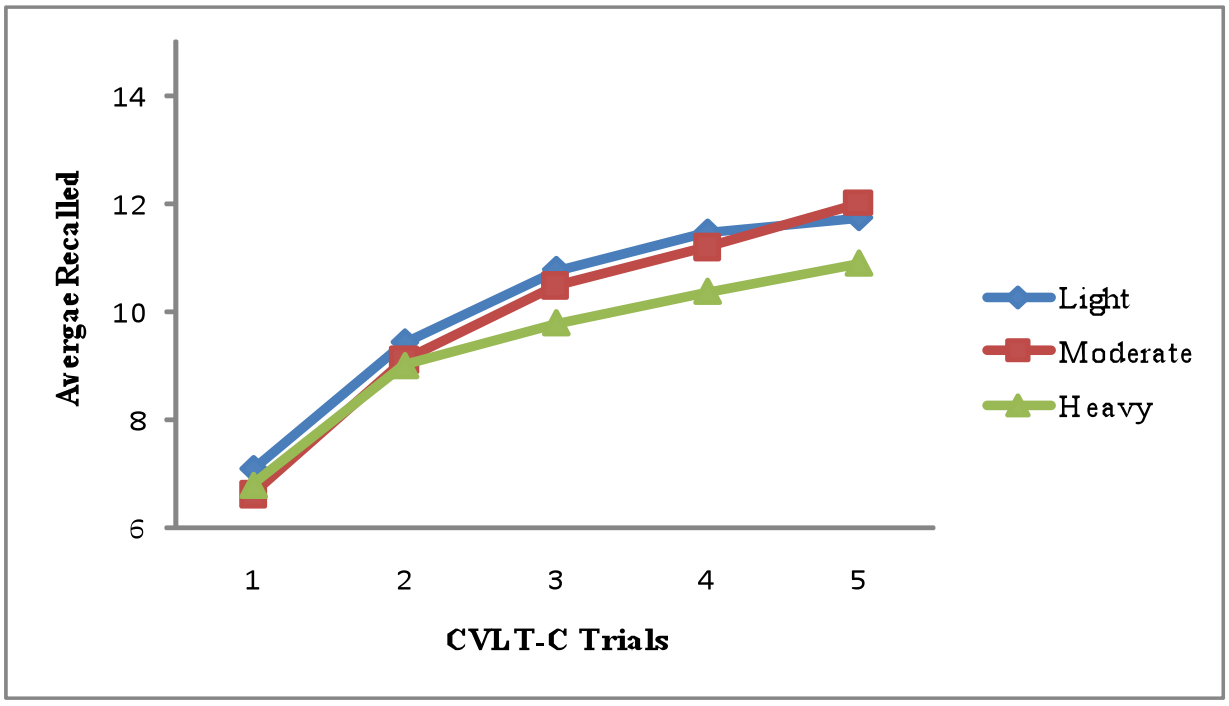

Figure 3. Mean recall of oz AA/day exposure groups across CVLT-C learning trials.

Detroit Cohort: Between-groups Comparisons for CVLT-C learning trials difference scores

Difference Scores	$F(2, 288)$	p	η^2
Trial 2 – Trial 1	0.080	.923	.001
Trial 3 – Trial 2	0.683	.506	.005
Trial 4 – Trial 3	0.028	.973	< .001
Trial 5 – Trial 4	1.088	.338	.007

Memory

Table 7

Detroit Cohort: Descriptive statistics for the CVLT-C learning trials

Exposure Group	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Light (n = 251)	7.08 (1.73)	9.42 (2.37)	10.76 (2.38)	11.45 (1.9)	11.72 (1.91)
Moderate (n = 21)	6.62 (1.88)	9.10 (2.77)	10.48 (2.36)	11.19 (2.09)	12 (2.03)
Heavy (n = 19)	6.79 (1.75)	9 (2.21)	9.79 (1.93)	10.37 (1.92)	10.89 (2.05)

Note. Means are presented with standard deviations in parentheses.

Cape Town cohort. Memory performance was assessed using five separate outcome variables: short- and long-delay recall, short- and long-delay percentage retention, and recognition discrimination accuracy. Table 8 presents group means for these variables.

One-way ANOVA showed that there was a statistically significant between-groups difference in terms of short-delay recall, $F(3, 43) = 3.778$, $p = .017$, $\eta^2 = .209$. Post-hoc pairwise comparisons located a significant main effect between the FAS and Control groups, $p = .029$, and between the PFAS and Control groups, $p = .004$. Interestingly, however, there was no statistically significant between-groups difference in terms of long-delay recall, $F(3, 43) = 2.058$, $p = .120$, $\eta^2 = .126$. These results indicated that between-group differences at Trial 5 persisted through short-delay recall, but not through long-delay recall.

One-way ANOVA also showed that there were no statistically significant between-groups differences in terms of short-delay or long-delay percentage retention, $F(3, 43) = 0.495$, $p = .688$, $\eta^2 = .033$, and $F(3, 43) = .348$, $p = .791$, $\eta^2 = .024$. These results indicated that both participants with a history of heavy alcohol exposure (FAS, PFAS, and HE) and non-exposed controls retained similar percentages of previously-learned information over both short and long retention intervals.

The distribution of recognition discrimination accuracy scores contained an outlier (a score that was very low relative to the overall mean of 91.49). The distribution was thus transformed by recoding all values smaller than 3 SD below the mean to 1 point below the lowest observed value, as recommended by Winer (1971). One-way ANOVA on the transformed distribution detected no statistically significant between-group differences, $F(3, 43) = 2.335$, $p =$

.087, $\eta^2 = .140$. It is clear from the *p* value and the effect size estimate, however, that a trend towards significance definitely emerged here.

Table 8
Cape Town Cohort: Descriptive statistics for CVLT-C memory outcome variables

	Group			
Memory Outcome Variable	FAS (*n* = 6)	PFAS (*n* = 14)	HE (*n* = 9)	Control (*n* = 18)
Short-delay recall	7.5 (2.88)	7.43 (2.65)	8.44 (2.4)	10.28(2.56)
Short-delay % retention	71.26 (26.05)	86.37 (50.28)	80.35 (12.48)	88.92 (22.99)
Long-delay recall	8.5 (2.88)	7.93 (2.56)	9.11 (2.21)	10.06 (2.39)
Long-delay % retention	79.22 (20.13)	105.89 (114.74)	88.01 (13.81)	86.48 (17.64)
Recognition discrimination accuracy	90.74 (10.18)	87.30 (12.49)	90.67 (13.18)	96.3 (2.95)

Note. Means are presented with standard deviations in parentheses. FAS = fetal alcohol syndrome; PFAS = partial fetal alcohol syndrome; HE = heavily exposed.

Detroit cohort. As with the Cape Town cohort, memory performance was assessed using five independent outcome variables: short- and long-delay recall, short- and long-delay percentage retention and recognition discrimination accuracy. Table 9 presents group means for these variables.

One-way ANOVA showed that there was a statistically significant between-groups difference in terms of short-delay recall, $F(2, 288) = 4.051$, $p = .018$, $\eta^2 = .027$. Post-hoc pairwise comparisons located the significant difference as being between the light- and heavy-exposure groups, $p = .005$. There was also a statistically significant between-groups effect in terms of long-delay recall, $F(2, 288) = 4.87$, $p = .008$, $\eta^2 = .033$. Post-hoc pairwise comparisons located this significant effect between the light- and heavy-exposure groups, $p = .002$, as well as between the moderate- and heavy-exposure groups, $p = .046$. Taken together, the absence of a significant between-groups difference on Trial 5 and the presence of between-group differences for both short- and long-delay recall indicated that alcohol exposure impacts negatively on the retrieval of previously learned information.

One-way ANOVA also showed that there were no statistically significant between-groups differences in terms of short- or long-delay percentage retention, $F(2, 288) = 1.606$, $p = .202$, $\eta^2 = .011$, and $F(2, 288) = 1.795$, $p = .168$, $\eta^2 = .012$. These results suggest that participants in the light, moderate, and heavy exposure groups retained similar amounts of previously-learned information over both short and long retention intervals.

The distribution of recognition discrimination accuracy scores for this cohort also contained 3 outliers (scores that were very low relative to the overall mean of 95.91). The same

transformation procedure as in the case of the Cape Town cohort was followed here. One-way ANOVA on the transformed distribution detected a statistically significant between-group difference, $F(2, 288) = 5.652$, $p = .004$, $\eta^2 = .038$. Post-hoc pairwise comparisons located this significant difference as occurring between the light- and heavy-exposure groups, $p = .004$.

Taken together, these results do not support the hypothesis that encoding difficulties are the primary verbal learning and memory impairment for children with a history of moderate to heavy prenatal alcohol exposure.

Table 9
Descriptive Statistics for CVLT-C Memory Outcomes in The Detroit cohort

Memory Outcome Variable	Light (n = 251)	Moderate (n = 21)	Heavy (n = 19)
Short-delay recall	10.51 (2.25)	10.29 (2.28)	9 (1.86)
Short-delay % retention	90.37 (18.58)	85.49 (10.19)	84.23 (17.9)
Long-delay recall	10.94 (2.14)	10.71 (2.13)	9.37 (1.83)
Long-delay % retention	94.37 (18.11)	89.86 (13.65)	87.53 (17.66)
Recognition discrimination accuracy	96.43 (4.09)	94.56 (6.04)	93.41 (5.66)

Note. Means are presented with standard deviations in parentheses.

DISCUSSION

The main aim of the current research was to investigate verbal learning and memory functioning in children with a history of moderate to heavy prenatal alcohol exposure. Results from both Cape Town and Detroit cohorts supported the hypothesis that such children display impairments in those cognitive domains when compared to typically developing controls. The pattern of these impairments was somewhat different to the *a priori* predictions, however.

Previous research has indicated that deficits in the initial encoding of information (rather than in the retrieval of that information) are the primary underlying mechanism for impaired verbal memory in children with moderate to heavy prenatal alcohol exposure (Mattson et al., 1998; Mattson & Roebuck, 2002; Willford et al., 2004). Patterns in the data from the Cape Town cohort were consistent with those extant studies. Data from the Detroit cohort suggested, however, that the primary deficit in that sample occurred at the level of retrieval. In addition, data from both of the current cohorts provided a novel finding: impairments in recognition memory appear to be present for children with moderate to heavy prenatal alcohol exposure.

Learning Impairments in FASD

In the Cape Town cohort, there were significant differences between the diagnostic groups (FAS, PFAS, HE and Control) in terms of the amount of information learned over the first 5 CVLT-C trials. These differences were primarily located in comparisons between the very heavily exposed participants (FAS and PFAS) and the control participants. Even though these between-group differences were present, the results do not support Mattson and Roebuck's (2002) suggestion that both alcohol-exposed and non-exposed participants benefit from repeated exposure to test materials. Instead, both exposed and non-exposed participants in the Cape Town cohort reached a learning plateau early on in the testing procedure. Control participants did, however, reach this plateau earlier than participants in the FAS, PFAS, and HE groups.

Taken together, these findings suggest that, in the Cape Town cohort, children with a history of heavy prenatal alcohol exposure display difficulties with the initial acquisition of information when compared to non-exposed, typically developing control participants. This finding replicates those of Mattson et al. (1998) and Mattson and Roebuck (2002). Furthermore, the absence of differences between the FAS, PFAS, and HE groups supports Mattson et al.'s (1998) proposal that a similar pattern of verbal learning deficits emerges for both individuals with and without the characteristic facial features of FAS.

Additionally, data from the Cape Town cohort supported the dose-response hypothesis that the heavier the prenatal alcohol exposure, the more severe the impairments in verbal learning and memory would be. Specifically, participants in the FAS and PFAS groups performed consistently more poorly than participants in the HE and Control groups.

Contrary to *a priori* predictions, and in contrast to the results from the Cape Town cohort, verbal learning performance differences were not present within the Detroit cohort. Participants with light, moderate, and heavy prenatal alcohol exposure learned similar amounts of information over the first 5 CVLT-C trials. Although participants with heavy prenatal alcohol exposure did perform slightly more poorly than participants with moderate and light prenatal alcohol exposure, this difference was not large enough to suggest a significant dose-response relationship. This lack of statistical significance may be attributed to the small number of participants in the heavily exposed group relative to the light and moderate exposure groups. Nevertheless, these findings do not support the notion that the primary deficit in verbal learning and memory for children with a history of moderate to heavy prenatal alcohol exposure is at the level of encoding. These results stand in contrast to those of Willford et al. (2004), who found

that impaired acquisition of verbal information underlies the verbal learning and memory deficits associated with moderate prenatal alcohol exposure.

Memory Impairments in FASD

Short- and Long-delay Free Recall

In the Cape Town cohort, participants with heavy prenatal alcohol exposure (i.e., those in the FAS and PFAS groups) recalled significantly less information about the target list immediately after presentation of a distractor list (i.e., on the short-delay free recall trial) than non-exposed control participants. When the amount of information recalled after learning trial 5 was controlled for, however, participants in the FAS, PFAS, HE, and Control groups all retained the same amount of information over the short-delay interval. Between-group differences at short-delay recall were, therefore, not due to a loss of information over the retention interval, or to a failure to retrieve items after the delay. These results are consistent with those of Mattson and Roebuck (2002). Specifically, one might conclude here that, when initial learning is controlled for, the primary deficit underlying verbal learning and memory impairments lies in the encoding of verbal information and not in retention or retrieval of that information.

Interestingly, the between-groups difference did not persist to the long-delay recall trial in the Cape Town cohort. On further examination of the descriptive statistics it appeared that participants in the FAS, PFAS, and HE groups showed a slight improvement from short- to long-delay recall. Explanations for this improvement are two-fold. Firstly, at short-delay recall participants with prenatal alcohol exposure (FAS, PFAS, and HE) may have been experiencing more interference from the Tuesday List than non-exposed control participants. The interference of the words on the Tuesday list may have decreased by the long-delay recall trial, therefore, improving recall of the correct target words. Secondly, the improvements may be due to the incorrect administration of the long-delay recall trial. If it was indicated to the participants that the long-delay recall trial was the final recall opportunity (e.g. “can you tell me the words from the Monday List one last time”) participants may have displayed improved recall by virtue of the incentive attached to correct recall on the long-delay recall trial.

A different pattern emerged in the Detroit cohort’s data. Participants in the heavy and moderate exposure groups recalled significantly less information than participants in the light exposure groups on both the short- and long-delay recall trials. In light of the absence of between-groups differences for total information learned over the first 5 CVLT-C trials, as well

as for the amount of information retained from learning Trial 5 to the delayed recall trials, these results indicate the presence of a retrieval deficit for participants with a history of moderate to heavy prenatal alcohol exposure. The presence of a retrieval deficit does not support the hypothesis that verbal learning and memory impairments would be at the level of encoding. These results, therefore, stand in stark contrast not only to those from the Cape Town cohort of the present study, but also to those of Mattson et al. (1998), Mattson and Roebuck (2002), and Willford et al. (2004).

A possible explanation for the aforementioned differences in verbal learning and memory impairments is that children with a history of moderate prenatal alcohol exposure do not display the same kind of memory deficits that are present for children with a history of heavy prenatal alcohol exposure, but rather display retrieval impairments that are rooted in executive functioning deficits. Typical development of executive functioning spans childhood and adolescence (De Luca et al., 2003). During adolescence, as the frontal lobes mature, executive functioning continues to develop such that complex working memory and goal-directed functions are acquired. This executive functioning developmental trajectory may, however, be stunted in children with a history of prenatal alcohol exposure (Rasmussen & Bisanz, 2009). Impairments across the executive functioning domains have been previously reported in the prenatal alcohol exposure literature (see Kodituwakku, Kalberg, & May, 2001; Rasmussen, 2005). Neuroimaging research has further reported that, when compared to typically developing controls, children with FASD display functional and structural abnormalities in the frontal lobes (Sowell et al., 2007; Spandoni et al., 2007). This gives further support to the suggestion that the development of executive functioning in children with a history of prenatal alcohol exposure may be delayed.

In the Detroit cohort, therefore, children with a history of moderate prenatal alcohol exposure may have 'grown into' their alcohol-related deficits. Where the mean age was 14, non- and lightly-exposed participants may have developed sufficient learning and memory strategies to aid in the retrieval process. Children with moderate prenatal alcohol exposure, however, may not show this same age-appropriate development and as a result display retrieval impairments (Rasmussen, Pei, Manji, Loomes, & Andrew, 2009). In a sense then, children with prenatal alcohol exposure will grow into their executive functioning deficits as the developmental gap widens. In contrast, children in the Cape Town cohort were younger (mean age = 9) and, therefore, may not have grown into the executive functioning deficit yet. As they grow up, and

the developmental gap between typically developing and alcohol-exposed individuals widens, evidence for executive functioning impairments may become increasingly prominent. Furthermore, the heavier levels of prenatal alcohol exposure present in the Cape Town cohort may have resulted in encoding deficits overshadowing any executive functioning deficits that were present. The presence of recognition memory impairments in participants with a history of moderate to heavy prenatal alcohol exposure further supports the role of delayed executive functioning development in explaining the verbal learning and memory impairments associated with FASD.

Recognition Memory

A pattern of impaired recognition memory for participants with moderate to heavy exposure, when compared to typically developing controls, was found in both the Cape Town and Detroit cohorts. Recognition memory impairments have not previously been reported in the prenatal alcohol exposure literature. The presence of such impairments is, however, in line with the proposal that the primary cognitive mechanism underlying the verbal learning and memory deficits present in FASD is that of an inefficient use of learning and/or retrieval strategies (Mattson & Roebuck, 2002; Rasmussen et al., 2009; Willford et al., 2004). Furthermore, the proposed presence of ineffective learning strategies supports the idea that impairments in higher executive functioning underlies impairments in verbal learning and memory functioning (Manji, Pei, Loomes, & Rasmussen, 2009).

In one example of a study that demonstrated the presence of these mooted executive functioning deficits, Rasmussen et al. (2009) investigated the developmental trajectory of verbal memory strategies (e.g., semantic clustering) in children with FASD and non-exposed controls. Interestingly, they found that both groups of children made use of verbal memory strategies at the age-appropriate intervals. Children with FASD, however, did not use these strategies as effectively as control participants. For example, Rasmussen et al. (2009) found that children with FASD did not use verbal rehearsal as consistently as non-exposed controls. In line with this Pei, Rinaldi, Rasmussen, Massey and Massey (2008) reported that children with FASD display considerable difficulty with verbal learning and memory tasks that are reliant on intact working memory. Specifically, tasks that focus on the phonological loop, the aspect of working-memory that underlies verbal rehearsal abilities, give evidence to the verbal learning and memory deficits associated with FASD (Pei et al., 2008). This will impair not only the initial encoding of

information, but also negatively affect later retrieval and recognition of previously learned information for children with FASD.

Further support for this proposal is provided by fMRI research. Sowell et al. (2007) found functional abnormalities in the left medial temporal lobe and dorsolateral prefrontal cortex in children with heavy prenatal alcohol exposure when compared to typically developing controls. Of particular interest in alcohol-exposed participants was the increased activation of the dorsolateral prefrontal cortices, particularly in the left hemisphere, as opposed to decreased activation in the medial temporal lobes, during performance of a verbal paired-associates test. Sowell et al. (2007) suggest that this pattern may provide evidence for the hypothesis that individuals with heavy prenatal alcohol exposure place increased demands on the encoding and retrieval functions of frontal memory systems because the functioning of the medial temporal lobes is compromised. They further speculated that widespread cortical activation during verbal recall in participants with heavy alcohol exposure may decrease the effectiveness of the retrieval process itself.

Taken together, the findings of Sowell et al. (2007) and Rasmussen et al. (2009) support the proposal that impairments in recognition memory performance in children with moderate to heavy prenatal alcohol exposure may be due to the ineffective use of learning and retrieval strategies. It was beyond the scope of the current research to analyse learning strategies. This area of research is, however, strongly recommended for future research.

Limitations and Recommendations for Future Research

In the Cape Town cohort, the translation of the CVLT-C testing materials into Afrikaans (see Appendix A) may have increased the difficulty level of the task. Afrikaans target words typically have more syllables and are, therefore, phonetically more complex than the English target words, which might make them more difficult to remember. The use of translated materials was further complicated by the diversity in Afrikaans dialect spoken. Standard Afrikaans translations may not be appropriate in cases where participants speak a local dialect that is classified as Afrikaans, but that may draw on words from other languages. In the present study, translation of the CVLT word lists was made by a native Afrikaans-speaking MA-level child psychologist with extensive experience working with the children in this cohort and communicating with them in their dialect. Future research in South Africa should, however, look

at developing a measure of verbal learning and memory that is both language- and culture-appropriate and that is normed for the South African population.

The research was further limited by the unequal diagnostic/exposure group sizes within both cohorts. Due to the difficulties associated with participant recruitment in this type of research, this limitation is difficult to remedy. However, future research should aim to increase the sample sizes for participants with a history of moderate to heavy prenatal alcohol exposure. One possible option for future research would be to over-recruit participants across the levels of prenatal alcohol exposure (i.e. light, moderate, heavy and very heavy).

In order to confirm the novel finding that recognition memory is impaired in children who have a history of moderate to heavy prenatal alcohol exposure, future research should investigate both recognition memory performance and specific learning strategies that facilitate optimal retrieval and recognition memory functioning. Longitudinal research designs would be particularly relevant to exploring the developmental differences in executive functioning for children across the alcohol-exposure spectrum. Tracking the development of executive functioning across the lifespan will allow for an investigation of how individuals with light, moderate and heavy prenatal alcohol exposure 'grow into' executive functioning deficits. Findings from such an investigation would provide a useful contribution to the growing body of literature that is working towards defining a behavioural phenotype for FASD.

Few studies have investigated the neural correlates of verbal learning and memory in FASD. Sowell et al. (2007) identified a pattern of functional impairment for children with FASD which supports the notion that an over-reliance on frontal memory systems is not beneficial for verbal learning and memory performance in children with prenatal alcohol exposure. Further neuroimaging research is necessary to replicate the findings of Sowell et al. (2007) as well as to provide a thorough investigation of the retrieval strategies of children with FASD.

It is important to note that the results presented above cannot be considered as isolated from the effects of the generally lowered IQ scores that are associated with prenatal alcohol exposure. Because verbal memory is such an important aspect of IQ testing, it is difficult to tease apart which aspects of verbal learning and memory impairments are due to alcohol exposure over and above the effects of IQ impairments. Although it is not always possible, future research into the outcomes of prenatal alcohol exposure should aim control for the effects of IQ. In line with this, future research should further aim to incorporate statistical analyses that control for the effects of potential confounding variables (e.g. differences in maternal characteristics).

Conclusion

Verbal learning and memory performance were investigated in children with a history of moderate to heavy prenatal alcohol exposure as well as in typically developing, demographically matched controls. In the Cape Town cohort, an encoding deficit emerged as the primary verbal learning and memory impairment for children with prenatal alcohol exposure when compared to typically developing controls from the same community. In the Detroit cohort, however, the primary deficit was apparent at the level of retrieval. Novel findings of relative impairments in recognition memory were reported for alcohol-exposed participants in both cohorts. These latter results support the proposal in previous literature that ineffective use of learning and retrieval strategies for children with prenatal alcohol exposure is the cognitive mechanism underlying verbal learning and memory deficits in FASD. Confirmatory research is, however, necessary.

The results of this research may be used to inform the development of educational tools that will aid in improving the use of learning and retrieval strategies. For example, the use of cognitive modelling by teachers may facilitate children's use of language functions to aid in the learning process (Watson & Westby, 2003). Furthermore, these results provide a significant contribution to the growing body of literature that is working towards defining a cognitive profile for FASD.