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Episodic Memory, Hippocampal Volume, And Effects Of Premature Birth In Young Children

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**EPISODIC MEMORY, HIPPOCAMPAL VOLUME, AND EFFECTS OF PREMATURE
BIRTH IN YOUNG CHILDREN**

by

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THESIS

Submitted to the Graduate School

of Wayne State University,

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CHAPTER 1 INTRODUCTION

Memory is a multifaceted phenomenon comprised of several distinct constructs or systems (i.e. Bauer et al., 2013). It is important to investigate the unique developmental trajectory of each memory system as previous research has found that developmental changes are not uniform across memory systems (Rajan & Bell, 2014). It has been theorized that the developmental changes that are observed in memory performance are paired with complex developmental changes in the hippocampus (Bachevalier, 2015; Daugherty, Bender, Raz, & Ofen, 2016; Daugherty, Yu, Flinn, & Ofen, 2015; Jabes & Nelson, 2015; Lavenex & Lavenex, 2015; Mullally, 2015; Newcombe, 2015), an essential brain region for episodic memory (Ofen, 2012; Scoville & Milner, 1957). Premature birth is linked to developmental differences in the hippocampus (de Kieviet, Zoetebier, van Elburg, Vermeulen, & Oosterlaan, 2012) as well as deficits in episodic memory (de Kieviet, van Elburg, Lafeber, & Oosterlaan, 2012; Rose, Feldman, & Jankowski, 2005).

With this study, I aim to investigate (a) the validity and reliability of behavioral assessment of episodic memory ability in young children and (b) the relationship between episodic memory ability and volume of the hippocampus in young children. Furthermore, I aim to explore the effect of extreme premature birth (born between 24 and 34 weeks of pregnancy) on the relationship between episodic memory and hippocampal volume. To accomplish these aims, we assessed children in the Metro Detroit area with both cognitive measures and magnetic resonance imaging (MRI).

Episodic Memory

Common distinction in considering memory is the division into two types of information storage: short-term memory and long-term memory. Long-term memory can be further

differentiated into procedural memory (memory for skills) and declarative memory (memory for information) (Squire, 1987). Declarative memory can be further differentiated into semantic memory (memory for facts) and episodic memory (memory for events) (Tulving, 1983). Episodic memory requires the association of multiple pieces of information (Allen & Fortin, 2013) and develops throughout childhood. Specifically, individuals do not appear to be able to fully utilize episodic memory until late childhood or adolescence (Bauer et al., 2013; Tulving, 2002).

More precisely, episodic memory involves the recognition or recall of previously learned material that is related to a specific time and references a specific person, place, or event with more detail than other memory systems (Tulving, 2002). The detail within episodic memories is so specific that the retrieval process has been referred to as “mental time travel” (Tulving & Markowitsch, 1998). Additionally, the extreme detail of episodic memories allows for association of particular aspects of an experience so that an event may become identifiable and differentiated from other similar events (Baddeley, 1998). Furthermore, this level of association of information is unique to episodic memory.

Episodic memory ability can be assessed with a variety of measurements. Examples of such measurements include a word-list recall task that requires the participant to recall specific words from the previous trial (e.g. Omizzolo et al., 2013); a source recall task that requires the participant to recall a fact and to identify the person that provided them with that fact (e.g. Rajan & Bell, 2014); a picture recall task that requires the participant to recall the content and location of a series of pictures (Bauer et al., 2013); and an associative memory task that requires the participant to recall both components of the associated pair (e.g. Salvan et al., 2014). In each of such tasks, specific aspects of episodic memory ability are being evaluated; however, it is not

clear which measurements provide the most accurate assessment of episodic memory across development (Tulving, 2002).

Brain Substrate of Episodic Memory

Structures within the medial temporal lobe (MTL), and in particular the hippocampus, is essential for episodic memory (Scoville & Milner, 1957). The maturation of the hippocampus is largely unknown, but what is known suggests a complex development with changes in structure and function. Some evidence suggests that the total volume of the hippocampus is similar to that of an adult by 4 years of age (Gogtay et al., 2006); however, developmental changes in the morphology of the hippocampus continue to occur until adulthood (Daugherty et al., 2016). When a relationship between volume of the hippocampus and memory performance is considered, there is a negative correlation between hippocampal volume and memory performance for children, adolescents, and young adults, but a positive correlation for adults. However, this analysis only included one study of young children with the youngest subject being 7 years of age (Van Petten, 2004). Moreover, it appears that the relationship between the volume of the hippocampus and episodic memory is task-dependent for children (Brunnemann et al., 2013).

Establishing this brain-behavior relationship becomes more complicated when multiple memory tasks are utilized.. Specifically, hippocampal volume is significantly related to performance on visual episodic memory tasks in typically developing children (ages 7-11) but not performance on a verbal episodic memory task (Brunnemann et al., 2013). The relationship between episodic memory and volume of the hippocampus also appears to be altered when deviations from normal development occur. Specifically, larger hippocampal volume is positively correlated with memory retention and discriminability in healthy adults (Pohlack et al.,

2014) but larger hippocampal volume is negatively correlated with memory performance for adults with impaired synaptic pruning (Molnar & Keri, 2014). Moreover, episodic memory performance is positively correlated to hippocampal volume for full-term born children, but not for preterm born children (Brunnemann et al., 2013). In this project I aim to provide additional evidence to enhance understanding of: (i) the relationship between hippocampal volume and episodic memory performance in young children, and (ii) the possible implications of preterm birth in instigating deviations from normal development that may be reflected in altered brain-behavior relationship.

Effects of Premature Birth on Episodic Memory and Hippocampus

Premature birth affects over 500,000 children in the United States annually (World Health Organization, 2014) and the number of preterm born children has increased in past 10 years (de Kieviet, Zoetebier, et al., 2012). The increase in preterm birth was accompanied by an increase in survival rate (de Kieviet, Zoetebier, et al., 2012) and the effects of preterm birth on behavior, cognition, and physical development are more prominent when the level of prematurity (number of weeks under 40) is more severe (S. Raz, Debastos, Newman, & Batton, 2010). Specifically, preterm birth is associated with deficits in immediate recall and everyday memory tasks (Isaacs et al., 2000; Rose et al., 2005), both of which include an episodic memory component. However, other evidence suggests that although young children struggle with episodic memory overall and children born preterm are at risk for developing memory difficulties, there is no significant difference in this ability between preterm and full-term born children at a young age (Briscoe & Gathercole, 2001; Brunnemann et al., 2013). These contradictory findings indicate that more research is needed to fully understand the effect of preterm birth on episodic memory performance.

Preterm birth is often accompanied by serious complications, such as hypoxia-ischemia (Isaacs et al., 2000; Omizzolo et al., 2013), to which the hippocampus is extremely vulnerable (Abernethy, Palaniappan, & Cooke, 2002). Therefore, preterm birth is also related to higher a risk of reduced hippocampal volume, which is present starting from a young age (Brunnemann et al., 2013; Isaacs et al., 2000; Omizzolo et al., 2013). The risk of hippocampus abnormalities following preterm birth is very high, as high as 67% in one sample (Fuller, 1983). In addition to the structural differences in the hippocampus at birth, preterm born children also exhibit decreased hippocampus growth compared to full-term born children (Thompson, 2014). However, a recent meta-analysis reported that although total brain volume is significantly less in preterm born children compared to full-term born children, other anatomical differences between these groups greatly depends on the experimental design of the research (a whole-brain approach verses a region-specific approach) (de Kieviet, Zoetebier, et al., 2012). Specifically, preterm birth is related to reduced hippocampal volume, but this relationship may or may not hold true when the volumes are corrected for total brain volume. This indicates that preterm birth may be related to decreased brain volumes overall, but not to unique reductions in hippocampal volume (de Kieviet, Zoetebier, et al., 2012; Isaacs et al., 2000; Omizzolo et al., 2013).

The decreased brain volume observed in preterm compared to full-term born children is related to cognitive deficits (de Kieviet, Zoetebier, et al., 2012). Specifically, reduced hippocampal volume is correlated with impairments in episodic memory performance (Isaacs et al., 2000), which indicates that the neuroanatomical differences between preterm and full-term born children can provide information about potential cognitive difficulties for preterm born children. Further research is needed to understand if deficits in episodic memory are related to

unique differences in hippocampal volume of preterm born children or if these deficits are due to overall reductions in brain volume.

The research reviewed above suggests that development of the hippocampus and the relation between volume of the hippocampus and episodic memory appears to be different in preterm born children compared to full-term born children. Specifically, hippocampal volume at term equivalent age does not strongly relate to cognitive development at the age of two years for preterm born children (Beauchamp et al., 2008), and hippocampus volume is not significantly related to learning and memory in preterm born children (Omizzolo et al., 2013). This null association could indicate that memory functioning is supported by additional brain regions in preterm individuals that suffered early damage to the hippocampus (Omizzolo et al., 2013). The understanding of episodic memory and development of the hippocampus in preterm children is vital. Understanding deficits at a young age can allow for early detection and identification of at-risk children and in turn, allow for prevention of severe negative outcomes following preterm birth (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009; Padilla, 2014).

Summary and Study Aims

In this study I focused on the unique system of episodic memory that allows for detailed recall of associated information (i.e. content with location). Episodic memory performance is assessed in many ways, but more research is required to discover the most reliable and valid method of assessment. The hippocampus is related to episodic memory but the exact relationship is unclear, especially for young children, due to complex developmental trajectories. These relationships can become more complex when deviations from normal development occur, such as preterm birth. Although preterm birth is thought to be associated with reduced episodic

memory performance and hippocampal volume, there are inconsistent findings of episodic memory performance at a young age in preterm born children compared to full-term born children. Furthermore, it is not fully understood how term status affects the relationship between hippocampal volume and episodic memory performance. A more complete understanding of this brain-behavior relationship could ultimately help with detecting and potentially alleviating cognitive deficits for preterm born children.

Aim 1- Behavioral assessment of episodic memory. Episodic memory performance is difficult to measure directly, because the “mental time travel” is very complex and detailed (Tulving & Markowitsch, 1998). Nevertheless, there are many tasks that potentially measure episodic memory performance. The purpose of this aim was to investigate how these different behavioral assessments relate to each other, and determine if a latent construct for episodic memory could be formed using both standardized and experimental performance-based tasks. It was hypothesized that the episodic memory tasks would load onto two separate factors. Specifically, it was theorized that there would be (a) an associative component that would contain all tasks that required simultaneous recall or recognition of more than one piece of information (i.e. content and location), and (b) an item component that would contain all tasks that required recall or recognition of only a signal piece of information (See Figure 1).

Aim 2- Assessment of relationship between episodic memory and hippocampal volume. As discussed above, the hippocampus is essential for episodic memory; however, the relationship between hippocampal volume and memory performance is not well understood, especially in young children. The purpose of this aim was to investigate the relationship between the performance on behavioral measures for episodic memory and hippocampal volume in young children. It was hypothesized that there would be a significant negative correlation between

hippocampal volume and episodic memory performance. Although all factor scores were investigated, it was hypothesized that the relationship with hippocampal volume would be specific to the associative component from the factor analysis.

Aim 3 (exploratory)- Assessment of effect of term status on episodic memory and the relationship between episodic memory and hippocampal volume. Preterm birth can lead to deficits in behavior, cognition, and physical development (S. Raz et al., 2010) that can impact the children later in life. The relationships between reduced brain volume and cognitive deficits need to be investigated further to fully understand the impact that these deficits may have as the children develop. Therefore, I aim to provide a more complete understanding of the effect of preterm birth on episodic memory performance and hippocampus development. This aim was tested using independent sample *t*-tests and Fisher *z*-tests to compare the findings from the first two aims for full-term born children verses preterm born children. It is hypothesized that there will be no difference in episodic memory performance between preterm born and full-term born participants. However, it is anticipated that preterm born participants will have reduced hippocampal volume compared the full-term participants. Additionally, it is hypothesized that there will be a differential relationship between hippocampal volume and episodic memory performance for preterm born children verses full-term born children such that the brain-behavior relationship will only be significant for the full-term born participants.

CHAPTER 2 METHODS

Participants

Fifty-two young children (ages 5-6 years) from the Metro Detroit area were recruited to participate in this study. Term status was determined based on birth weight with 2,500 grams (5 lbs., 8 oz.) as the minimum weight for the full-term group. Of note, there were four participants born between 36 and 37 weeks gestation that met the birth weight requirement and were included in the full-term sample. Additionally, there were five full-term participants that did not provide birth weight or gestational age data; all of these individuals were included in the full-term group. Of the 52 participants recruited, one full-term born participant was excluded from all analyses for brain anomalies observed on the MRI. Additionally, two full-term born participants were excluded from all group differences analyses due to not meeting the minimum birth weight requirement for inclusion into the full-term group. Therefore, 49 participants (25 preterm born) were included in the analyses. However, only 32 of these participants (12 preterm born) completed the MRI portion of the experiment due to voluntary withdrawal or inability to be scanned for safety reasons (i.e. metal in body).

The full-term born children were recruited through Wayne State University Pipeline and flyers handed out in the community. The preterm born children were recruited from the participant list of a previous study, which recruited participants from the neonatal intensive care unit at William Beaumont Hospital in Royal Oak, Michigan. The sample size of the study is smaller than ideal based on many recommendations for minimum sample size for factor analysis (Osborn & Costello, 2004); however, it is sufficient based on an n-to-k ratio of 10:1 (Nunnally, 1978). Additionally, using G*Power and the results of a similar study (Brunnemann et al., 2013), it was determined that the sample size in the study was sufficient to investigate group differences

in episodic memory performance and hippocampal volume ($N = 12$, $1 - \beta = .80$) and to investigate an overall relationship between episodic memory performance and hippocampal volume ($N = 31$, $1 - \beta = .80$). However, the sample size of each group was smaller than recommended ($N = 31$) to investigate group differences in the brain-behavior relationship. Nevertheless, a larger sample size was not feasible at this time due to the nature of the preterm sample recruitment method. Also, this sample size was consistent with similar published works (Briscoe & Gathercole, 2001; Brunnemann et al., 2013) and this study was intended to provide knowledge for future studies with larger samples.

Procedure

The participants were assessed with two four-hour sessions, which were made child-friendly with techniques such as a space theme and numerous practice sessions (Barnea-Goraly et al., 2014; Raschle et al., 2009). The children were provided with an “astronaut’s training manual” that was used to track their progress through each phase of the study. The first session was completed on the Wayne State University campus and consisted of behavioral assessments (i.e. intelligence and memory) and an initial exposure to an artificial MRI scanner. During the initial exposure, the experimenters emphasized the importance of staying still and relaxed in the MRI and allowed the children to practice this skill.

The second session was completed at the Wayne State University MR Research Facility within Harper Hospital and consisted of additional MRI training, the MRI scan, and additional behavioral assessments. The MRI training monitored the children’s ability to remain motionless with a temporal motion-tracking device and acted as a second exposure with an artificial MRI scanner that was similar to the actual scanner (i.e. sounds, response boxes, and video screen). Following the behavioral assessments of the second session, the participants were compensated

for their time. In addition to compensation, the parents of the participants received a brief psychological report of the behavioral assessment results and images of their children's brains.

Behavioral Measures of Episodic Memory

WPPSI-IV: Picture Memory and Zoo Locations. The Wechsler Preschool and Primary Scale of Intelligence, fourth edition (WPPSI-IV) is a standardized measure intended for children ages 2 – 7 years. Although there are several subtests that make up the WPPSI-IV, the subtests of interest for this study are Picture Memory and Zoo Locations. These subtests are intended to measure the ability to store and recognize or reproduce visual information within a short time frame (Wechsler, 2012). The Picture Memory subtest consists of stimulus items and test items. The participants view each stimulus for 3 or 5 seconds, depending on difficulty, and complete the corresponding test item immediately following this presentation. The stimulus consists of one to seven target stimuli and the same images appear in several stimuli. The test item consists of the target stimuli and additional foil stimuli. The participants continue to complete items until they make an error on three consecutive test items. A response is considered an error if any image from the target stimulus is not recalled.

The Zoo Locations subtest consists of a learning period (viewing the item for 3 or 5 seconds) and a testing period (replicating the item from memory). Each item consists of animal cards placed in specific locations on a grid. The first trial includes one animal in a 2x1 grid and the items increase in difficulty up to seven animals in a 3x3 grid. Each animal is repeated in multiple items, but is not in the same grid location across items. The participants continue to complete items until they make an error on two consecutive test items. A response is considered an error if any animal from the target stimulus is not recalled in the correct location. Performance on both subtests was evaluated based on participants' accuracy. Both subtests have strong

internal consistency (Picture Memory $r_{xx} = .91$; Zoo Locations $r_{xx} = .86$) and moderate validity with measures of executive functioning ($r = .26-.54$) (Differential Ability Scales, second edition and A Developmental Neuropsychological Assessment, second edition; Wechsler, 2012).

CVLT-C. The California Verbal Learning Test, Children's Edition (CVLT-C) is a standardized measure intended for children ages 5 – 16 years. This task is intended to measure verbal memory with a list of 15 words from three semantic categories (Delis, Kramer, Kaplan, & Ober, 1994). This task consists of five learning trials that include a verbal presentation of the list by the examiner and a verbal free-recall phase by the participant. The presentation order is consistent from trial-to-trial and includes all 15 words, presented approximately 1-second apart. The free-recall phase does not have a specific order, as the participants are instructed to “say them in any order- just say as many of them as you can” (Delis et al., 1994, p. 11). Only the data from the five learning trials were utilized in this study, even though this task also includes a distraction trial, a short-delay trial, a long-delay trial, and a recognition trial.

Performance on this task was evaluated by correct total recall for the first five learning trials. This task has acceptable psychometric properties including strong average across-trial recall consistency ($\alpha = .85$) and strong average across-word recall consistency ($\alpha = .81$). In addition, validity is acceptable for this task, as evidenced by an exploratory factor analysis that included a General Verbal Learning factor and a significant correlation ($r = .33$) with a verbal subtest (Vocabulary subtest of Wechsler Intelligence Scale for Children-Revised) (Delis et al., 1994).

Picture Sequencing. The NIH Toolbox Picture Sequence Memory Task (Picture Sequencing) is summarized here, for a full description of the task see Bauer et al. 2013. The Picture Sequencing task is a computerized task administered through the Internet and consists of

a practice phase and two test items. The stimuli are color images that represent actions (i.e. “bake the cake”) and all images of one trial correspond to a common theme (i.e. “how to have a birthday party”). The images are presented individually, in a fixed order, at the center of the screen as an audio recording describes the action. Each image is then assigned a unique location on the outer edge of the computer screen. During the practice phase, the participants are presented with two different themes of four images each. During both trials of the test phase, the participants are presented with the same theme of nine pictures. Performance on this measure was evaluated by the participants’ ability to place the images in consecutive ascending order.

This task has moderate convergent validity with a sentence repetition task (A Developmental Neuropsychological Assessment, second edition) [$r(110) = .50, p < .001$] but poor discriminant validity with a vocabulary task (Peabody Picture Vocabulary Test, fourth edition) [$r(112) = .58, p < .001$] (Bauer et al., 2013). However, it should be noted that this discriminant validity concern was not present with older participants (Bauer et al., 2013). Despite this validity concern with young participants, this task was utilized, because Picture Sequencing is a unique measurement of memory in that it requires recall of the content and location of an image.

Picture-Pair. Associative Line Drawing Memory (Picture-Pair) is an experimental computerized task developed in our lab, specifically designed to test associative memory, and adapted for assessment in children (Daugherty & Ofen, 2015). Picture-Pair consisted of a practice phase and two trials, which consisted of a study phase, a 1-minute distraction task (counting backwards by three from a random number), and a recognition phase. The stimuli used for this task were 132 black line drawings within a $2\frac{5}{8} \times 2\frac{5}{8}$ inch white square.

During the study phase, participants were randomly presented with 26 picture pairs for 5 seconds each with a 1-second inter-trial interval. The drawings were presented with a black background on a 13-inch screen of a MacBook Pro laptop with a resolution of 1280 x 800 and a refresh rate of 60 Hz. The group of 26 image pairs that each participant was presented was counterbalanced based on participant number. When one stimulus was presented, it appeared in the center of the screen. When a pair of stimuli were presented, they were presented 3-inches apart on opposite sides of the screen. Stimuli that could have been encoded differently due to their position in the presentation order (i.e. first and last) were removed from the testing phase.

The recognition phase was completed in two parts, an item recognition test and a pair recognition test, and the order of these tests was counterbalanced based on participant number. The item recognition test consisted of 16 individual line drawings (8 target drawings shown in the study phase and 8 foils not shown in the study phase). The pair recognition test consisted of 16 drawing pairs comprised entirely of images presented during the study phase. Half of the pairs were presented in the test phase exactly as they appeared in the study phase (complete pairs) and half were comprised of two drawings that were not paired together in the study phase (recombined pairs). Performance on both tests of the recognition phase was evaluated based on correct recognition of target images (hits) minus recognition errors (false alarms). The average performance across both trials was used as an overall measure of task performance for both tests of the Picture Pair task. As this is an experimental task, no validity or reliability measures were available.

Object Memory. Object Memory is an experimental computerized task designed to test memory recognition for objects in addition to considering the effect of category inclusion on object memory. This task was adapted for children from a more complex task that was developed

in our lab to test differences between scene and object memory in adults. Object Memory consisted of a practice phase and two trials. A trial consisted of a study phase, a 1-minute distraction task (counting backwards by three from a random number), and a recognition phase. The stimuli used for this task were 256 color-images of objects. Half the stimuli were equally distributed into eight distinct object categories (i.e. bread, cars, etc.) and the other half of the stimuli were from unique object categories. There were six additional images used during the study phase as an image repetition test to ensure the participants were attempting to memorize the pictures.

During the study phase, participants were randomly presented 70 images (64 target images and 3 images for the image-repetition task) for three seconds each with a 1-second inter-trial interval. Half of the target images were from four distinct object categories (within category images) and half were from unique categories (across category images). The images were presented with a black background on a 13-inch screen with a resolution of 1280 x 800 and a refresh rate of 60 Hz. The group of 70 images was counterbalanced based on participant number. For the image-repetition test of the study phase, the participants were asked to indicate, with a button press, when an image repeated. Although the participants were not aware of the repetition pattern, the two copies of the image were separated either by zero, one, or two intervening images.

The recognition phase was completed in two parts, an old-new recognition test and a two alternative-force choice test (2AFC), and the order of these tests was counterbalanced based on participant number. The old-new recognition test consisted of 64 images (32 target images and 32 foil images) presented individually. The participant was required to indicate if the image was “old” (target image shown during the study phase) or “new” (foil). Half of the images during the

old-new test were within-category images and half were across-category images. The 2AFC test consisted of 32 trials of one target image and one foil presented simultaneously. The participant was required to select the target image. Half of the foils were from the same object category (within category item) as the target image and half were from a different object category (across category item). Performance for Object Memory was evaluated based on accuracy of detecting the target picture. This accuracy was evaluated for within category images as well as for across category images in both the old-new recognition test and the 2AFC test. The average performance across both trials was used as an overall measure of task performance for both tests of the Object Memory task. As this is an experimental task, no validity or reliability measures were available.

Brain Measures

MRI acquisition and post-acquisition processing. Hippocampal volume measures were taken for a T1-weighted magnetization prepared rapid gradient echo (MPRAGE) sequence that was collected using a 32-channel head coil in a 3 Tesla Siemens Verio (Siemens Medical AG, Erlangen, Germany) scanner at Wayne State University (WSU). The 3D sequence was acquired in the coronal plane, perpendicular to the anterior-posterior commissural axis with the following parameters: echo time = 4.26 ms; repetition time = 2200 ms; inversion time = 1200 ms; flip angle = 9.0°; pixel bandwidth = 130 Hz/pixel; GRAPPA acceleration factor PE = 2; interpolated voxel size 0.5 mm × 0.5 mm × 1.0 mm.

Prior to hippocampus manual demarcation, the T1 MPRAGE image set was corrected for inhomogeneity, resampled to a 0.5 mm³ isotropic voxel, and manually realigned to be perpendicular to the horizontal axis of the hippocampus, aligning the interhemispheric fissure. Individual differences in tilt and roll were also corrected manually. All preprocessing and manual

demarcation was completed with Analyze v11.0 (Biomedical Imaging Resource, Mayo Clinic College of Medicine, Rochester, MN, USA).

Hippocampal volumetry. Manual demarcation procedures were modified from (N. Raz, Rodrigue, Head, Kennedy, & Acker, 2004). Images were displayed (magnified $\times 2$) on a 21-inch digitizing tablet (Wacom Cintiq) and manually demarcated with a stylus by three independent raters. Prior to data collection, the independent raters were required to meet high reliability standards with an intra-class correlation coefficient (ICC(2)) (Shrout & Fleiss, 1979) of at least 0.85 for hemispheric measures, and 0.90 for bilateral total.

The hippocampus was measured in the coronal plane on every third slice extending from the mammillary bodies to the most posterior slice on which the pulvinar nucleus is still visualized, for a total of 15 – 22 slices. Volume was calculated as the sum of the area across measured slices and the computed volume from slices that were omitted. Hippocampal volumes were corrected for differences in Intracranial volume (ICV) via analysis of variance (Jack et al., 1989).

Intracranial volume measurement and volumetry correction. ICV was measured from the anterior-posterior commissures aligned T1 MPRAGE that was resampled to a voxel size of 0.5 mm^3 during post-processing. Prior to data collection, the independent raters were required to meet high reliability standards for manual demarcation with an intra-class correlation coefficient (ICC(2)) (Shrout & Fleiss, 1979) of .90 or greater. ICV was measured on every 20th slice, beginning with the most dorsal slice on which brain tissue was visualized and extending 10 slices ventrally. Volume of the hippocampus was corrected for individual differences in ICV via analysis of covariance (Jack et al., 1989).

Analytic Approach

All data were screened for missing data, outliers, non-linearity, homoscedasticity, normality, and multicollinearity across the entire sample. Grouped data screening was not completed because the group difference aim was an exploratory analysis. The ungrouped data screen included comparing participants with values to those without values on individual variables of interest, evaluation of z-scores with a univariate outlier cutoff of $z > |3.29|$, evaluation of skew and kurtosis with a cutoff of $z > |2.57|$, a regression with participant number as the dependent variable to find values for Mahal's distance with a multivariate outlier cutoff of $MD > 39.25$ (based on chi-square distribution with $\alpha = 0.001$ and $df = 16$), visual evaluation of pairwise scatter plots for extreme non-linearity and homoscedasticity, and evaluation of bivariate correlations between episodic memory variables with a multicollinearity cutoff of $r > .9$ (univariate) or Tolerance < 0.01 (multivariate). Group differences on demographic variables were evaluated using independent sample t-tests. A general linear modeling analysis was completed to explore potential differences between the corrected volumes of the left and right hippocampus.

A confirmatory factor analysis was completed with the episodic memory variables using Principal Component Analysis (PCA). As these episodic memory tasks were intended to measure similar aspects of memory, it was anticipated that the factors would be correlated. Thus, an oblique rotation with $\Delta = 0$ was used in this PCA. Individual factor loadings were only considered relevant at greater than .400 in an attempt to account for the small sample size. A factor was defined as any component with an Eigenvalue greater than 1.00 (Crawford et al., 2010). One PCA was completed for the whole sample without investigation of group differences in factor structure due concerns with the small sample size of each individual group.

The relationships between the factor scores from the PCA and the volume of the hippocampus were evaluated using bivariate correlations. The potential relationship between the composite scores of the PCA and hippocampal volume was evaluated further with a partial correlation to control for birth weight, income, gender, and age. The relationship between performance on the individual episodic memory tasks and the volume of the hippocampus was evaluated to investigate the potential of a task-dependent relationship. Additional partial correlations were performed to evaluate these potential task-dependent relationships while controlling for birth weight, income, gender, and age.

Prior to assessing potential term differences in the brain-behavior relationship, independent sample t-tests were completed to determine if there were term differences in episodic memory performance (factors of the PCA and individual tasks) or volume of the hippocampus. These potential group differences were evaluated further with analysis of covariance (ANCOVA) accounting for income, gender, and age. Then the relationship between episodic memory performance and volume of the hippocampus was evaluated for each term group separately. Separate bivariate correlations between the composite scores of the PCA and the volume of the hippocampus were completed for each group and Fisher z -tests were used to compare these correlations. Next, separate partial correlations were completed to control for income, gender, and age in the relationships between the composite scores and the volume of the hippocampus and Fisher z -tests were used to compare these correlations. Finally, separate bivariate correlations and partial correlations (accounting for income, gender, and age) were completed for each task to assess the potential task-dependent relationship between episodic memory performance and volume of the hippocampus for each term group separately and Fisher z -tests were used to compare these correlations.

CHAPTER 3 RESULTS

The data screen indicated there were no multivariate outliers, no concerns for non-linearity, homoscedasticity. However, there were concerns for multicollinearity, univariate outliers, and non-normality. The multicollinearity concerns were resolved when gestational age was removed from the analysis as gestational age was highly correlated ($r = .94$) with birth weight. There was one outlier on both overall socioeconomic status (Hollingshead, 2011) and parent rated family income as the scores were lower than the other scores on these variables. This issue was resolved by making the values less deviant by increasing them by one point. This transformation still allowed this participant to have the lowest score on socioeconomic status and income. Additionally, there were three significant findings in the missing data analysis. Participants without Picture Sequencing data ($N = 2$) had significantly higher scores on two variables of the Object Memory task ($p < .01$) than those with Picture Sequencing data. Those without birth weight and gestational age data ($N = 5$) had significantly lower verbal intelligence than those with birth weight ($p = .04$) and gestational age ($p = .02$) data. Those without hippocampal volume data ($N = 18$) had significantly lower birth weight ($p < .01$) and gestational age ($p < .01$). The missing data concerns were resolved by using pairwise deletion on all analyses. There were significant concerns with non-normality for one measure of Object Memory (2AFC across) but as the other three measures within normal limits, no transformations were performed to prevent interpretation confusion.

When investigating potential group differences on demographic variables, it was determined that the preterm born participants had higher parent rated family income on average compared to the full-term born participants ($t = -2.07, p = .05$); no other demographic variables were significantly different between groups (See Table 1). As expected, birth weight ($t = 15.37,$

$p < .01$) and gestational age ($t = 12.53, p < .01$) were lower for the preterm born participants on average when compared to the full-term born participants. The comparison of the right and left corrected hippocampal volumes determined that there was no difference between hemispheres ($F(1,29) = 1.24; p = .27$); therefore, the combined corrected volume of both hippocampi was used in all analyses.

Aim 1- Behavioral assessment of episodic memory

A PCA was completed to test if individual task performance would separate into distinct factors based on the level of association required during recall or recognition. The analysis indicated there were three distinct factors (See Table 2 and Figure 2). Factor 1 included measures from Picture Memory, Zoo Locations, Picture Sequencing, and the Picture-Pair pair recognition test. Because each of these tasks required a certain level of association, such that at least two components of stimuli (i.e. content and location) be recalled or recognized simultaneously, we termed Factor 1 ‘Associative’. Of note, when compared to the other tasks, these four measures require two or more components to be remembered or recalled simultaneously. Inclusion of associations between pieces of information is a hallmark of episodic memory; therefore, this ‘Associative’ factor is likely the best factor to capture individual differences in episodic memory performance.

Factor 2 included measures from CVLT-C, the Picture-Pair item recognition test, and the Object Memory old-new recognition test. The common aspect contributing to performance in all of the measures included in Factor 2 is that they require only one piece of information to be recalled at a time. This factor was thus termed ‘Item’ factor.

Factor 3 included measures from the Picture-Pair pair recognition test and the Object Memory 2AFC test. Although these measures include multiple stimuli during the test phase

similar to the tasks in Factor 1, these tasks are unique in that they require an additional level of decision making and higher-level processing of the information that are not required for performing the tasks included in the Associative Factor. Specifically, they include interference, or the simultaneous presentation of target stimuli with foil stimuli, following a delay. This combination of interference with delay is thought to require a more in-depth comparison between the target image and the foil image to make the correct decision. This factor was thus termed ‘Decision’ factor. Although it was unexpected that the Picture-Pair pair recognition test loaded onto two factors, it is the only task that requires both associative memory and a complex decision to complete successfully.

Aim 2- Assessment of relationship between episodic memory and hippocampal volume

The composite scores, specifically the Associative Factor score is thought to be a more robust measure of episodic memory because it accounts for performance across different types of associative memory. Thus, composite scores from all three factors of the PCA were used to assess the potential factor specific relationship between episodic memory performance and volume of the hippocampus. None of the factor scores were significantly correlated with volume of the hippocampus ($r \leq .28$, $p \geq .23$) even after controlling for birth weight, income, gender, and age ($r \leq .34$, $p \geq .28$; See Table 3).

Although the composite scores from the PCA are thought to be more robust measures of episodic memory, it is possible that using these overall measures to evaluate the brain-behavior relationship would mask a task-dependent effect. Therefore, the relationship between episodic memory performance and hippocampal volume was evaluated for each task separately. None of the individual task performances were significantly related to the volume of the hippocampus even after controlling for birth weight, income, gender, and age (See Table 4). Nevertheless, the

Picture-Pair pair recognition test had a non-significant trending correlation with hippocampal volume ($r = .29, p = .097$; See Figure 3).

Aim 3 (exploratory)- Assessment of effect of term status

Although preterm birth is related to decreased episodic memory performance, these differences do not appear to be present at a young age; however, there appears to be a different relationship between episodic memory performance and volume of the hippocampus at this young age (Brunnemann et al., 2013). I therefore tested not only term differences in episodic memory performance and volume of the hippocampus, but I also tested term differences in the relationship between episodic memory performance and volume of the hippocampus. Term differences in episodic memory performance were investigated using the composite scores from the PCA and the individual task scores. Although the preterm born participants performed significantly better on the Picture-Pair item recognition task before ($t = -3.11, p = .003$) this was not significant after controlling for income, gender, and age ($F(1,29) = 2.85, p = .10$). There was no significant difference between the preterm born and the full-term born participants in episodic memory performance on any other task (See Table 5).

Preterm birth is also associated with decreased hippocampal volume, even at a young age (Brunnemann et al., 2013). Surprisingly, it was determined that the preterm born participants in this sample had significantly larger hippocampal volume than the full-term born participants even after controlling for income and gender ($t = -3.52, p = .001$; See Table 4).

Last, we investigated the relationship between episodic memory performance and hippocampal volume by term, as it was anticipated that the full-term born participants would exhibit a stronger relationship than the preterm born participants due to their risk for decreased performance and brain volume. Although the relationship between the factor scores and the

volume of the hippocampus was not significantly different between the two groups ($z \leq |0.24|$, $p \geq .81$; See Table 6), there were significant and non-significant trending relationships for the full-term born participants that were not present for the preterm born participants when the individual task scores were evaluated (See Table 7). Specifically, performance on the Picture-Pair item recognition test was significantly negatively correlated with hippocampal volume when age, gender, and income were controlled for ($r = -.52$, $p = .04$; See Figure 3) and the performance on Zoo Locations had a non-significant trending correlation with the hippocampal volume when age, gender, and income were controlled for ($r = -.47$, $p < .06$; See Figure 4) for the full-term group only.

CHAPTER 4 DISCUSSION

As anticipated, the individual episodic memory measures reliably separated into different components based on task demands. Specifically, the episodic memory measures loaded onto separate factors based on the level of association that was required for the task. Additionally, the measures separated based on the level of decision making required. This factor structure was fairly defined with only one task loading onto more than one factor. Although this cross loading was not ideal, it was not entirely unexpected due to the uniqueness of this measure (required both a high level of association and a complex decision). Although the composite scores of the factor analysis were not significantly correlated with the volume of the hippocampus for the overall sample, performance on an individual task (Picture Pair pair recognition test) displayed a trending relationship with volume of the hippocampus. Additionally, when potential term differences were evaluated, there was one significant and one non-significant trending brain-behavior relationship for the full-term born participants that were not present for the preterm born participants.

The hippocampus is essential for episodic memory (Scoville & Milner, 1957) but this relationship is rarely tested in young children (ages 5-6 years) as evidenced by a recent meta-analysis that only had studies with participants older than six years of age (Van Petten, 2004). Additionally, research with children and adolescents (ages 7-18) reveal that episodic memory performance is significantly related to volume of the hippocampus with certain tasks but not others (Brunnemann et al., 2013; Van Petten, 2004). It is possible that these inconsistent findings are indicative of true developmental changes as both episodic memory (Bauer et al., 2013; Tulving, 2002) and hippocampus morphology (Bachevalier, 2015; Daugherty et al., 2016; Daugherty et al., 2015; Gogtay et al., 2006; Jabes & Nelson, 2015; Lavenex & Lavenex, 2015;

Mullally, 2015; Newcombe, 2015; Omizzolo et al., 2013) continue to change throughout childhood and into adulthood. However, these inconsistent findings may also be related to the suboptimal use of individual task performance as a measure of episodic memory but the data in this study do not support the theory that the composite scores will be more consistently correlated with the volume of the hippocampus. However, it is possible that the composite score null findings in this study are reflecting a developmental phenomenon; specifically, that the measures we use to evaluate episodic memory in adults are not appropriate to measure episodic memory in young children.

When preterm born participants were compared to full-term born participants in this sample, the preterm group had significantly larger hippocampal volume and better episodic memory performance. It is unclear as to why the preterm born participants had larger hippocampal volume and performed better on some measures of episodic memory. One possibility is bias in selection criteria of the participants included in each of the groups. For example, there may be differences in socioeconomic status that were unaccounted for in the measures used in this study, or there may be systematic biases in the high attrition of the preterm born participants in the MRI portion of the study that contributed to the findings.

It was discovered that the full-term participants displayed a significant relationship between performance on some episodic memory tasks that the preterm group did not, despite the fact that the preterm group was not characteristic of the population (i.e. had larger hippocampal volume than the full-term born participants). It is possible that some of the term group differences would become more apparent after accounting for injuries at birth and interventions received since birth as it is known that each of these variables effect preterm children's outcomes (Abernethy, Cooke, & Foulder-Hughes, 2004; Als et al., 2004). Additionally, there were several

non-significant term group differences in the relationship between episodic memory performance and volume of the hippocampus, such as the difference in dispersion seen in the correlation between the Associative Factor and volume of the hippocampus (See Figure 5), that may become more apparent with a larger sample size.

Although the findings of this study indicated that volume of the hippocampus was significantly related to performance on two of the episodic memory tasks and there were differences in the relationship between preterm born and full-term born participants, there was not strong evidence for this brain-behavior relationship overall. However, it is possible that there is a brain-behavior relationship in this sample that is unrecognizable in this study, as total hippocampal volume is not as sensitive to changes in hippocampus development as regional volumetry measures (Daugherty et al., 2016; Daugherty et al., 2015). Nevertheless, this was the measurement utilized in this study because the more sensitive measurements are not well defined and have less refined methods of measurement at this time. Additionally, it is possible that the relationship between episodic memory and hippocampal volume is not present at this young age. A recent study found no significant relationship at 4 years of age but there was a significant relationship at 6 years of age (Riggins, Blankenship, Mulligan, Rice, & Redcay, 2015).

Limitations and Future Directions

Researchers were not blind to term-status during testing. Although there are multiple reasons that the researchers were aware of this variable at the time of testing, the main reason was to ensure proper counterbalancing on the experimental tasks. The counterbalancing for these tasks was automated and based on participant number (i.e. odd verses even) and the most comprehensive method to ensure that full-term and preterm participants had the same counterbalancing was to provide them with different types of participant numbers (100 vs. 300).

An additional limitation to interpretation is that the full-term sample was recruited from a different location than the preterm sample due to authorization limitations, as the study was only approved to recruit preterm born participants from the hospital. However, efforts were made to match the samples on age, gender, and socioeconomic status to counteract some of the potential bias of different recruitment locations methods. Although there was a significant difference between the groups on family income, all reported analyses were also completed without the lowest income families in the full-term group and similar results were found. Due to the nature of the sample, the sample size is small and the analyses did not have sufficient power for all analyses (recommended $N = 31$ for $1 - \beta = .80$). The obtained power for the term group analyses varied due to differences in sample size and effect size (FT $1 - \beta \leq .50$; PT $1 - \beta \leq .40$). The sample size was considered in the interpretation of the results of all analyses. This study is part of a larger ongoing study that intends to recruit more participants to increase our confidence in the findings discussed above. Additionally, a longitudinal study is planned to investigate the development of episodic memory performance and hippocampal growth, specifically in preterm born children.

Conclusions

Episodic memory is related to the volume of the hippocampus in adults but this relationship is unclear in young children, especially children born preterm. The findings from this study suggest that, although episodic memory can be described with a composite variable, the relationship between hippocampal volume and episodic memory performance may be task dependent and may be different in preterm born children compared to full-term born children. Additionally, it is possible that the tasks that are used to assess episodic memory performance in

adults are not adequate for measuring episodic memory in young children. Additional research is needed to verify these findings.

Table 1

Preterm Born Participants compared to Full-Term Participants on Demographic Data

Variable	Full Sample				MRI Sample			
	Full-Term		Preterm		Full-Term		Preterm	
	Mean (SD)	Range	PT Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
<i>N</i> (Female:Male)	24 (11:13)	--	25 (17:8)	13S:12T	20 (9:11)	--	12 (7:5)	6S:6T
<i>C:AA:O:NR</i>	16:6:0:3 16:5:0:3	--	18:2:4:1	18:2:4:1	14:4:0:2	--	10:4:0:2 10:1:0:1	--
Age	6.05 (0.65)	5.05- 6.90	6.12 (0.63)	5.14- 7.04	6.09 (0.63)	5.05- 6.89	6.16 (0.60)	5.14- 7.04
Age Adj	6.04 (0.65)	5.05- 6.90	5.94 (0.62)	5.01- 6.87	6.09 (0.63)	5.05- 6.89	6.01 (0.60)	5.02- 6.87
Verbal IQ	108.54 (16.77)	73-143	109.52 (12.12)	85-141	107.90 (18.27)	73-143	109.58 (12.60)	88-141
Verbal IQ Adj	108.54 (16.77)	73-143	110.60 (12.54)	88-141	107.90 (18.27)	73-143	110.08 (12.65)	88-141
Overall SES	48.50 (13.26)	19-66	52.20 (10.45)	32-66	48.56 (12.94)	19-66	56.17 (6.80)+	37.5- 66.0
Maternal Edu	16.00 (2.31)	12-20	16.08 (2.12)	12-18	16.21 (2.39)	12-20	16.00 (2.09)	12-18
Paternal Edu	14.90 (3.01)	12-20	15.44 (2.27)	12-20	14.88 (2.92)	12-20	16.50 (1.73)	12-20
Income	7.41 (1.87)	3-9	8.36 (1.25)*	5-9	7.26 (1.94)	3-9	8.75 (0.87)*	5-9
Subjective SES	5.78 (1.76)	2-8	6.38 (1.28)	4-9	5.63 (1.83)	2-8	6.36 (1.36)	4-8
Birth Weight	3248.84 (455.05)	2500- 4054	1335.88 (370.81)**	810- 1935	3262.73 (461.78)	2500- 4054	1520.08 (348.35)**	940- 1935
Gestational Age	38.44 (1.63)	36.0- 41.0	30.32 (2.61)**	24.7- 33.5	38.64 (1.51)	36.0- 41.0	31.59 (1.28)**	28.1- 33.5

Note. S = Singleton; T = Twin; C = Caucasian; AA = African American; O = Other; NR = No Response; Adj = adjusted- Adjusted age was based on estimated due date; Edu = education in years. The overall SES measure is Four Factor Index of Social Status (Hollingshead, 2011). Subjective SES was parental ratings of where the family's status would be compared to other families in the United States on a 10-point scale. Gestational age is listed in the form of week.day.

+ $p = .07$; * $p \leq .05$; ** $p \leq .001$

Table 2

Episodic Memory Task Descriptions

Task	Stand [^]	Input Modality	Verbal/ Nonverb	Study Phase		Delay	Test Phase		Inter ⁺	Assoc.
				Ind. Stim.	Sim. Stim.		Ind. Stim.	Sim. Stim.		
Picture Memory	X	Visual	Both		X		X	X	Stimuli w/ each other	
Zoo Locations	X	Visual	Nonverb		X		X		Content w/ location	
Picture Sequencing	X	Visual, Auditory	Both		X		X		Content w/ location	
Picture-Pair pair test*		Visual	Both		X	X	X	X	Stimuli w/ each other	
CVLT-C Total Recall	X	Auditory	Verbal		X		X		--	
Picture-Pair item test		Visual	Both		X	X	X		--	
Object Memory old/new within		Visual	Nonverb	X		X	X		--	
Object Memory old/new across		Visual	Nonverb	X		X	X		--	
Object Memory 2AFC within		Visual	Nonverb	X		X	X	X	--	
Object Memory 2AFC across		Visual	Nonverb	X		X	X	X	--	

Note: Red text = the tasks that loaded onto the Associative Factor; Green text = tasks that loaded onto the Item Factor; Blue = tasks that loaded onto the Decision Factor; Purple = the task that loaded onto both the Associative Factor and the Decision Factor. Ind. Stim. = Individual Stimuli; Sim. Stim. = Simultaneous Stimuli.

*Cross-loaded onto Associative Factor (red) and Decision Factor (blue)

[^]Standardized tasks that can be compared to other children of the same age; raw scores were used for these tasks

⁺Interference is defined as the simultaneous presence of foil item(s) with target item(s)

Table 3

Relationship Between PCA Composite Scores and Total Corrected Hippocampal Volume for Whole Sample

Episodic Memory Variable	Bivariate Correlation ($N = 23$)		Partial Correlation ($df = 12$; birth weight, income, gender, age)	
	r	p	r	p
Associative Factor	.14	.53	.19	.51
Item Factor	-.13	.56	-.01	.98
Decision Factor	-.17	.44	.17	.55

Note. The partial correlations were statistically adjusted for birth weight, parent reported family income, gender, and age. Volume of the hippocampus of each hemisphere was corrected for total intracranial volume and the two corrected volumes were added together to create the total corrected volume of the hippocampus.

Table 4

Relationship Between individual task performance and Total Corrected Hippocampal Volume for Whole Sample

		Bivariate Correlation			Partial Correlation (birth weight, income, gender, age)		
Episodic Memory Variable		<i>r</i>	<i>p</i>	<i>N</i>	<i>r</i>	<i>p</i>	<i>df</i>
Associative Factor	Picture Memory	-.04	.84	34	.06	.78	22
	Zoo Locations	-.24	.18	34	-.30	.15	22
	Picture Sequencing	.07	.72	30	.10	.66	18
	Picture Pair pair test	.29	.097	33	.28	.19	22
Item Factor	CVLT-C	-.14	.44	34	-.32	.12	22
	Picture Pair item test	.05	.77	33	-.14	.53	22
	Object Memory old-new within	-.03	.90	26	-.08	.74	16
	Object Memory old-new across	.17	.39	26	.05	.84	16
Decision Factor	Object Memory 2AFC within	.12	.54	27	-.02	.94	16
	Object Memory 2AFC across	.17	.39	27	-.12	.64	16

Note. The partial correlations were statistically adjusted for birth weight, parent reported family income, gender, and age. Volume of the hippocampus of each hemisphere was corrected for total intracranial volume and the two corrected volumes were added together to create the total corrected volume of the hippocampus.

Table 5

Preterm Born Participants compared to Full-Term Born Participants on Episodic Memory Performance and Total Corrected Hippocampal Volume

Episodic Memory Variable	Full-Term		Preterm		<i>p</i> (<i>t</i> -test)	<i>p</i> (ANCOVA)
	Mean (SD)	<i>N</i>	Mean (SD)	<i>N</i>		
Associative Factor	.10 (0.76)	14	-.14 (1.25)	15	.54	.89
Picture Memory	16.25 (4.55)	24	15.92 (4.27)	24	.80	.56
Zoo Locations	11.29 (1.90)	24	10.48 (1.83)	25	.13	.02
Picture Sequencing	412.73 (84.09)	22	419.84 (91.61)	22	.79	.48
Picture Pair pair test	.10 (0.19)	23	.22 (0.27)	25	.08 ⁺	.32
Item Factor	.22 (1.10)	14	-.11 (0.94)	15	.40	.65
CVLT-C	32.21 (11.34)	24	33.68 (10.80)	25	.64	.32
Picture Pair item test	.46 (0.24)	23	.66 (0.21)	25	.003*	.10
Object Memory old-new within	.72 (0.10)	15	.69 (0.12)	18	.55	.56
Object Memory old-new across	.82 (0.12)	15	.83 (0.10)	18	.90	.92
Decision Factor	.15 (1.27)	14	-.08 (0.74)	15	.55	.79
Object Memory 2AFC within	.80 (0.13)	16	.79 (0.10)	18	.85	.56
Object Memory 2AFC across	.85 (0.16)	16	.89 (0.08)	18	.32	.40
Total Correct HCV	6441.71 (461.61)	20	7155.46 (687.49)	12	.001**	.008**

Note. The analyses of covariance (ANCOVAs) were statistically adjusted for parent reported family income, gender, and age. Volume of the hippocampus of each hemisphere was corrected for total intracranial volume and the two corrected volumes were added together to create the total corrected volume of the hippocampus (Total Corrected HCV).

⁺*p* = .08; **p* ≤ .05; ***p* ≤ .001

Table 6

Relationship Between PCA Composite Scores and Total Corrected Hippocampal Volume by term

Episodic Memory Variable	Bivariate Correlation ($N_{FT} = 14, N_{PT} = 7$)			Partial Correlation ($df_{FT} = 8,$ $df_{PT} = 2$); income, gender, age)		
	FT r	PT r	z (p)	FT r	PT r	z (p)
Item Factor	.14	.27	-0.23 (.82)	.06	.23	-0.16 (.87)
Associative Factor	-.12	-.32	0.36 (.72)	-.21	-.28	0.07 (.94)
Decision Factor	-.11	-.58	0.95 (.34)	-.15	-.39	0.24 (.81)

Note. The partial correlations were statistically adjusted for parent reported family income, gender, and age. The z value is the result of the two-tailed Fisher z -test used to compare the correlation or partial correlation of the full-term born participants to that of the preterm born participants. Volume of the hippocampus of each hemisphere was corrected for total intracranial volume and the two corrected volumes were added together to create the total corrected volume of the hippocampus. The Fisher z score could not be calculated with a df of 2 so a df of 4 was used for the preterm group to get an estimation of the term comparison for the partial correlations.

Table 7

Relationship Between individual task performance and Total Corrected Hippocampal Volume by term

Episodic Memory Variable	Bivariate Correlation				Partial Correlation (income, gender, age)				
	FT <i>r</i>	PT <i>r</i>	<i>z</i> (<i>p</i>)	(<i>N</i> _{FT} , <i>N</i> _{PT})	FT <i>r</i>	PT <i>r</i>	<i>z</i> (<i>p</i>)	(<i>df</i> _{FT} , <i>df</i> _{PT})	
Associative Factor	Picture Memory	.08	-.21	0.71 (.48)	(20, 12)	.05	-.18	0.34 (.69)	(14,7)
	Zoo Locations	-.43 ⁺	-.01	-1.09 (.28)	(20, 12)	-.47 ⁺	-.08	0.23 (.46)	(14,7)
	Picture Sequencing	.02	.12	-0.22 (.83)	(18, 10)	.02	-.28	0.34 (.73)	(12,5)
	Picture Pair pair test	.05	.31	-0.65 (.52)	(19, 12)	.05	.45	-0.9 (.37)	(13,7)
Item Factor	CVLT-C	-.12	-0.28	0.41 (.68)	(20, 12)	-.16	-.43	0.51 (.61)	(14,7)
	Picture Pair item test	-.48*	.10	-1.5 (.13)	(19, 12)	-.52*	.12	-1.18 (.24)	(13,7)
	Object Memory old-new within	.37	-.13	1.04 (.30)	(15, 9)	.44	-.47	0.91 (.36)	(9,4)
	Object Memory old-new across	.39	.16	0.50 (.62)	(15, 9)	.37	.02	0.34 (.73)	(9,4)
Decision Factor	Object Memory 2AFC within	.31	.20	0.24 (.81)	(16, 9)	.31	.06	0.24 (.81)	(10,4)
	Object Memory 2AFC across	.09	.17	-0.16 (.87)	(16, 9)	-.04	-.14	0.09 (.93)	(10,4)

Note. The partial correlations were statistically adjusted for parent reported family income, gender, and age. The *z* value is the result of the two-tailed Fisher *z*-test used to compare the correlation or partial correlation of the full-term born participants to that of the preterm born participants. Volume of the hippocampus of each hemisphere was corrected for total intracranial volume and the two corrected volumes were added together to create the total corrected volume of the hippocampus.

⁺*p* = .06; **p* ≤ .05

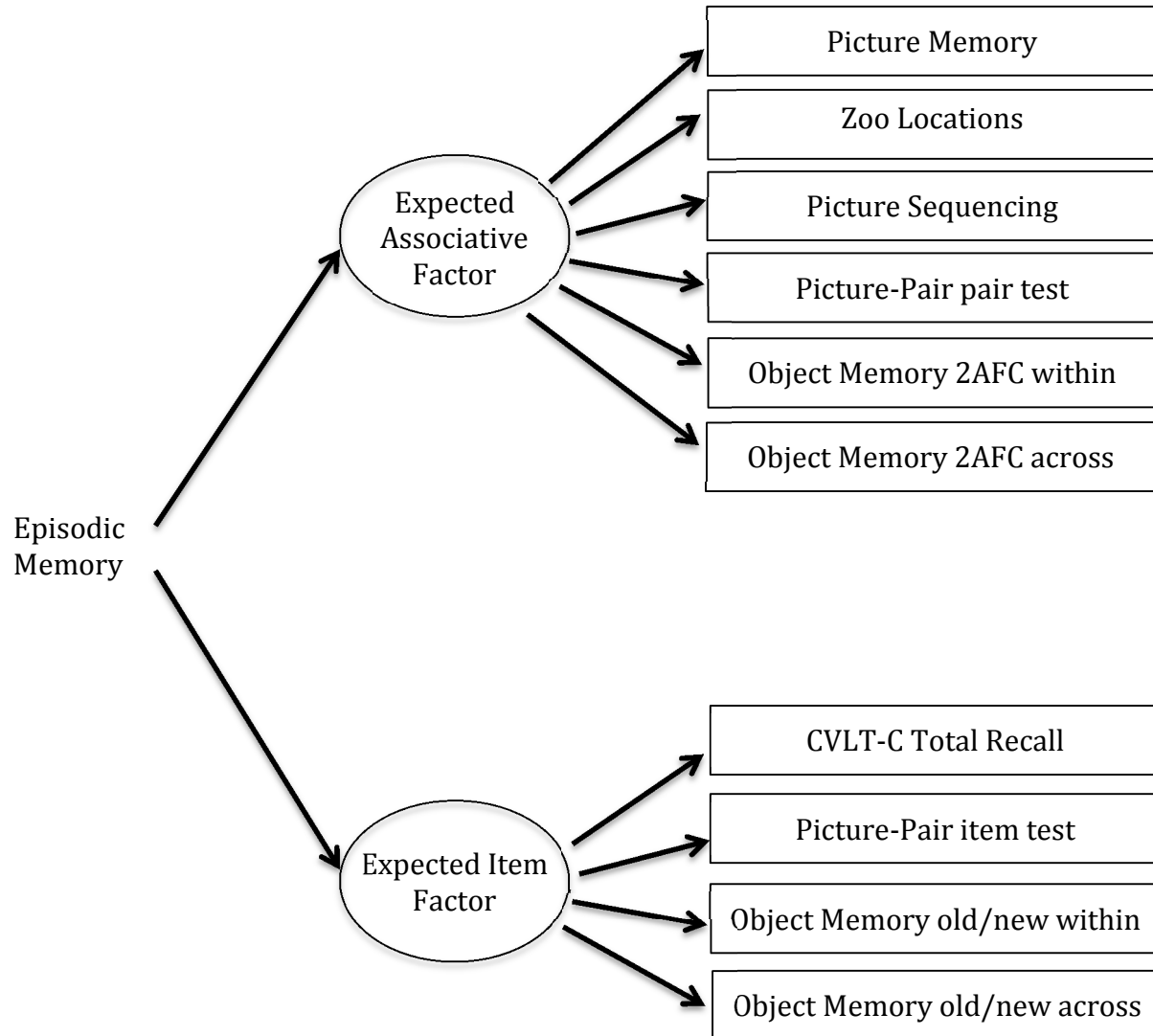


Figure 1. Expected outcome for episodic memory factor analysis.

It was hypothesized that the episodic memory tasks would load onto two separate factors based on the level of association required for correct memory recall or recognition.

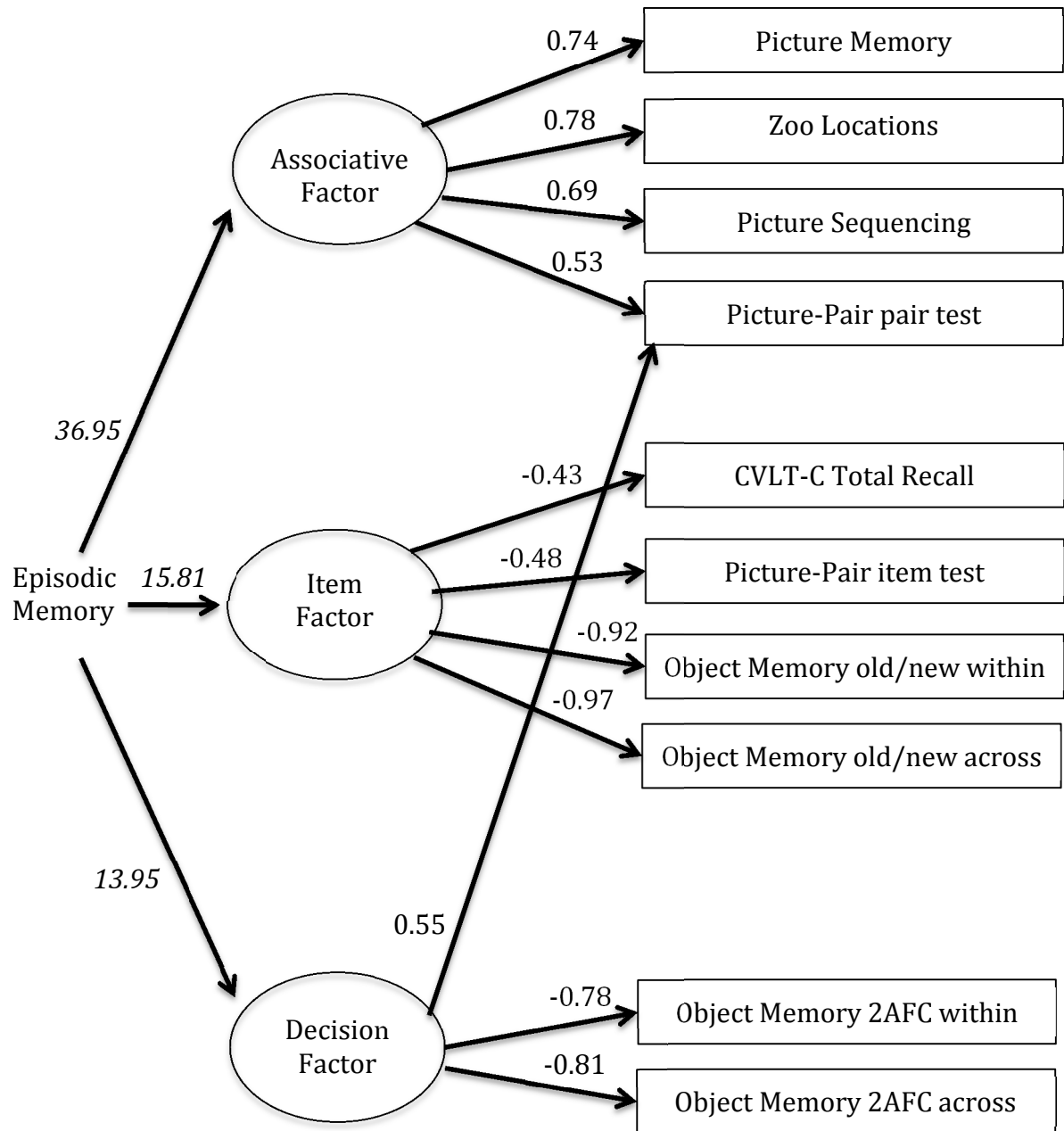


Figure 2. Observed outcome for episodic memory factor analysis.

A Principal Component Analysis was completed with oblique rotation ($\Delta = 0$) and there were three relevant factors. The numbers in italics indicate the percent of variance accounted for in each factor. The non-italicized numbers indicate the factor loading of each individual task onto each factor.

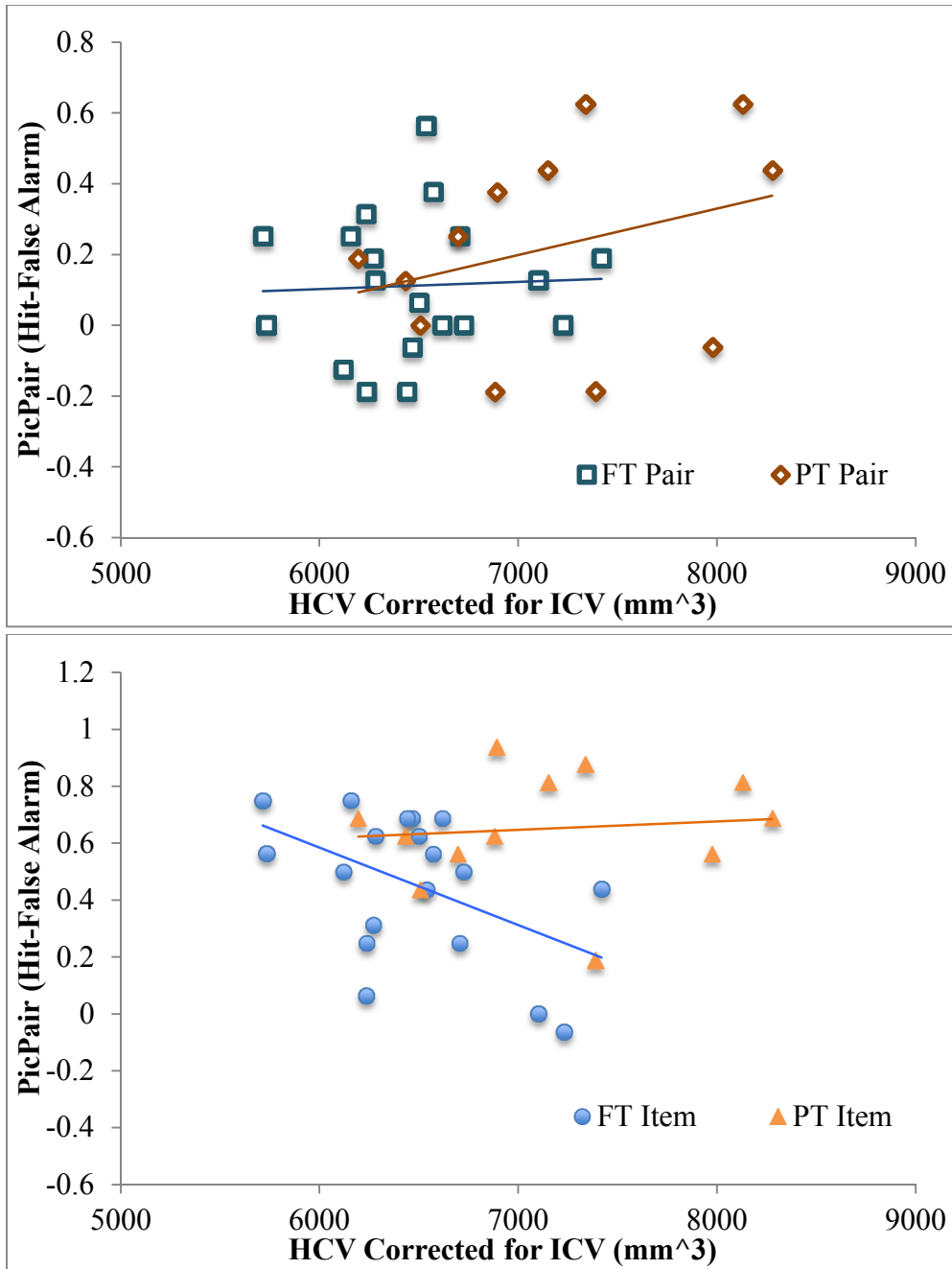


Figure 3. Correlation between performance on the Picture Pair pair recognition test and total corrected volume of the hippocampus.

Scores on the Picture Pair pair test (open markers) had a trending correlation with the volume of the hippocampus (HCV) corrected for intracranial volume (ICV) across the whole sample ($r = .29$, $p = .09$) but this relationship was not significant for either group. However, the scores on the Picture Pair item recognition test (solid markers) were correlated with HCV in the full-term born participants (FT; blue markers) after controlling for parent reported family income and gender ($r = -.52$, $p < .05$) but not for the preterm born participants (PT; orange markers).

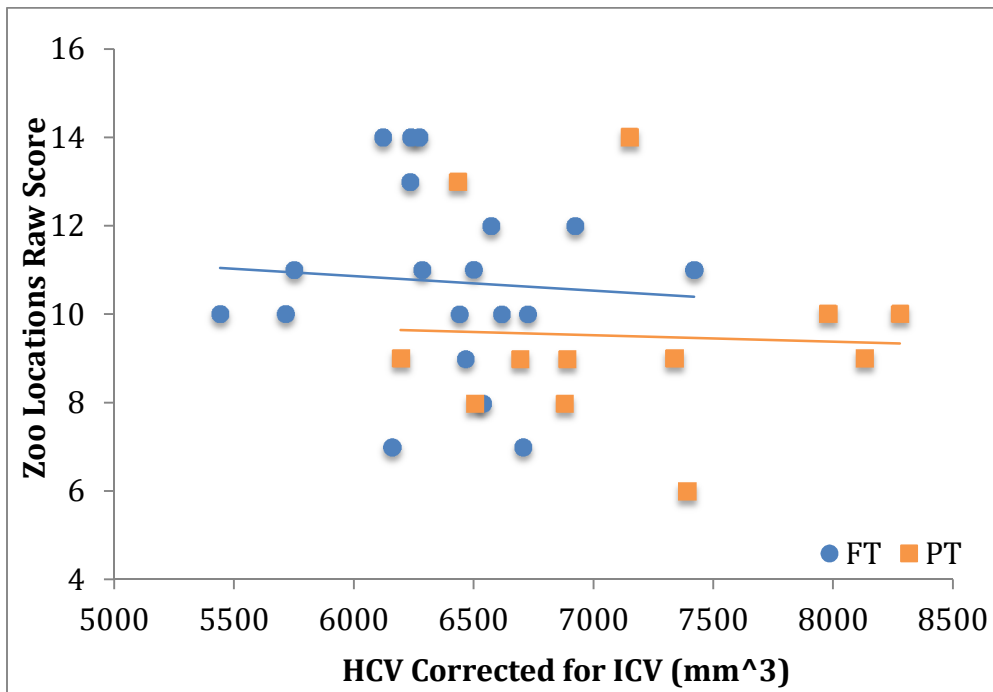


Figure 4. Correlation between performance on Zoo Locations and total corrected volume of the hippocampus.

Scores on Zoo Locations were not significantly correlated with the volume of the hippocampus (HCV) corrected for intracranial volume (ICV) across the whole sample ($r = -.24$, $p = .18$), but they did have a trending correlation with HCV for the full-term born participants (FT; blue markers) when parent reported family income and gender were control for ($r = -.47$, $p = .06$) that was not present for the preterm born participants (PT; orange markers).

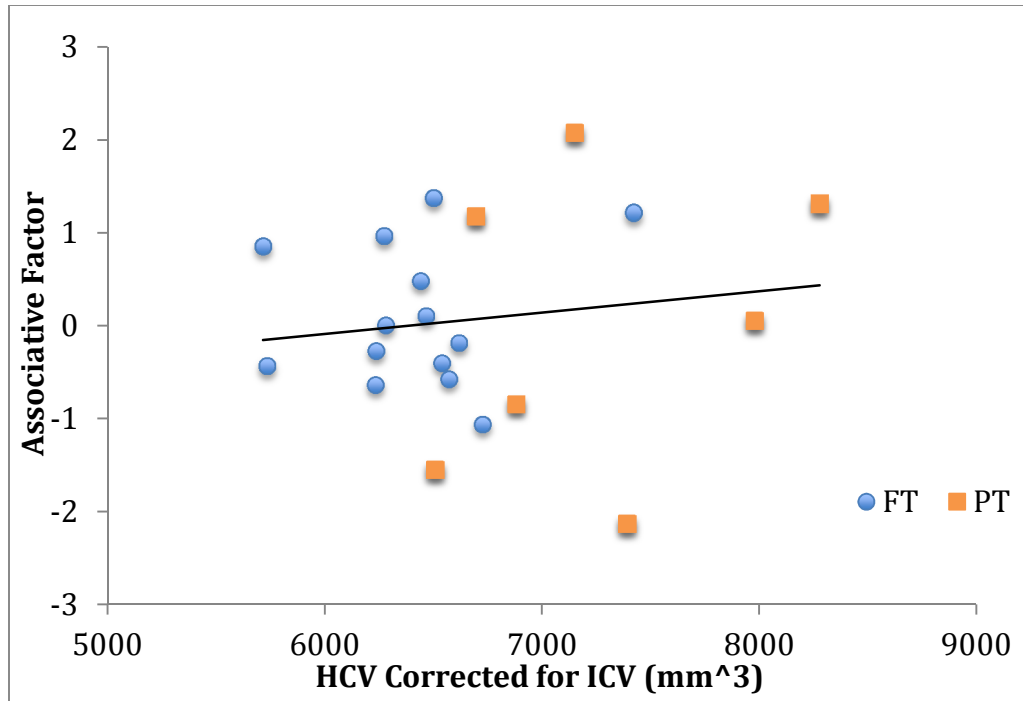


Figure 5. Correlation between composite scores of the Associative Factor and total corrected volume of the hippocampus.

Although the Associative Factor was not significantly correlated with total corrected hippocampal volume (HCV), it appears that there is a different pattern of relationship for the preterm born participants compared to the full-term born participants. Specifically, it appears that the preterm born participants display greater dispersion than the full-term participants. The trend line displayed here is for the sample as a whole.

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ABSTRACT**MEMORY PERFORMANCE, HIPPOCAMPAL VOLUME, AND EFFECTS OF
PREMATURE BIRTH IN YOUNG CHILDREN**

by

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The hippocampus is essential for episodic memory. Preterm birth is associated both with deficits in episodic memory and with alteration on hippocampal structure; however, the effect of term status on the relation between episodic memory and hippocampal volume (HCV) is unclear. We studied the potential of a latent construct of episodic memory as well as the relation between episodic memory and HCV in full-term and preterm born children (ages 5-6). The individual episodic memory measures separated into different components based on the level of association and decision that was required for the tasks. The composite scores were not significantly correlated with the volume of the hippocampus but performance on an individual task displayed a trending relationship with hippocampal volume. Additionally, there were brain-behavior relationships for the full-term born participants that were not present for the preterm born participants. The relationship between hippocampal volume and episodic memory performance may be task dependent and may be different in preterm born children compared to full-term born children. Additionally, it is possible that the tasks that are used to assess episodic memory performance in adults are not adequate for measuring episodic memory in young children.

AUTOBIOGRAPHICAL STATEMENT

Dana is a third year Clinical Psychology student at Wayne State University and a practicum student at Children's Hospital of Michigan with a focus in developmental neuropsychology. She has accumulated comprehensive clinical experience, research, and coursework as part of her work towards a PhD in Clinical Psychology. Specifically, she has completed psychological assessments and psychotherapy with adults and children. Dana is from a small town in Iowa and plans to return to the Midwest following graduation. Additionally, Dana values spending time and playing board games with family and friends. Following completion of her degree, Dana plans to work in a pediatric rehabilitation facility with a specialization in brain injury rehabilitation.