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Episodic memory—memory for events in the context of a particular time and place—is a complex construct with a protracted development. One defining and critical feature of episodic memory is memory for temporal order, or the ability to remember the order of sequences of events (e.g., X happened before Y). Memory for temporal order is largely thought to be dependent on a neural structure in the medial temporal lobe (MTL), the hippocampus. Previous work has shown continued behavioral improvements in episodic memory in general and specifically memory for temporal order across middle to late childhood (i.e. 7-11-years-old). However, the underlying factors contributing to this development are unclear. One factor may be the structural changes in subregions along the longitudinal axis of the hippocampus that also occur during middle to late childhood. However, these behavioral and neural changes have yet to be linked during development. The present study examined, in a group of children (7-11-year-olds) and young adults, age-related differences in performance on a memory for temporal order task, age-related difference in volume along the longitudinal axis of the hippocampus using structural MRI, and the relation between memory performance and hippocampal volume. Age-related improvements were found in both the encoding and retrieval of temporal order. Manual parcellation of the hippocampus replicated previous work: adults had smaller hippocampal head and tail and larger body than children. While no relation between hippocampal subregions and retrieval of temporal order were found, some differential

patterns for adults and children emerged for the relation between encoding of temporal order and hippocampal subregions.

EXAMINING THE DEVELOPMENT OF MEMORY FOR TEMPORAL ORDER AND THE NEURAL SUBSTRATES THAT SUPPORT IT

by

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CHAPTER I

INTRODUCTION

What would life be like without the ability to remember the events that make up our past? How would we make sense of our life story? Episodic memory—memory for past events in the context of a particular time and place—allows us to make sense and organize the vast amount of experiences we encounter throughout life (Tulving, 2001). From this ability to remember our past, including the specific features that make up past events (e.g., memory for *when* a past event occurred), we can create an autobiography, form a sense of self and learn from previous experiences (Tulving, 1972; Nelson, 1997). Research on episodic memory has largely focused on its emergence and early childhood development. For example, many studies have examined different developmental aspects of episodic memory such as the stability, length of retention, and memory for features of events themselves, both in preverbal infants over the first 1-2-years of life (e.g., Bauer & Leventon, 2013; Lukowski & Bauer, 2014; also see Bauer, 2006; 2007 for review) and in the post-verbal preschool years (e.g., Fivush & Hamond, 1990; Hamond & Fivush, 1991; Fivush & Haden, 1997). Over both of these time points, these studies show improved robustness of individual memories, increases in the amount of time this information is retained, and in the number of accurate details reported about an event itself. However, we also know that this development continues into middle and late childhood (e.g., from 7-to-12-year-olds; Bauer, 2007; Pathman, Doydum & Bauer, 2013; Lee, Wendelken,

Bunge & Ghetti, 2015). Together, these studies have found improvements in the features of episodic memory (e.g. spatial or temporal memory) and collectively (temporal and spatial together) during this time in development—thus, we know that important and protracted developmental changes are still occurring late into childhood. However, the underlying factors contributing to these changes in middle to late childhood are still unclear.

Memory for temporal order—the ability to remember the order of sequences of events—is a defining and critical feature of episodic memory and is largely thought to be dependent on an important brain structure for memory, the hippocampus. It allows past events to be placed on a continuous timescale and provides additional contextual information about what happened before or after an event (e.g. X happened after Y) even when the exact time of event is not recalled (e.g., X happened on Tuesday morning). Thus, information about the order of past events allows for our memory representations of past events (i.e. episodic memories) to flow consecutively and have continuity (Tulving, 1972). And because of its importance in forming complete memory representations, memory for temporal order has been studied with multiple populations and across development including animal models (e.g. Fortin, Agster, & Eichenbaum, 2002; Kesner et al., 1998, 2002; Fouquet et al., 2010; Devito & Eichenbaum, 2011; Templer & Hampton, 2013), human infants (Bauer & Thal, 1990; Bauer, 2006; Pathman & Bauer, 2013) and younger and older adults (Suzuki et al., 2002; St.Jacques et al., 2008; Lehn et al., 2009; Jenkins & Ranganath, 2010).

Little is known about the factors underlying age-related changes in episodic memory and memory for temporal order across childhood. One factor that has been examined is the development of neural substrates implicated in episodic memory, and specifically the hippocampus, a structure within the medial temporal lobe. The focus of this research has been on infants and early childhood because of developmental researcher's use of animal models that suggests relatively early hippocampal development and functional maturity by the preschool years (see Bauer, 2006; 2008, for discussion). However, more recent work has shown that the hippocampus undergoes continued structural development well into middle to late childhood (Herschkowitz, 2000; Gogtay et al., 2006; Otsby et al. 2009; DeMaster & Ghetti, 2012; DeMaster, Pathman, Lee & Ghetti, 2014; Townsend, Richmond, Vogel-Farley & Thomas, 2010). Given that memory for temporal order is dependent on the hippocampus, and the hippocampus undergoes structural changes, it is possible that age-related improvements in memory for temporal order could be driven by hippocampal changes, as discussed below.

Development of Memory for Temporal Order

Two separate lines of research have examined the development of memory for temporal order across the life span. In one, in which the majority of studies have been conducted, age-related differences have been examined between younger and older adults (Cabeza, Anderson, Houle, Mangels, & Nyberg, 2000; Newman, Allen & Kaszniak, 2001; Dumas & Hartman, 2003; Blachstein, Greenstein, & Vakil, 2012). Consistent with other aging adult studies, Fabiani and Friedman (1997) found that younger adults were

more accurate than older adults in recall of temporal order judgments for both word and picture stimuli.

In another line of research, memory for temporal order has been examined in childhood. The emergence of long-term memory for temporal order has been documented through the use of imitation paradigms in infancy and over the first two years of life in which infants are able to demonstrate recall for sequences of events. In the imitation-based memory tasks, an experimenter models a sequence of actions, and then immediately or after a delay infants are given the opportunity to imitate the actions and in correct temporal order. For example, infants have been tested on their ability to order events such as taking a mitten off a puppet's hand, shaking the mitten and then placing the mitten back (Barr, Dowdden, & Hayne, 1996; Pathman, San Souci & Bauer, 2010). Also, beyond the first two years of life, in early childhood, age-related differences have been observed for temporal order both in arbitrary laboratory and autobiographical tasks on many occasions (Friedman, 1991, 1992; Friedman & Kemp, 1998; Friedman et al., 1995; Pathman, Doydum, & Bauer, 2013; Pathman et al., 2013). Often this is measured by using stimuli presented as words or pictures in a list or through the use of personally-experienced events in which participants are asked to judge which came first (primacy) or last (recency; see Friedman, 1993 for discussion on types of tasks used to measure time).

Only four studies have examined the development of temporal memory in middle to late childhood. Further, only three of these studies also had a young adult comparison group. These few studies have shown that this ability improves throughout childhood with significant improvements in accuracy for temporal order judgments from middle to

late childhood. Picard et al. (2012) used depictions of a house and everyday events to test multiple aspects of episodic memory. In particular, Picard and colleagues found that during a temporal task in which children had to order a series of these everyday events, 4-6-year-olds performed significantly less accurately than any other age group (6-16). Importantly, 6-8-year-olds also preformed less accurately than 10-12-year-olds demonstrating the continued age-related improvements in memory for temporal order. In another study, Pathman, Doydum and Bauer (2013) used a daily photo-taking paradigm where children and adults took photographs of personally experienced events of their choosing for four weeks. At the end of the four weeks, participants were evaluated on their memory for temporal order. Participants were given pairs of their photos, and asked to indicate which of the two events occurred first (primacy) or more recently (recency). Difficulty was experimentally manipulated by varying the distance (temporal lag) between the events/photographs (e.g., long lag: the photos were taken weeks apart; short lag: photos were taken days apart). Results revealed that while 8-10-year-olds and adults had similar patterns of performance on judgments of primacy/recency for photos across differing levels of difficulty (i.e. greater or less lag time between photos), overall children performed less accurately than adults for temporal order judgments of photos within a pair. Therefore, even by late childhood, children are not performing at adult-like levels.

Pathman and Ghetti (2014) found significant age-related improvements in temporal order memory accuracy between 7-year-olds, 10-year-olds and young adults. During study (encoding phase) researchers used a working memory task adapted from Jenkins and Ranganath (2010) in which participants viewed quadruplets of arbitrary

images shown one at a time and then were shown one the four items again (a "probe"). Participants were asked to indicate the ordinal position of the "probe" item (i.e. was it presented first, second, third or fourth). Encoding task accuracy was high overall, but showed age-related improvements across each age group. After a 10 minute delay, during an unexpected test (retrieval phase), participants were shown one of the previously viewed probes. Following the probe, they were shown an array of three objects including one "target" item and two distractors. Participants were required to indicate which object came immediately after the probe during the encoding phase (i.e. the target item). Results showed that 7-year-olds (middle childhood) performed less accurately than 10-year-olds (late childhood) and 10-year-olds performed less accurately than young adults.

Lastly, Lee, Wendelken, Benge, and Ghetti (2015) presented triplets of items to 7-11-year-old children and young adults. Later, during test, participants were required to indicate whether the items were presented in the same order as before. Lee et al. found that adults performed more accurately on this task than all 8-10-year-olds, but not 11-year-olds. Together, this limited number of studies converge to show that memory for temporal order continues to develop in middle to late childhood. While the developmental trajectory of memory for temporal order has begun to be examined, the underlying neural mechanisms for this developmental change in middle to late childhood has never been examined.

Contributions of the Hippocampus to Memory for Temporal Order

Memory for temporal order is supported by the hippocampus (Davachi & DuBrow, 2015; Eichenbaum & Fortin, 2003). Animal studies provide consistent and

complementary reports that the hippocampus is important for temporal memory (e.g. McDonald, Lepage, Eden, & Eichenbaum, 2011). For example, Fortin et al. (2002) exposed rats to sequences of odors and later tested both their recognition and ability to order these odors. Results showed that rats were able to remember temporal order above chance and accuracy increased when a larger lag between odors was present. Rats with hippocampal damage did not perform above chance except for the largest lag. In another study, Hoang and Kesner (2008) found that rats who sustained smaller hippocampal lesions showed impairments in primacy temporal judgments but when they sustained larger dorsal and ventral hippocampal lesions both primacy and recency temporal judgments were impaired—suggesting not only the importance of the hippocampus in memory for temporal order but also possible regional differences within the hippocampus contributing to different aspects of temporal memory.

In studies with adults who have sustained hippocampal damage, results show a deficit in recalling the order of both objects and words but not in their recognition accuracy (Mayers et al., 2001; Spiers et al., 2001). Also, findings from the adult neuroimaging literature provide evidence of activations in hippocampal and medial temporal lobe (MTL) cortical regions during both the encoding (Jenkins & Ranganath, 2010; Tubridy & Davachi, 2011) and retrieval (Konishi et al., 2006; Lehn et al., 2009; St. Jacques et al., 2008) of temporal sequences. For example, Lehn et al. (2009) had participants (young adults 23–29-years-old) watch a novel movie and then recall sequences of events during functional magnetic resonance imaging (fMRI). The results showed significant activation in the MTL and the adjacent bilateral parahippocampal

cortex during sequence recall as well as activation in the right hippocampus, which was predictive of correct recall of sequences of scenes from the novel movie viewed. Overall, multiple lines of research including studies with animal models, adult lesion studies, and adult neuroimaging studies show that the hippocampus is necessary for memory for temporal order.

Structural Changes in the Hippocampus across Development

While most studies examining structural changes in the hippocampus have come from the adult literature (Maguire, Gadian, Johnsrude, Good, Ashburner, Frackowiak, & Frith, 2000; Poppenk & Moscovitch, 2011), a few studies have examined the structural changes that occur in the hippocampus across childhood and adolescence. Although findings are somewhat inconsistent at first glance, there is evidence of protracted development in the structure of the hippocampus that continues in middle to late childhood (DeMaster, Pathman, Lee & Ghetti, 2014; Ostby et al., 2009). Some previous studies report either very little or no structural changes in the hippocampus (Giedd et al., 1996; Yurgelun-Todd et al., 2003). However, these findings may be due to the examination of the hippocampus as a whole. Instead, when the hippocampus is parsed along its longitudinal axis into subregions via anatomical landmarks, including the head, body, and tail, structural changes with age can be observed. For example, Gogtay et al. (2006; also see Insausti et al., 2010) found that hippocampal anterior regions decreased in volume with age, more posterior regions (which included much of the body) increased in volume with age, and the very posterior region of the tail either did not significantly change with age or was shown to decrease on the left side. In a study with children (8-11-

year-olds) and adults DeMaster, Pathman, Lee & Ghetti (2014) found both a significant correlation in total hippocampal volume with age as well as within subregions, including age-related decreases in the right (and not as significantly in the left) head and right tail, as well as an age-related increase in both the right and left body.

Brain-Behavior Relations

Although no study has examined the link between temporal memory and the development of the structure of hippocampus, structural changes in the hippocampus have been examined in relation to other types of contextual information (e.g. spatial details). DeMaster, Pathman, Lee and Ghetti (2014) had participant's complete two separate tasks intended to assess memory for the contextual information associated with an item: a color task and a spatial task. During the color task, participants first completed an encoding portion where they would view black and white images of items with a color border. After a 20 minute break, participants were tested on their ability to a) recognize the item as "old" (rather than a completely novel item) and b) to retrieve the correct contextual detail associated with the item (in this case, color). In the second task administered on another day, the task was identical except for during encoding the items were presented on the screen in a particular location (right or left; and no color border). At retrieval, again they had to a) discriminate old versus new items and b) identify the correct contextual detail associated with the item (this time, spatial location). In both tasks, adults performed better than children. Performance on each of the tasks was reliably correlated and therefore combined into one "source score". Importantly, researchers found significant relations between volume of subregions of the hippocampus

and source score. Specifically, better source score was associated with a smaller hippocampal head and larger hippocampal body in adults and a larger hippocampal tail in children. Differential development of these regions may be due to some regions of the hippocampus (e.g. the anterior portion) being implicated in flexible recall of certain contextual information (e.g. spatial memory). Flexibility may be indicative of more experience and may be due to a greater reliance on anterior subregions of the hippocampus, as seen in adult's retrieval abilities. These findings provide support for the general role of the hippocampus in certain types of contextual memory. Further, these results also reflect that differential patterns in volume along the longitudinal axis of the hippocampus between children and adults have implications for behavior, such as in the successful recall of certain types of contextual information. However, a link between the hippocampus and the context of temporal memory across development has never been studied. Therefore, an examination of this relation could provide support that the protracted development of the hippocampus is one of the factors of the observed age-related behavioral differences in memory for temporal order.

The Present Study

Our program of research examines the development of episodic memory and the underlying neural substrates that support it during middle to late childhood based on the significant changes that occur during this time both in recall accuracy and brain development. In the present study, we focus on memory for temporal order (memory for the sequence of past events), a critical and defining feature of episodic memory. As noted in previous sections, we know that memory for temporal order is supported by the

hippocampus. We also know that structural changes in the hippocampus continue throughout middle and late childhood (see above, DeMaster, Pathman, Lee & Ghetti, 2014). However, the link between the hippocampus and memory for temporal order across development has never been studied.

The present study uses an adapted version of the task used in Pathman and Ghetti (2014). This task uses arbitrarily grouped items to evaluate memory for temporal order. The use of arbitrary items is important so that participants are unable to rely on other memory processes, such as script knowledge. Children often can rely on script knowledge, or event schemas, which contain general knowledge about when or where a typical daily event occurs (see Hudson & Nelson, 1986, for review). Therefore, it is important to use arbitrary items in a laboratory setting to examine temporal order memory development, and to pinpoint the relation between temporal order memory and hippocampal development.

The primary goals of the present study were to: a) examine the development of memory for temporal order in middle to late childhood (7-to-11-year-olds) and young adults; b) examine structural changes in the hippocampus between middle to late childhood and young adults using structural MRI; and c) examine the relations between hippocampal structure and accuracy of memory for temporal order between middle to late childhood and young adults. Based on previous studies that have used similar hippocampal parcellation in relation to episodic memory measures, it is hypothesized that we will find a) age-related differences in memory for temporal order, b) structural changes in the volume of the subregions of the hippocampus across age groups, including

a smaller right hippocampal head, larger hippocampal body bilaterally, and smaller right hippocampal tail in adults compared with children; and b) relations between subregion volume and memory for temporal order including different patterns between children and adults that may mimic the patterns seen between hippocampal subregions and other types of context memory reported in DeMaster et al. (2014). However, because the relation between subregions and temporal order memory has never been studied, no specific predictions will be made. It is possible that we will find the same relation as DeMaster et al. (2014) if memory for temporal order is processed by the hippocampus similarly to other types of contextual information. On the other hand, no relations or different relations will be found if memory for temporal order is a capacity that is organized differently in terms of the structure along the longitudinal axis of the hippocampus.

CHAPTER II

MATERIALS AND METHODS

Participants

This study was designed with two sessions. The first session, which is described in more detail below, is considered a training session to collect secondary behavioral measures and to provide all participants with more information about MRI. The second session, in which the MRI scan occurred is to collect the primary behavioral measure (a temporal order task) and the imaging data. There was no obligation for participant's to complete the scan session. Two separate IRB consenting procedures were used for the training session (session 1) and the scan session (session 2), as described in the Procedures below.

A total of 148 participants completed the training session of this study (7-11-year-old children: *n*=82 and young adults: *n*=66). Only participants who passed all eligibility requirements (i.e. there were no contraindications for MRI, child participants passed the play tunnel game, and there were no scheduling conflicts) were asked to come back for the scan session. This resulted in a total of 89 participants who participated in the scan session: 48 7-11-year-old children and 41 young adults. Of those who completed the MRI, usable scans were obtained for 29 children and 37 young adults. Unusable scans were due to movement (2 adults, 16 children), scanner error (2 adults, 2 children), dental work artifacts (1 child) or because the participant did not want to complete the scan (1

child). Participants with a WASI score that was more than two and a half standard deviations below the mean were excluded (1 adult). In addition, if participant's encoding was at chance (25%) they were excluded (1 child). Because this was such a large study with multiple portions for participant's to complete, each analysis uses a subset of the total available data set. Please see *Table 1* for the number of child and adult participants with available data for each level of analysis.

Table 1

Sample Size (n) and Mean Age for Each Level of Analysis.

Analysis	Children	M_{age}	Young Adults	M_{age}
Encoding (behavioral)	45	9.84	41	21.88
Retrieval (behavioral)	38	9.98	34	21.63
Useable scan	29	9.92	37	21.88
Encoding (behavioral) + Scan	28	10.01	37	21.88
Retrieval (behavioral) + Scan	25	10.26	32	21.73

All child and adult participants were right-handed. Child participants were recruited through community advertisements and adults were recruited through the Psychology Department participant pool and community postings. All parents provided written consent for their child and children provided written assent. Families were compensated $5 for participation in the training session, $30 for the scan session, and children received a small toy or book after each session. Adult participants provided written consent and were compensated with course credit for their participation (participant pool) or with $5 and $15 for each session, respectively (community recruitment). For screening purposes, participants were pre-interviewed (via phone or

email) for information on handedness, history of neurological disorder or trauma, learning or attention disorders, any possible contraindications (e.g. pacemakers, aneurism clips, metal in the body, etc.). Those who did not meet the eligibility (described further below) and safety screening requirements to have an MRI scan were not allowed to participate in the study, or if these were discovered during the training session, were not asked to complete the scan session.

Stimuli

Images for the temporal order task were drawn from the same stimuli bank as in Pathman and Ghetti (2014). Six hundred seventy two stimuli images were selected from the normative versions 1.0 and 2.0 Bank of Standardized Stimuli (BOSS; Brodeur, Dionne-Dostie, Montreuil & Lepage, 2015). Images were selected based on their appropriateness for children and in order to eliminate any stimuli that closely resembled another from the set (e.g., if there are two images such as 'African elephant' and 'Indian elephant', only one was used). The final list of stimuli images was randomized and images were grouped into fours (i.e. quadruplets). Each quadruplet of images acted as a single trial, for a total of 168 encoding trials. The 168 trials were split into six runs (each containing 28 trials).

Procedure

Training session

The training session lasted approximately 1-1.5 hours and took place in the Memory Development Lab at the University of North Carolina, Greensboro. The goal of this session was to provide participant's with information about the MRI scanner and to

either talk about (for adults) or simulate (for children) the scanning experience (i.e., lying motionless, sounds of scanner, focusing on a screen directly above them). This "mock scanner" training was intended to evaluate each participant's ability to complete the second session successfully. All participants were told what an MRI scanner is, what kinds of information can be obtained from the scanner, the importance of laying still while in the scanner, and were acquainted with the sounds they would hear inside the scanner. Child participants then went on to play games to mimic the scanning environment. This was done by asking children to lie down on their back in a play tunnel that was the same diameter as the scanner bore. The children were asked to play a game in which they had to lie still for a consecutive 10-minute period of time while watching a movie. The movie was displayed on an iPad mini positioned directly above their head so they could comfortably watch while laying on their back (this would be similar to how they would view the stimuli images inside the scanner on the mirror attached to the head coil directly above their head). In the game, researchers would place toy bowling pins with a bell inside each one around the participant's head and shoulders and place a small ball on the center of their forehead. The bowling pins and ball were used as indicators of movement in the following ways: if the ball shifted or fell off of their forehead, if the bowling pins made a ringing noise, or if the bowling pins shifted or fell to the side. Children were given three opportunities to "complete or pass" the task (i.e. there were no indicators of movement). If they were unable to successfully do this, they would not be asked to complete the scan session.

In addition, during the training session all participants completed a handedness questionnaire (parents completed this for child participants). All participants completed a standard old/new recognition memory task. Participants viewed twenty-five images of objects on a computer screen during an encoding phase and after a 10-minute delay[1], during the retrieval phase, participants were asked to distinguish images as "old" or "new" between twenty-five of the previously viewed images ("old") and twenty-five novel images of objects ("new"). Lastly, participants completed two subsets (vocabulary and matrix reasoning) of the Wechsler Abbreviated Scale of Intelligence (WASI).

Scan session

Approximately 1-3 weeks later, eligible participants would complete the scan session at the Gateway MRI center located in the Joint School of Nanoscience and Nanoengineering (Greensboro, NC). The scan session lasted approximately 2-2.5 hours. All participants (and parents of child participants) were safety screened again for eligibility to complete an MRI scan both with a participant checklist form and a trained MRI operator interview. Next, a temporal order memory task (adapted from Pathman and Ghetti, 2014) was administered. The temporal order memory task included an encoding portion outside of the scanner and a retrieval portion inside of the scanner in which participants were asked questions about their memory for sequences of images.

Scan Session: Encoding. Participants sat in front of a laptop in the screening room of the MRI suite (i.e. outside of the scanner) to complete the encoding portion of the

[1] During the delay, participants completed an Experiment-Child interview. The Experimenter-Child Interview consists of an experimenter having a structured conversation about two reported past events the participant has experienced. This interview includes a free recall portion and a cued recall portion about pieces of contextual information associated with each event. However, this will not be discussed in the results section, as this interview/task is outside the scope of this thesis.

temporal order task. They were instructed that they were going to view the quadruplets of items, and after a brief delay they would see one of those items again. They were asked to indicate whether the item that appeared after the delay was the first, second, third, or fourth item in that set. Participants were instructed to focus on the order of the items and to try and get as many of them correct as possible. Once the encoding portion began on the laptop, each item of the quadruplet would appear one at a time, each for 1.5 seconds, in the center of the screen. Following an 8 second fixation (the brief delay), participants were presented with one of the four items again (a probe) and asked to indicate its ordinal position (first, second, third or fourth; see Jenkins & Ranganath, 2010 and Pathman & Ghetti, 2014 for similar procedures; see *Figure 1* for sample trial). The probe remained on the screen until the participant's response for ordinal position was selected. Participants completed six runs (each with 28 trials and separated by a 2 minute delay). Following the six runs of encoding, participants were given a 10-15-minute break as they transitioned to the scanner.

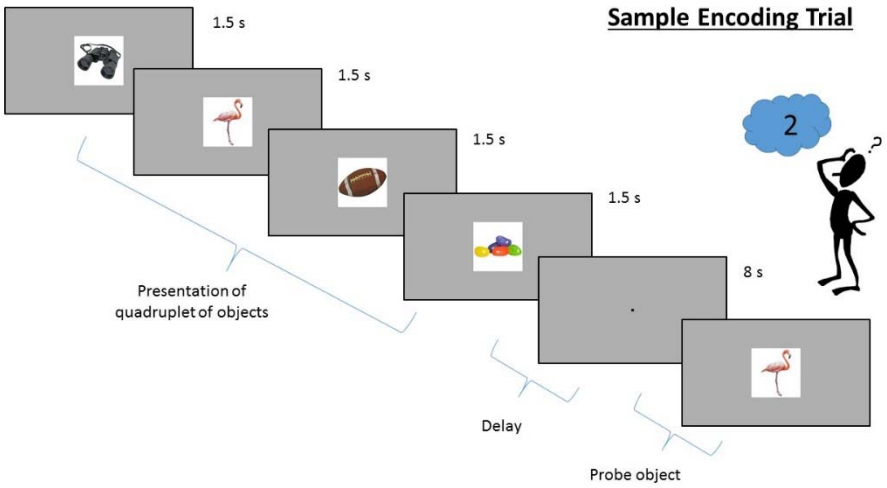

Figure 1. Sample Encoding Trial that Participants Completed Outside of the Scanner.

Scan session: Retrieval. After encoding, but before participants went into the scanner, the retrieval instructions were described with example trials (on a powerpoint). Once inside the scanner, participants were read the instructions again. Participants were instructed on how each trial would be presented: first they would see one of the items that they indicated the ordinal position of during encoding (i.e. the probe), then after a brief delay, an array of the other items from that quadruplet would appear. They were asked to indicate the item from the array that came immediately after the presented probe item (i.e. the item that followed in ordinal position during encoding). Participants were shown each probe for 1.5 seconds in the center of the screen followed by a 2 second delay screen and then the array of the three previously accompanied items from that trial (one target, two distractors) for 4 seconds. The array was followed by an extended response screen for an additional 2 seconds. Participants could respond via button press during either the retrieval array or extended response screen. There was a variable inter-trial interval averaging 7.7 seconds between every trial and presented as a fixation (ITI=5.7, 7.7, or 9.7 seconds; see *Figure 2* for sample retrieval trial).

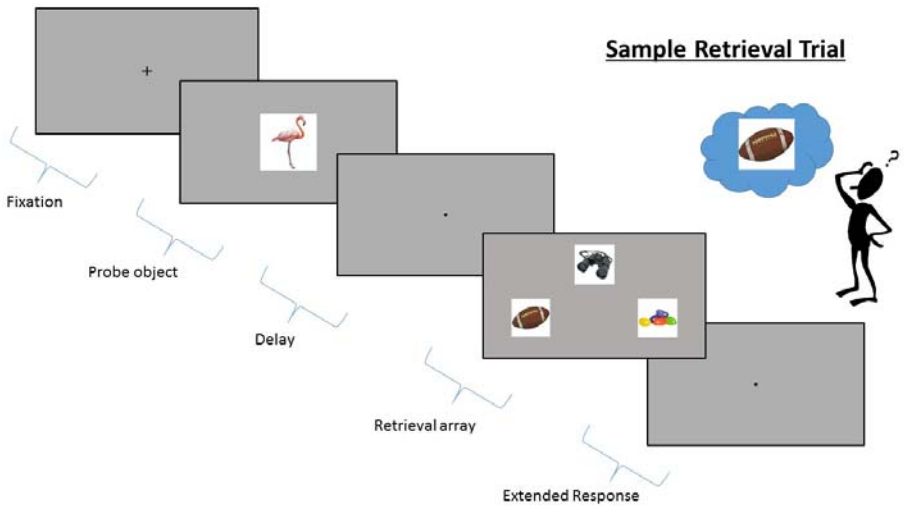

Figure 2. Sample Retrieval Trial that Participant's Completed Inside of the Scanner.

Of the 168 trials presented during encoding, 126 of them were presented during the retrieval phase. (These 126 trials were ones in which the encoding probe was presented in ordinal positions 1, 2, or 3. The trials in which the encoding probe was presented in ordinal position 4 cannot be used in the retrieval task since no item followed it. These fourth position items were included during encoding so that participants would attend to the ordinal position of all items in the quadruplet.) For each retrieval trial array, the spatial arrangement of the three items were presented equidistant from the fixation point, as well as equidistant from one another. The three images appeared in top, left, and right positions on the screen. The target item was randomly selected to appear an equal number of times in each of the possible positions (top, left, right).

MRI Imaging Acquisition

The structural MRI data was acquired using a 3T Siemens Magnetom Tim Trio scanner equipped with a 12-channel phased-array receiving head coil. Headphones and

adjustable padding around the neck and head were used to minimize motion. Whole-brain structural data was acquired using a rapid gradient-echo (MP-RAGE) sequence to acquire T1-weighted images using the following parameters: TR = 2000ms; TE= 28ms; flip angel= 76°; matrix size= 64 x 64; A > P phase encoding direction; slice thickness= 5mm; voxel size=1.0 x 1.0 x 1.0. Stimuli were presented using E-prime software onto a projector located at the head of the scanner. Participants viewed the stimuli through the mirror attached to the head coil. All participants responded using a Lumina LU444-RH 4-button response pad (and were trained on how to respond prior to and again once inside the scanner).

Hippocampal Parcellation

Commercially available software (*Freesurfer v5.3.0)* was used to examine the structure of the hippocampal formation by using the automated segmentation tool for cortical and subcortical regions. After validation provided by Tae et al. (2008), multiple subsequent studies have utilized *Freesurfer* for identification of the outer boundaries of the hippocampal formation in relation to memory in both children and adults (Gilmore et al., 2012, Bramen et al., 2011; Ostby et al., 2012). After the software's initial segmentation, a trained researcher manually identified the following subregions of the hippocampus: head, body, and tail via anatomical landmarks (see DeMaster, Pathman, Lee & Ghetti, 2014 for detailed description on landmarks and procedure used for hippocampal parcellation). To identify the change from the head of the hippocampus to the body, researchers began in the coronal view at the anterior hippocampal slice as identified by the software and continued through slices caudally. To identify the last slice

containing the hippocampal head, researchers looked for the slice where no digitations are present, and the hippocampus began to round (see *Figure 3A and B*). Researchers continued to move caudally through the hippocampus until they reached the fornix. The slice in which the fornix is clearly discernible from the hippocampus reflected the initial slice of the hippocampal tail (see *Figure C and D*). Lastly, the software identified the final slice of the hippocampal tail. See *Figure 3E* for example child participant hippocampus from the sagittal view with head (red), body (green), and tail (blue) parcellation. Another trained researcher segmented 20% of the adults and 20% of the children for reliability and reached agreement within 3 or less slices for each subregion for 94.6% of the decisions. Volume of the hippocampal head, body and tail for both the left and right hippocampus was calculated for all participants.

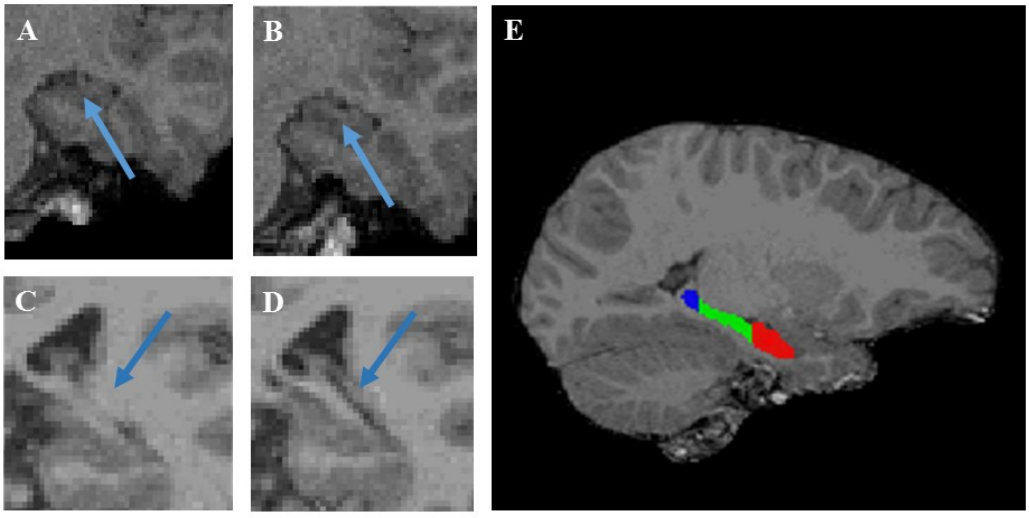

Figure 3. Hippocampal Parcellation Landmarks. Shown in the coronal view: Images A and B show the distinction between the last slice of the head where digitations are still present (A) and the first slice of the body where there are no longer digitations and it is

rounded (B). Images C and D show the distinction between the last slice of the body (C) and the first slice of the tail where the hippocampus becomes completely separate from the fornix (D). Image E is an example participant's structural image (T1-weighted, MPRAGE) with hippocampal subregions segmented along the longitudinal axis: head (red), body (green), and tail (blue) in the sagittal view.

In addition, intercranial volume (ICV) was calculated using automated procedures with *Freesurfer* software by isolating all intercranial volumes from the skull, including gray matter, white matter and all cerebrospinal fluid spaces. In order to consider variation of hippocampal volume due to overall age-related differences in brain volume, hippocampal subregion volumes were corrected for intercranial volume with the following calculation: Volume (adj)=Volume(rawí) – b x (ICV(í) – mean ICV), where Volume(adj) is the adjusted volume for the participant, Volume(rawí) is the unadjusted hippocampal subregion volume for the participant, b is the slope of the regression of hippocampal subregion volume (Volume(rawí)) on ICV, ICV(í) is the ICV for the participant, and mean ICV is the sample mean for all participant's average ICV (Raz et al., 2005; DeMaster et al. 2014). The same mean ICV was used for the entire sample (i.e. for both children and adults) because of a preliminary analysis in which regional volume was regressed on ICV, Age Group, and ICV x Age Group. The interaction of ICV x Age Group was insignificant in all cases (p's>0.153) and thus children and adults were considered as a single sample for mean ICV. All subsequent statistical analyses use the ICV-corrected subregional volumes. This procedure was based on the analysis of

variance formula (ANOVA) and identical to that used in DeMaster et al (2014; for age) and Raz et al. (2005; for gender).

CHAPTER III

RESULTS

Behavioral Performance

Recognition

Overall recognition accuracy was calculated by the proportion of "correct" responses: the number of hits plus the number of correct rejections divided by the total number of trials. An independent samples t-test did not yield significant differences in overall recognition accuracy between children (M=0.88, SD=0.19) and adults (M=0.89, SD=0.19), $t(81)$=-.49, p=0.63. In addition, a corrected recognition score was calculated subtracting the proportion of false alarms from the proportion of hits. This also did not yield significant results between children (M=0.77, SD=0.38) and adults (M=0.78, SD=0.37), $t(81)$=-.51, p=0.61. Therefore, children did not have lower recognition accuracy than adults and were equally as accurate in identifying "old" versus "new" objects. We can assume any differences in the memory for temporal order task are not due to differences in children's and adult's abilities to recognize stimuli.

Memory for Temporal Order

The primary measure in this study was the memory for temporal order task. During encoding (outside of the scanner), participants viewed quadruplets of items and indicated the ordinal position of a probe item from each quadruplet. There were a total of 168 encoding trials. On average, adults (M=163.90, SD=11.82) completed more

encoding trials than children (M=145.26, SD=23.99), $t(84)$=20.80, p<0.001. The number of trials was lower for children than adults based on a number of factors that occurred during the session in which the researcher had to make decisions on. For example: children's ability to maintain focus on the task (i.e. if they clearly weren't trying, not looking at the computer screen with the stimuli, getting out of their chair, turning around and talking, etc), fatigue, or in an attempt to keep the session under 2.5 hours (based on the IRB protocol).

Later, during retrieval (inside the scanner), participants were shown the probe item again, followed by an array of the three other items from the quadruplet, and were asked to identify the item that came immediately after the probe. There was 126 total possible retrieval trials across six runs. On average, adults (M=111.82, SD=23.78) completed more retrieval trials than children (M=66.74, SD=31.09), $t(71)$=6.05, p<0.001. Again, children completed less trials because they were fatigued, ready to get out of the scanner, or in an effort to keep the session under 2.5 hours.

The following patterns and effects reported remained the same regardless of whether analysis included all participants with behavioral data or when only considering those with a usable structural scan. Therefore, in order to have the largest sample size possible, reported are analyses for all participants who had behavioral data (regardless of if they also had a useable structural scan).

Encoding. First, for the encoding data (45 children, 41 adults), one-sample t-tests were conducted for both age groups (children and adults) to compare encoding performance to chance (25%). Both groups were significantly above chance: children

(*M*=70.94%, *SD*=0.20), *t*(44)=15.50, *p*<0.001; adults (*M*=94.82%, *SD*=.01), *t*(40)=92.43, *p*<0.001. An independent samples t-test revealed a significant difference in encoding accuracy between age groups, *t*(84)=80.52, *p*<0.001, *d*=1.69, where children preformed less accurately than adults. Therefore, because of this age difference, only correct encoding trials were considered when calculating retrieval accuracy.

Retrieval. Again, for the retrieval data (38 children, 34 adults), one-sample t-tests were conducted for both age groups to compare retrieval performance to chance (33%). Both age groups were significantly above chance: children (*M*=0.38, *SD*=0.11), *t*(37)=2.77, *p*<0.01; adults (*M*=0.57, *SD*=0.13), *t*(33)=10.55, *p*<0.001. There was a significant difference between age groups: adults were more accurate than children in retrieving the correct temporal order of items, *t*(69)=1.768, *p*<0.001, *d*=1.58. Bivariate correlations and partial correlations controlling for age produced no significant relations between temporal order encoding or retrieval scores and either of the recognition scores (accuracy or corrected accuracy; *p's*>0.28).

WASI (Wechsler Abbreviated Scale of Intelligence)

There was not a significant difference between age groups on their WASI standard score (children: *M*=110.53, *SD*=13.44; adults: *M*=109.53, *SD*=11.57; *t*(85)=.37, *p*=0.71) or percentile (children: *M*=69.09, *SD*=24.69; adults: *M*=69.15, *SD*=22.12; *t*(85)=-.01, *p*=0.99). Pearson correlations between WASI standard score and encoding accuracy were significant for both children (*r*=0.46, *p*<0.01) and adults (*r*=0.33, *p*<0.05). However a different pattern emerged for Pearson correlations between WASI standard score and retrieval accuracy in that it was significant for children (r=0.43, p<0.05) but did not reach

significance for adults (r=0.18, p=0.31). To corroborate these results, partial correlations for the full sample, controlling for age in months, were conducted and revealed significant correlations between WASI standard score and encoding accuracy (r=0.36, p<0.01) but did not reach conventional levels of significance for retrieval accuracy (r=.213, p=0.08).

Hippocampal Volumes

There were 29 children and 37 adults with useable scan data. To examine the relation between total hippocampal volume (both left and right hemispheres) and age group, a correlation was conducted and revealed a significant positive correlation, r=0.25, p<0.05. Therefore, because of this significant relation even after adjusting for total ICV, and in order to replicate previous analysis procedures (e.g., DeMaster et al, 2014), total hippocampal volume was included as a covariate in further analyses. A 2 (age group: children, adults) x 3 (subregion: head, body, tail) x 2 (hemisphere: left, right) analysis of covariance (ANCOVA), with total hippocampal volume as a covariate, revealed a significant subregion x age group interaction, $F(2, 128)=7.36$, $p<0.01$, $\eta^2=0.11$. To follow-up this interaction, composite scores were calculated for each subregion collapsed across hemispheres (i.e. an average of each head, body, tail subregions). Independent t-tests revealed significant differences between children and adults for all subregions such that adults had smaller a hippocampal head, larger body, and smaller tail than children (p's<0.01; see *Figure 4*).

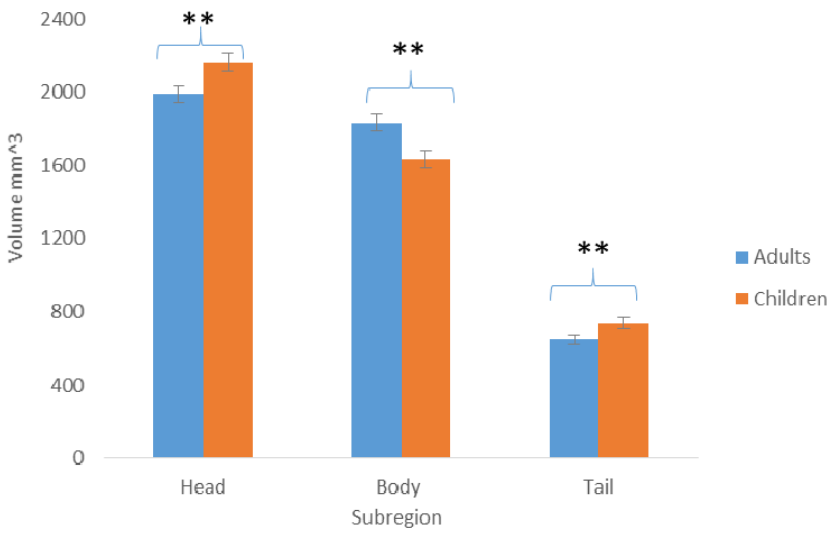

Figure 4. Composite (Right and Left) Hippocampal Subregion Volumes for Children and Adults. Shown with standard error bars (p's<0.01).

Additionally, the subregion x hemisphere x age group interaction was nearly significant, $F(2, 126)=2.47$, $p=0.06$, $\eta^2=0.04$. To further investigate these interactions, ANCOVAs were conducted for both the right hippocampus and left hippocampus separately with the respective (right, left) hippocampal hemisphere as a covariate. The ANCOVA for the right hemisphere revealed a significant subregion x age group interaction, $F(2, 126)=9.471$, $p<0.001$, $\eta^2=0.14$ where adults had smaller head, larger body, and smaller tail than children (*p's*<0.02; See *Figure 5A*). In the left hemisphere, the ANCOVA showed nearly significant effects for subregion, $F(2, 126)=2.63$, $p=0.07$, $\eta^2=0.04$ and a subregion x age type interaction, $F(2, 126)=2.54$, $p=0.08$, $\eta^2=0.04$. The left head subregion did not reach conventional levels of significance, $t(63)=1.91$, $p=0.06$, but there appeared to be a similar pattern as the right hemisphere, where adults had

smaller hippocampal head than children. There was not a significant difference between age groups in the left body. Lastly, again adults had a similar pattern to the right hemisphere with a smaller left tail than children ($p<0.05$; see *Figure 5B*).

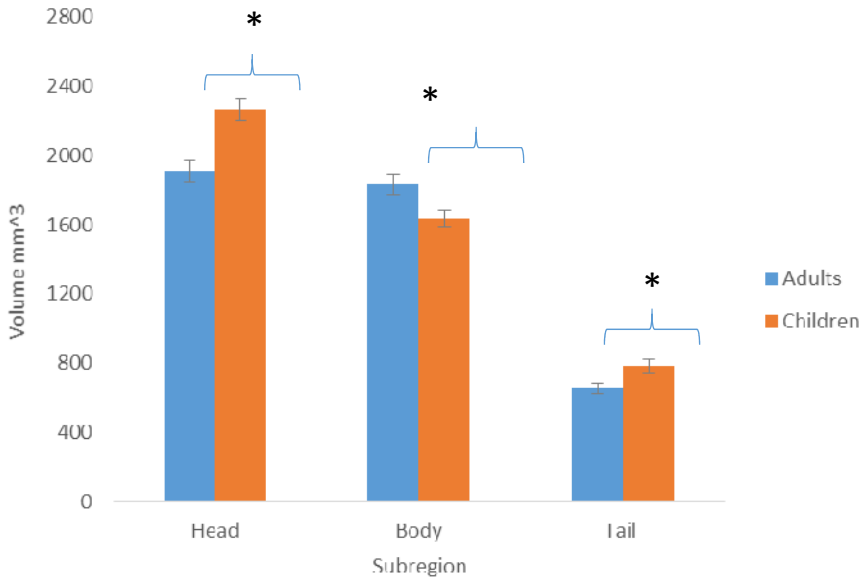

Figure 5A. Right Hippocampal Subregion Differences Between Children and Adults (p's<0.05). All values are adjusted for ICV with right hippocampal volume as a covariate and shown with standard error bars.

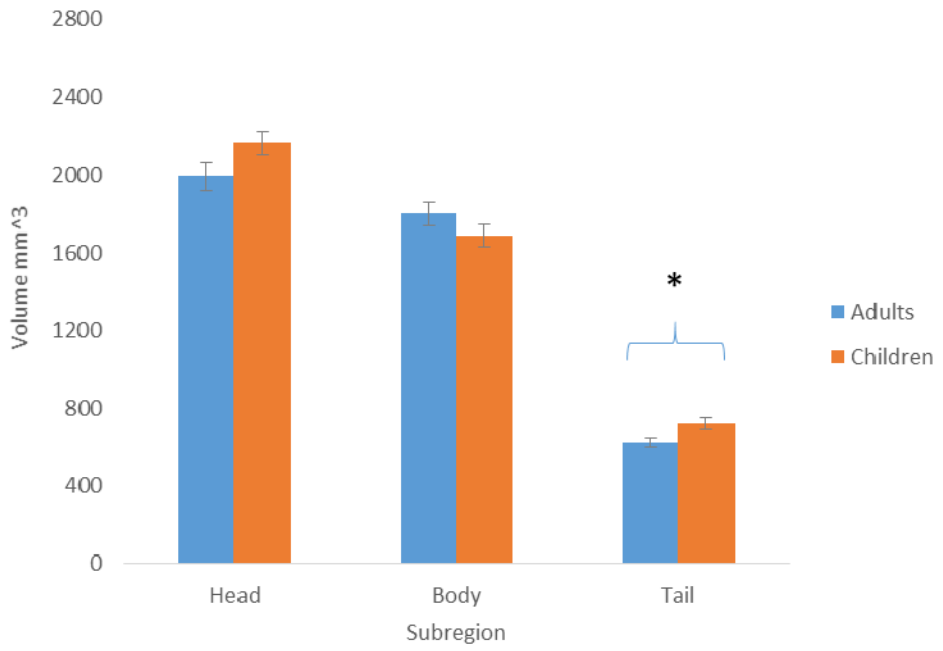

Figure 5B. Left Hippocampal Subregion Differences Between Children and Adults ($p<0.05$). All values are adjusted for ICV with left hippocampal volume as a covariate and shown with standard error bars.

Relations between Hippocampal Volumes and Memory for Temporal Order

To evaluate the relation between hippocampal subregion volumes and memory for temporal order, we replicated the procedure by DeMaster et al. (2014) and conducted correlational analyses using the standardized residuals of each variable of interest for each group (child and adults separately). By using the residuals, we were able to control for age-related variance within each of these groups for our dependent variables of interest: each subregion volume for child and adult groups separately, retrieval proportion correct, and encoding proportion correct (again, both retrieval and encoding proportion correct with adults and children separately). We also conducted the same analyses

controlling for both age and ICV, but these yielded the same results and thus the results controlling for age only are reported. This mirrors the method (including the variables controlled for) in DeMaster et al. (2014).

Encoding

Relations between hippocampal subregion volume and encoding accuracy on the temporal order task were evaluated (28 children, 37 adults). For adults, smaller left head was marginally related to encoding accuracy (r= -0.30, p=0.075; see *Figure 6A*). There was a significant difference in the correlations of children and adults with left hippocampal head volume (Fisher's z=2.40, p<.01). For children, larger right body (r=0.45, p<0.05) was significantly related to encoding accuracy (see *Figure 6B*). Again there was a significant difference in the correlations of children and adults with right hippocampal body volume (Fisher's z=2.87, p<0.01).

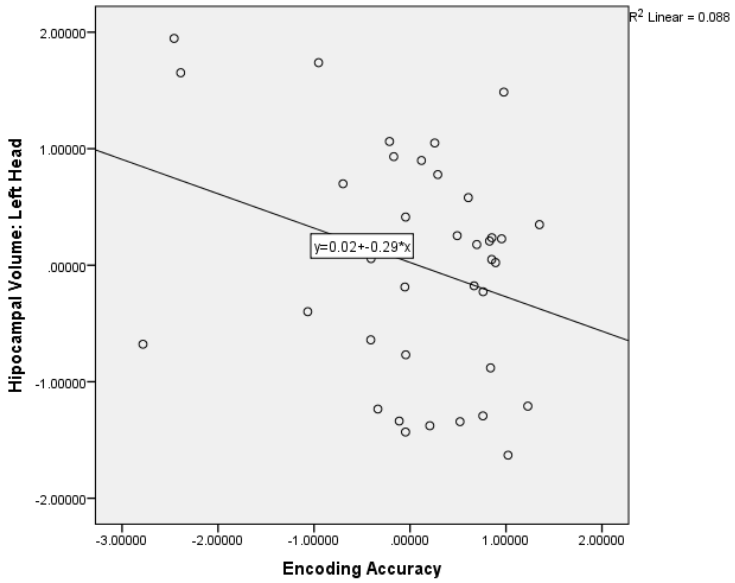

Figure 6A. Negative Correlations Between Hippocampal Volume in Left Head and Encoding Accuracy in Adults.

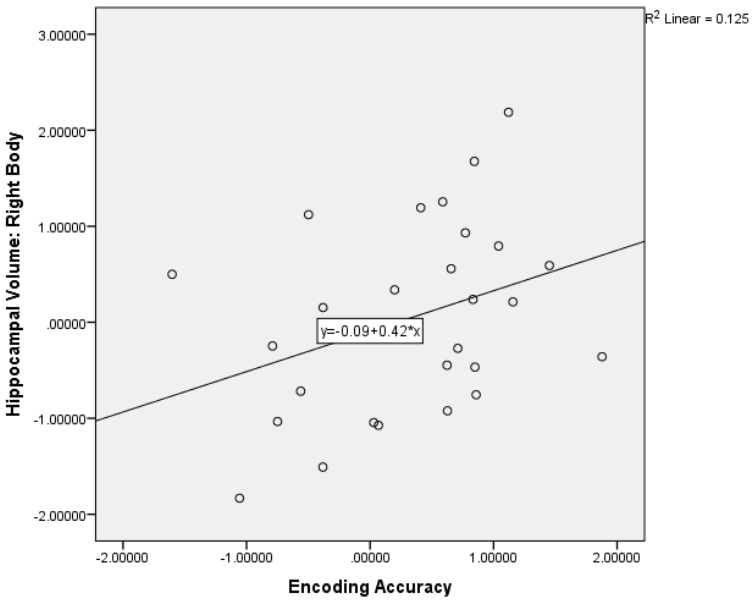

Figure 6B. Positive Correlations Between Hippocampal Volume in Right Body and Encoding Accuracy in Children.

Retrieval

For children (n=25), there were no significant correlations between any left or right subregion volume and retrieval accuracy on the temporal order task (p's>0.178). Similarly, for adults (n=32) there were no significant correlations between any left or right subregion volume and retrieval accuracy on the temporal order task (p's>0.140).

CHAPTER IV

DISCUSSION

To our knowledge, the present study was the first to examine the relation between temporal memory and the structural development of hippocampal subregions along its longitudinal axis in middle to late childhood. Separately, previous work has found age-related differences across this developmental time period in both memory for temporal order (a specific kind of temporal memory and a component of episodic memory) and in hippocampal subregions. Behaviorally, we predicted that we would see improved performance in memory for temporal order between children (7-11-years-old; middle to late childhood) and young adults. In terms of the hippocampus, we expected to see different patterns among subregion volume between children and adults: adults with smaller right head, larger body bilaterally, and smaller right tail than children. This pattern would replicate that found previously by DeMaster et al. (2014). No specific predictions were made about the relation between specific hippocampal subregions and performance on memory for temporal order tasks—although, we did expect different patterns to emerge between age groups.

We found that young adults performed more accurately than children both during the encoding and retrieval portions of the memory for temporal order task. From manual hippocampal parcellation, we found that adults had smaller right head, larger right body, and smaller tail bilaterally than children. While there were no significant relations

between retrieval of temporal order (long-term memory task) and hippocampal subregions, we found a significant positive relation between encoding performance (working memory task) and right hippocampal body in children (but not adults). And in adults, we found a marginally significant relation in the negative direction between encoding performance and left hippocampal head (but not in children). Thus, for encoding of temporal order information, children's performance was higher for those with larger right body while adult's performance tended to be higher for those with smaller left head.

The task we used to assess memory for temporal order was adapted from Pathman and Ghetti (2014). In their study, there were three age groups (7-year-olds, 10-year-olds and young adults) and their task included three conditions (temporal order, temporal context, recognition). In the encoding portion (which remained exactly the same between the two studies), we found nearly identical results for the adult groups (~94%). For children, our 7-11-year-old's as a whole performed similarly to their youngest child group (7-year-olds; ~70%). A slight decrease in performance was expected due to the novel and possibly disquieting nature of the scanning environment (even from just being in the MRI suite and particularly for children) so this was not surprising. For the retrieval portion, both child and adult participant's performance decreased by about 10% from the findings in Pathman and Ghetti (2014). Again, accuracy was expected to decrease given the scanning environment (especially during retrieval inside the scanner). Another possibility for the decrease in retrieval accuracy may be the decision to only include temporal order trials in our study. In Pathman and Ghetti, there were also recognition

trials (which only required participants to correctly identify the target item from an array with one "old" item and two completely "new" or novel items not seen during encoding). Participants across all ages performed more accurately on these types of trials than in the temporal order or temporal context conditions (a condition in which the array included one target and two distractors that were from other quadruplets). Therefore, the inclusion of these recognition trials may have boosted participant's confidence, provided some "relief" on their cognitive load during retrieval, and ultimately increased their performance on other types of trials (i.e. temporal order).

Our findings of improved accuracy in memory for temporal order also coincides with other studies examining temporal order in middle to late childhood and adults. For example, Lee et al. (2015) also found that adults performed significantly better than 8-10-year-olds in a task that required participant's to remember the order of triplets of items presented one at a time at different locations on a screen. However, adults did not perform better than 11-year-old's in their study, suggesting that the shift from middle to late childhood is an important developmental time period for memory for temporal order. This is further supported by Picard et al. (2012) who used tasks requiring children to order a series of everyday events from a story told by a researcher. Picard et al. (2012) found that improvement in this ability occurred between their 6-8-year-old (middle childhood) and their 10-12-year-old (late childhood) groups, but no further improvements occurred in their 14-16-year-old group. Further, Pathman, Doydum and Bauer (2013) showed that even for personally experienced autobiographical events with visual cues (photo-taking paradigm), 8-10-year-olds did not perform as accurately as adults when

making temporal order judgments. Taken together, the few studies that have examined memory for temporal order in middle to late childhood consistently find that this is a particularly important developmental period for memory for temporal order. And, more broadly, because temporal memory is a crucial and defining component of episodic memory, middle to late childhood is a critical developmental time point for episodic memory.

But what are the contributing factors to this development? We also know that during this time there are changes in the volumes of hippocampal subregions and that the hippocampus has been implicated in memory for temporal order from research with animal models, human infants, adult neuroimaging, and clinical cases. Overall, our imaging findings replicate the previous work that there is a differential pattern between children and adults along the longitudinal axis of the hippocampus (i.e. an age x subregion interaction; DeMaster et al., 2014; Gogtay et al., 2006). Our composite volumes calculated for the head, body, and tail of the hippocampus reveal that adults have smaller head and tail, and larger body than children.

Taking a closer look, our results replicate identically the significant differences in child and adult subregion volumes found by DeMaster et al. (2014) in the right hemisphere, and nearly so in the left hemisphere (although similarly, we both find age-related differences in more anterior regions; i.e. the body and tail). These also closely resemble developmental findings by Gogtay et al. (2006). Although Gogtay et al. (2006) did find significant changes (i.e. decreases in volume) in both hemispheres for the head across development, they also reported a more protracted development of the right

hippocampus relative to the left hippocampus. Thus, while the non-significant pattern we found in the left head is consistent in terms of direction, the effect may have been washed out by the larger number of older children (10-11-year-olds) in our child group. Also consistent with the current study, Gogtay et al. (2006) found increased volume in the "posterior third" (i.e. the tail) region bilaterally over development. Overall, across development, the present study adds to the small number of studies studies that show that changes do occur along the anterior-posterior longitudinal axis of the hippocampus that otherwise may not be apparent when examining the structure as a whole (e.g., Giedd et al., 1996). Ultimately these findings confirm the importance of examining subregions within the hippocampus, particularly across middle to late childhood when many of these changes may occur.

Lastly, this study aimed to explore the relation between temporal memory and hippocampal subregions during middle to late childhood for the first time. DeMaster et al. (2014) examined other aspects of episodic memory retrieval (e.g. spatial memory, color context) and hippocampal subregion volume and found differential relations between children and adults: Smaller right head and larger bilateral body predicted higher performance in adults, while larger left tail predicted higher performance in children. There are multiple possibilities for why a similar pattern was not found with retrieval of memory for temporal order including: a) aspects of our task or design, b) restrictions of the sample, or c) retrieval of temporal order information is, in fact, not as sensitive to the structural heterogeneity along the longitudinal axis of the hippocampus as other components of episodic memory might be during this period of development. Each of

these will be discussed in addition to the current study's findings of an association between encoding (working memory task) accuracy and hippocampal subregions.

The task difficulty, coupled with the distractions of the scanner affecting performance, may have contributed to the lack of relations found between performance on the retrieval phase and hippocampal structure. One possibility would be to use more salient or personally meaningful stimuli to help boost performance. However, our group of adult's retrieval accuracy of about 57% is similar and even slightly higher than a study by Burt, Kemp, Grady and Conway (2000) that used a task requiring adults to order photos they had taken themselves in the last 2-weeks. Burt et al. (2000) found that adults were only about 53% accurate in ordering across these personal events, and about 42% accurate when ordering within an event. Thus, memory for temporal order seems to be difficult in general and other factors may contribute this difficulty outside of the hippocampus itself (e.g., functional development and connectivity, discussed more below). Another possibly is to have used a task that incorporated multiple types or levels of context (similarly to DeMaster et al., 2014 in which they had both spatial and color details). For example, similar to Pathman & Ghetti (2014), we could have included both temporal order and temporal context trials. Temporal memory can be tested by asking about events in relation to one another (temporal order: X happened before or after Y) or by placing an event in time (temporal context: X happened on a particular day or time of day). Because we know the hippocampus is essential for binding together pieces of contextual information (e.g., Cohen & Eichenbaum, 1993, 2001; Konkel & Cohen, 2009),

creating a task with multiple types of contextual relations to be bound into memory representations could have been a more sensitive measure.

In addition, our sample size may have been too small to detect these relations. Ideally because this is such a sensitive developmental time both for memory for temporal order and for the hippocampus, we would have had two groups of children: 7-9-year-olds (middle childhood) and 10-11-year-olds (late childhood). Our group of children had a larger number of late childhood participants than middle childhood (11 7-9-year-olds, 18 10-11-year-olds) and thus the older children may have been driving the effects (or lack therefore) we see in terms of relations between behavioral accuracy and volume of subregions. However, because we have replicated both previous behavioral findings and imaging findings from this developmental time, a final possibility is that these null findings between retrieval and structure are valid and just as informatory as a significant result. We examined the longitudinal axis of the hippocampus because it has been found to be implicated in the retrieval of other contextual details. Memory for temporal order although dependent on the hippocampus itself may not be as sensitive to these structural changes. Other factors may contribute or be more sensitive to measures of memory for temporal order such as functional development or more complex circuitry and connectivity to other cortical areas.

Not only does the hippocampus endure nuanced structural changes along the longitudinal axis but posterior-anterior functional changes have also been proposed to occur—and these may be important for episodic memory performance (Giovanello et al., 2009; Ghetti et al., 2010; Ghetti & Bunge, 2012). For example, an fMRI study by

DeMaster and Ghetti (2014) found that for adults, anterior regions of the hippocampus predicted successful retrieval of episodic details (color context of black and white images) while it was posterior regions that predicted successful retrieval in children (8-11-year-olds). Future studies should examine this possibility with other components of episodic memory, such as temporal memory.

However, recently in a group of adults, Kyle, Smuda, Hassan and Ekstrom (2015) did not find specific subregion activation associated with retrieval of memory for temporal order information. Kyle et al. (2015) had adults participate in a virtual reality in which they delivered objects to stores in a specific location and order (importantly these were presented in an incongruent manner such that spatial location would not support the retrieval of order). Later during retrieval and high resolution fMRI of the hippocampus, participants completed both spatial and temporal blocks in which they were presented with three of the store locations: one "reference" store and two other stores. In the temporal trials (of importance to us), they were required to indicate whether the two stores were the same, equal temporal distance from the reference store, whether they were unequal, or whether they were "lures" or new store locations. While temporal and spatial trials did activate the hippocampus, there were no specific clusters of activation that differentiated between these trials or showed specific subregion activation based on the type of context retrieved. Although this finding may be somewhat task specific, it is important to consider there may be other contributing brain regions outside of the hippocampus.

Another long hypothesized contributing factor to both episodic memory in general and specifically temporal memory is the role or function of the prefrontal cortex (PFC). Studies using fMRI and PET methods with adults have demonstrated these contributions with both episodic and autobiographical retrieval of temporal order (e.g., Cabeza et al., 2000; Suzuki et al, 2002; St. Jacques et al. 2008). No study has examined temporal memory in development using fMRI. Therefore, more work needs to be done to examine the functional activation of the prefrontal cortex across age groups, particularly during this crucial period of middle-to-late childhood.

The current study found differential relations or patterns between the encoding of temporal order and subregions of the hippocampus. In adults, smaller left anterior region (head) tended to be associated with better encoding (echoing similar relations in head with adults from DeMaster et al., 2014) while the right more posterior region (body) was significantly associated with better encoding in children. Again, because our sample included more children who are considered to be in late childhood, this could explain why we see this association in the body subregion and not the most posterior tail. Had we been able to have two separate child groups (younger and older) or a larger number of younger children in our sample, we may have seen an association instead with the most posterior region, similar to findings in DeMaster et al. (2014). One possibility, as suggested by other studies examining the role of experience and hippocampal volume (as with spatial memory in the London taxi driver study; Maguire et al., 2000), is the importance of experience-driven maturation of the hippocampus. Maguire et al. (2000) found that high levels of experience in spatial navigation (measured as the amount of

time as a London taxi driver) had smaller hippocampal heads than controls. Smaller hippocampal head in relation to experience and behavioral performance for spatial context in adults was also found in DeMaster et al. (2014) and approached significance in the current study. Particularly with temporal memory, the role of experience might especially be important. As children age, experience with time becomes more prevalent in their lives (e.g., keeping their own schedule, learning to tell time on a clock, understanding the calendar, important dates, and the cyclical nature of time). If these experiences are either driving or bi-directionally associated with structural changes along the anterior-posterior regions of the hippocampus, then the ability to even understand—or encode—temporal information may depend on this combined effort of experience and maturation.

Differential hippocampal subregion patterns may also be due in part to encoding strategy differences between adult and child groups and supported by the novelty-encoding hypothesis which states that anterior regions of the hippocampus have been found to support encoding of novel items whereas posterior regions are implicated in the repetition of items (Tulving & Kroll, 1995; Gonsalves et al., 2005; Lepage et al., 1998). Thus, adults in our study may be more focused to the novel information presented in each trial during encoding because of the relation with hippocampal head (anterior region). On the other hand, children may spend more of their time during encoding trying to remember or repeat previous trials as a method of rehearsal rather than focus on the novel information at the present moment it occurs, based on the relation to a more posterior hippocampal region (body).

A few fMRI studies have also explored the relation between both the hippocampus and prefrontal cortex during *encoding* of episodic details and even specifically of temporal information (Jenkins & Ranganath, 2010; Tubridy & Davachi, 2010). In adults, differential recruitment of the hippocampus and surrounding parahippocampal cortices, along with varying PFC regions have been found during encoding even between levels of temporal memory (i.e. more fine-grain temporal order versus more broad or coarse tests of placing events in time; Jenkins & Ranganath, 2010). In a study with both children and adults (ages 8-24), Ofen et al. (2007) found age-related increases in the recruitment of areas in the PFC during encoding that was associated with later better episodic performance. Therefore, other regions and connectivity to these regions may contribute to the differences in behavioral performance consistently reported during middle-to-late childhood.

Taken together, the current study combined with this small group of studies shows the importance of considering the complexity of the components and development of episodic encoding and retrieval. This study adds to our knowledge of both the development of a defining feature of episodic memory, memory for temporal order, and the development of a complex structure important for memory—the hippocampus. While no relations between retrieval and structure were found, there were different patterns of relations between encoding and structural development in children and adults. Future studies examining the development of episodic memory—and the defining features of it—should consider the structural nuances of the hippocampus, the relation between these subregion structures and their function, as well as other circuity and connections within

the brain, such as the PFC. As a whole, these add to our understanding of both the underlying binding mechanisms needed for complete memory representations and the strategies used across development to successfully encode and retrieve episodic memories. Further, while these are all important aspects of episodic memory, there is no unifying and cohesive theory of episodic memory development. With continued work on the multiple components that make up our episodic memories (e.g., temporal and spatial memory), how these components relate to one another and the underlying contributing factors (e.g., structural and function development of hippocampus and PFC) to their development, we can then incorporate these into a cohesive theory or model.

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