Investigating the Relationship Between Hippocampal Volume and Spatial Memory in Early Childhood

by Andrew Bunnell

The hippocampus is known to have a key role in memory, spatial navigation, and emotional behavior. The brain structure continues to develop postnatally during neurogenesis as the hippocampus integrates new neurons into existing neural circuits. The overall size of the hippocampus can be assessed through structural magnetic resonance imaging (MRI). Despite the knowledge of hippocampus function in adults and older children, it is unknown if the hippocampus supports spatial memory in young children. The current study leverages structural MRI and cognitive assessments from the Baby Connectome Project, specifically the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) Zoo Locations task, to investigate the relationship between hippocampal development and spatial memory in young children. MRI images were obtained when children were 1 to 2 years old. Automated algorithms were used to segment the brain into its distinct parts. The hippocampus was further manually segmented to compute the volume of the hippocampal subregions (bilateral head/body/tail). A linear regression analysis was performed to evaluate the association between hippocampal volume and spatial memory performance, controlling for sex assigned at birth and age at MRI scan. The results of the regression indicated that total hippocampal volume was negatively associated with Zoo Location Score ($F(4, 31) = 3.65$, $p = 0.0058$) with a regression coefficient of ($B = -0.002$, $p = 0.0058$). Follow up analyses of the hippocampus bilateral head, body, and tail indicated that only the right head volume was negatively associated with zoo location score ($B = -0.006$, $p = 0.0017$). No other statistical tests were significant. Understanding this relationship could provide valuable insights into hippocampal development and its association with spatial memory in young children.

Introduction

Hippocampus and its Functions

The hippocampus is a structure that is buried deep within the brain, at the floor of the lateral ventricle. Part of the cortex called the allocortex, the hippocampus contains two parts: the hippocampus proper (cornu ammonis) and the dentate gyrus (Anand & Dhikav, 2012). Together, the hippocampus proper and the dentate gyrus form the hippocampal formation (Anand & Dhikav). The term hippocampus is derived from its regular resemblance in a dissection to a seahorse (Knierim, 2015). In standard magnetic resonance imaging studies, landmarks are identified for the division of the hippocampus. The subdivision of the hippocampus is typically head, body, tail (Hannula & Duff, 2017). The hippocampal head is anterior to the body and the tail, and the body is located in between the head and the tail (Massoud, 2022). The three regions of the hippocampus project to different areas of the brain.

The hippocampus is known to have many functions, such as regulating emotions and behavioral inhibition. The hippocampus has strong connectivity when processing emotions relating to others' mental circumstances (Immordino-Yang & Singh, 2013). This shows that the hippocampus and emotion are tied together. Additionally, larger hippocampus volume is associated with higher behavioral inhibition system activity (Barros-Loscertales et al., 2006).

However, the hippocampus is most commonly associated with playing a key role in memory, particularly in the formation and retrieval of long-term memories. It also helps with spatial memory and emotional behavior, as it is a main player in the limbic system (Anand & Dhikav, 2012). The hippocampus is an interesting structure, as it will continue to grow postnatally (Anand & Dhikav). It is not fixed after the first few months a baby is born. Neurogenesis, the process of forming new neurons is continued throughout the development of the hippocampus. The neurons present in the hippocampus will continue to grow and integrate into mainstream neurons (Anand & Dhikav). This

integration is critical for allowing the hippocampus to play a key role in our daily lives.

Structural and Functional Variations

Asymmetry in the brain refers to the morphological and functional differences of the left and right side of the brain. The average pattern of human brain asymmetry is not set in stone prenatally (Kong et al., 2022). It is determined by the age, sex, size of brain, and heredity, but concluding findings are still in progress (Guadalupe et al., 2017). There still tends to be variation across individuals regarding the specifics of asymmetry. Each lateralization of the brain is associated with different roles and functions within the structure. As in the brain, the hippocampus is also divided into a right and left. However, there is no concluding evidence that there are specific functions of the left and right hippocampus. (Ezatti et al., 2016). The retrieval of spatial memory can be linked to the hippocampus as a whole and not specific sides.

There is also variation in the size of the hippocampus. Throughout development after birth, there is a large increase in the volume of the hippocampus. The growth of the hippocampus slows after the age of two (Nichols et al, 2024). For healthy humans, the average unilateral hippocampus size is 3,917 mm^3 within a range of 2,500 to 5,000 mm^3 (Ashbrook et al., 2014). There is large variability in the size of the hippocampus, which can be used to correlate to certain cognitive functions such as spatial memory.

Imaging of the Hippocampus

One main way to view and track hippocampus growth is through structural magnetic resonance imaging. This type of imaging uses the properties of different parts of the brain having different proportions of water (Rosenbloom & Pfefferbaum, 2008). It allows for visualization of the interior of the brain. When an MRI is taken, the difference in color shown is due to these different proportions of water. In an adult T1 MRI, white matter tends to be paler in color than the gray matter because the axons are wrapped in myelin (Rosenbloom & Pfefferbaum). Myelin is beneficial to brain function as it speeds up and synchronizes neural communication (Fields, 2008). During infancy, the volume of the white brain matter increases by 6-16%, demonstrating this development and change in the child (Knickmeyer et al., 2008). In infants, the white matter appears gray and the gray matter appears white. The colors are reversed. This change highlights that overall brain development is still occurring postnatally.

Spatial Memory and Hippocampus

Spatial memory plays a critical role in many cognitive skills. It is the ability to remember the locations, directions, and arrangements of objects in the environment (Kostakos et al., 2024). It serves as the foundation for spatial navigation. Throughout the development of a child, spatial memory consolidation grows. Spatial representation starts developing at the age of two but is limited in function until the age of five (Newcombe et al., 1998). As the child grows, cognitive mapping and spatial navigation strategies improve. It is not until the age of twelve or older where the spatial memory reaches a point similar to adults (Newcombe et al., 2019).

Age differences in spatial memory consolidation are significant. During the memory consolidation, the representations of spatial memory will shift from the hippocampus dependent to neocortical brain structure integration (Winocur & Moscovitch, 2011). Several studies have found that larger hippocampus volumes indicate better spatial memory. One study found that overall hippocampus size can be used as an indicator for spatial memory performance (Biegler et al., 2001). In a different study with adults, lesions in the hippocampus (decrease in hippocampus volume) can impair spatial memory processes (Shrager et al., 2007). Finally, in a separate study done with older children (ages 9-15 years old), a reduced hippocampal size was positively associated with poorer memory performance overall (Wheeler et al., 2011).

As adults age, however, there is a decrease in hippocampus size that is correlated to lower cognitive functioning such as episodic memory, working memory, and processing speed (O'Shea et al., 2016). All of these studies together show that the relationship between spatial memory and hippocampus size is positively associated in older children. In aging adults, the relationship shifts because age-related reductions in hippocampal volume are associated with decreases in spatial memory.

Assessing Spatial Memory

Assessing spatial memory in adults and older children is quite easy through surveys and answering questions. It is more difficult to measure cognitive function in young children, so many clinicians use the Wechsler Preschool and Primary Scale of Intelligence (WPPSI). WPPSI is a specific test for general IQ. The tasks were designed to be completed by children from 2 to 7 years old. WPPSI has published different versions with its most recent version (WPPSI-IV) coming in 2012. There are many subtests within the WPPSI that test different aspects of cognitive function. Two new working memory measures were released with the WPPSI-IV, including the picture memory and zoo locations tasks (Pearson WPPSI Brochure, 2012). Working memory refers to the amount of information that is held in the mind and used to carry out cognitive functions like problem solving (Oberauer et al., 2018). These two new tests on the WPPSI-IV provide opportunities to standardize working memory tasks from children as young as 2 years and 6 months all the way up to 7 years (Wechsler, 2012). The tasks remain nonverbal to allow children at a younger age to still perform. The previously used tests started at 6 years of age (Cowan, 2021). The zoo location task specifically can look into the visual working memory of a child.

Current Study

Despite the knowledge of the hippocampus and its association in adults and older children, there is little known about the current relationship between the hippocampus and spatial memory in children, specifically young children. Additionally, the current studies around this topic investigate concurrent spatial memory rather than using the hippocampus as a predictor for spatial memory in the future.

This study aims to examine the correlations between the hippocampus at an early age (1 to 2 years old) and assess the spatial memory through the WPPSI zoo location task at a later school age (6 to 7 years old). Given the current data about the positive relationship between the hippocampus volume and spatial memory, a positive correlation is anticipated between hippocampus volume at early age and spatial memory at school age. The results of this study can offer insights into the relationship between neural development and the spatial memory abilities of children. Understanding these connections and relationships can provide benefits for early identification of developmental delays.

Materials and Methods

Participants

The Baby Connectome Project (BCP) recruited a sample of 500 typically developing infants, toddlers, and preschool-aged children. The participants were selected for this study from existing registries at the University of North Carolina/University of Minnesota which were based on birth records. Additional participants also were recruited from "broader community centers" to create a representative sample of all children based on the US Census. The final way participants were recruited was through approaching new mothers at the "The Birthplace" (Name of Birthing Center) at the University of Minnesota/University of North Carolina hospitals. Data was collected in an accelerated longitudinal design. Specifically, participants were placed into cohorts of different ages. These cohorts were then followed for up to seven behavioral or imaging visits between the ages of 0 years to 5 years. Parental consent was obtained prior to participation. For more details, see Howell et al., 2016.

Inclusion/Extension

Participants were eligible for BCP recruitment if they were between the ages of 0 - 60 months. The participant could also be eligible if born at a gestational age of 37-42 weeks, had a birth weight appropriate for their age, and was born without pregnancy complications. Participants that were excluded were born prior to 37 weeks of gestation, had a birth weight lower than 2000 grams, or had a delivery complication. Participants were also excluded if they were adopted, had a first degree relative with autism or intellectual disability, had genetic conditions affecting growth, development, or cognition, or had any contraindication to MRI. Finally, participants were excluded from the study if their caregivers could not communicate in English to provide informed consent.

Procedure

Demographic and medical history information was collected from caregivers by telephone, the day prior to their lab visit. Once the information

was reviewed and the child was deemed eligible, a visit was scheduled. The child can be scanned either awake or sleep depending on the information provided by the parent. Awake scans need two BCP visits, one for training and the other for the scan. The training session mocks the scanning environment and prepares the child to reduce fear and anxiety. The second scan is recorded for results.

The data used in this study was a subset of the Baby Connectome Project Data. For these current analyses, BCP participants were filtered and selected if the participant had at least one MRI brain scan between 12 - 24 months and participated in the school-age follow-up visit of the BCP study. Participants with more than one MRI had one of their MRIs randomly selected for this study. The sample size for this study was 36.

Structural MRI Imaging

Images for the MRI were acquired on 3T Siemens Prisma MRI scanners using a Siemens 32 channel head coil at the Center for Magnetic Resonance Research (CMRR) at the University of Minnesota and the Biomedical Research Imaging Center (BRIC) at the University of North Carolina at Chapel Hill. The procedure consists of four main sequences: T1w, T2w, resting-state functional connectivity, and diffusion magnetic resonance imaging (dMRI). The images were collected by lengthening the TR from 8 msec to 30 msec and the TE from 4 to 5 msec to minimize waking. The T2 weighted images were generated with a variable flip angle turbo spin-echo sequence (turbo factor = 314, echo train length of 1166 msec, TR 3200 ms, Te 564 ms, resolution = 0.8 x 0.8 x 0.8 mm3). The T1 and T2 weighted images helped to provide structural brain development. T1 and T2 weighted images were prioritized first followed by the dMRI and rfMRI. If scans were not high enough quality because participants may have been moving during scanning or for some other reason, the scans were reacquired if possible. For more details, see Howell et al., 2016.

Hippocampal Subregion Segmentation

The MRI images were then run through a computer segmentation that used an algorithm to automatically label the parts of the brain including the hippocampus. The segmentation program is Baby Image Brain Segmentation Network also known as BIBSnet (Hendrickson et al., 2023). This program segmented the brain into its respective parts based on the algorithm it was programmed with (see Appendix A1). Because the hippocampus is the particular area of interest in the study, this area was manually segmented further. All of the borders were redefined and cleaned around the edges (see Appendix A2). To determine the difference between the body and head, the uncal apex was used. This is where the folded over structure retracts to the single layered body in the coronal view (see Appendix B). For the body and tail boundary, the line of fornix was used. This boundary occurs when the line of fornix was broken by the thalamus in the coronal view (see Appendix C).

After manual segmentations of the T1 and T2 images were completed, the images were converted back into native space. The volume was extracted from the T1 and T2 segmentations. The hippocampus volume is calculated based on the number of voxels labeled by the hippocampus as head, body, and tail for left and right. If a subject had a T1 and a T2 segmentation, the volumes were averaged across the T1 and T2 native spaces for the hippocampus because there was some degree of variability due to the probabilistic nature of the alignment algorithm in BIBSnet.

Behavioral Task WPPSI Zoo Location

At the school-age visit of the BCP, participants completed the standard WPPSI-IV battery, including the Zoo Locations task. In this task, a variable number of cards with pictures of animals is shown in a grid separated by walls. The instructions ask the child to remember where the monkey and animals live. The child is allowed to study the animals for 1 minute. After the study period, the cards are quickly collected and handed to the child. The task asks the child to place the animals in their respective locations. Two animals cannot be placed in the same location. If they get all the animals in the correct position, it is marked as a 1; otherwise, it is marked as a 0. The final score is the average across the number of trials until the child scores a 1. The orientation of the animal card is not mandatory for correctness. For more details, see Cowan, 2021.

Analysis

Descriptive statistics were consulted first through scatter plots. This was followed by a linear regression analysis to evaluate the association

between hippocampal volume and spatial memory performance, controlling for sex assigned at birth and age at MRI scan.

Results

Following the methods above, participants were selected for the project (see Table 1 for descriptive values). Age at MRI scan and sex were added as covariates. Other possible covariates that were looked at were race, ethnicity, and education of parents. There was not enough variability between those variables to the hippocampus size and WPPSI scores to contribute meaningfully to the data. Because WPPSI scaled scores are age normed standardized, the WPPSI age at follow-up visit was not included as a covariate.

A scatter plot was generated comparing the hippocampus size to the WPPSI Zoo Location scale score, separating participants based on sex assigned at birth (see Figure 1). Another scatter plot was generated as an exploratory analysis using the same axes but separating children based on being above or below the mean age of 17.44 months (see Figure 2).

Linear regression analysis was performed to evaluate the association between hippocampal volume and spatial memory performance, controlling for sex assigned at birth and age at MRI scan. The overall omnibus F was statistically significant ($F(4, 31) = 3.65$, $p = 0.0058$), indicating that the model explained a significant proportion of the variation in Zoo Location Score. The fitted regression coefficient for total hippocampal volume was negative and statistically significant ($B = -0.002$, $p = 0.0058$), suggesting that children with larger hippocampal volumes performed less well on the spatial memory task on average. Follow up analyses of the hippocampus bilateral head, body, and tail, indicated that only the right head volume was negatively associated with zoo location score ($B = -0.006$, $p = 0.0017$). No other statistical tests were significant (see Table 2 and Figure 3).

Discussion

This study found that there was a statistically significant negative correlation between hippocampus volume when children are between the ages of 1 and 2 years old and their spatial memory performance at school age. It was determined that the statistical significance of the model was driven only by the right hippocampus head (see Table 2).

Figure 3 demonstrates that this negative relationship is present in both the male and female participants. While the lines of the graph are not superimposed, the lines run parallel. This indicates that the relationship was unchanged based on sex assigned at birth. The offset in sex is likely due to the known difference in head size of males and females. Because males have larger heads than females and hippocampi are relative to head size, the males have a line that is parallel in slope but shifted to the right slightly along the x axis. Figure 2 demonstrates that this negative relationship is still mostly present in both the young children and the older children, although possibly attenuated in older children. This relationship can be tested in a further study.

The data from this study is not consistent with data of a study done on older children between the ages of 9 to 15 years olds (Wheeler et al., 2015), where a positive correlation between hippocampal volume and memory was found. Another study mirrors a similar result, where hippocampus volume can be used as an indicator for overall spatial memory performance (Biegler et al., 2001). However, both of these studies examine concurrent memory rather than using the hippocampus as a predictor for memory. The results of this current study suggest that the relationship between hippocampus volume and spatial memory is not positively correlated. The negative correlation could indicate that hippocampus volume alone cannot be the only predictor for spatial memory in the child. Spatial memory develops throughout puberty as the child explores and interacts with the environment (Kostakos et al., 2024). There could be other factors that influence spatial memory performance. This negative association identified between hippocampus volume and spatial memory calls for further research on this topic due to possible alternative explanations. One alternative explanation could be that the larger hippocampus indicates that there is inefficient processing of memory, not an advantage in spatial memory processing. Also, considering that this is one of the first studies analyzing this relationship at a young age, it might suggest that the relationship is indeed different at this younger age. The younger age children might also represent the children who mature the most rapidly between the scan and the WPPSI.

Despite the findings of this study, there were several limitations. One is the sample size. Although the sample was normally distributed in age at MRI scan, a sample size of 36 is relatively small. It impacts the ability for one to generalize the results. The low sample size occurred by filtering the BCP data to only contain the children whose data from the MRI scan and WPPSI zoo location task test was complete. Another limitation of this study is that overall brain size (intracranial volume) was not controlled for in this study. The hippocampal volumes available for this study were raw volumes and intracranial volume was not available to include as a covariate. Although age and sex were included as covariates, they do not fully account for global brain size. As a result, the negative association between hippocampal volume and spatial memory may partially be due to the differences in overall brain volume rather than hippocampal size specific effects.

Also, because the study relied on data at a specific time point, overall development could not be mapped out. If a child had multiple MRI scans between the ages of 1 to 2 years old, only one scan was randomly selected to be used for that child. There was no longitudinal data because the study compared discrete time points in the child's life (one to two years old and school age). Finally, the finer structural differences of the hippocampus such as the subfields of the hippocampus (Cornu Ammonis, Entorhinal Cortex, Dentate Gyrus, etc.) track more with the histological differences. The subfields, synaptic organizations, and projections of the hippocampus were beyond the scope of this study but could play a role in this correlation.

Due to a low sample size and a possibility of cohort effect, the negative relationship might have been seen. Participants with lower hippocampus volumes simply had higher WPPSI scores on the zoo location task. This effect might be from selection bias where the result only represents the characteristic of the sample and not of reality. This could lead to a Type I error where this study found something that is not actually present in society, a false positive.

Future directions of this study include expanding the overall sample size, while controlling for overall brain size, to increase the generalizability of the results. Also, it would be beneficial to run these same analyses with different age bins such as 0-1 years old and 2-3 years old. This could help to see if the results are applicable across a child's development or only found between 1-2 years old. This study also could encourage the investigation of the correlation between hippocampal volume and other aspects of memory such as episodic memory.

Overall, while this study finds that there is a statistically significant negative relationship between hippocampus volume and spatial memory, the results show the complexities of human development. The study demonstrates the need for further research of this relationship. Understanding this relationship could provide valuable insights into hippocampal development and its association with spatial memory in young children.

Figures and Tables

Table 1: Descriptive Values of data collected for participants and their respective hippocampal sizes

	n = 36 **Mean (SD) / n (%)**
Age at scan (months)	17.44 (3.28)
WPPSI Age (months)	62.40 (10.09)
Ethnicity	
Hispanic	2 (5.6%)
Non-Hispanic	34 (94.4%)
Race	
White	34 (94.4%)
>1 Race Endorsed	2 (5.6%)
Income	
<100K a year	19 (52.8%)
>100K a year	17 (47.2%)
Education	
No college	1 (2.8%)
Some/grad of college	17 (47.2%)
Some/grad of graduate school	18 (50%)
Total Hippocampal Volume (mm^3)	5855.35 (633.17)
Left Hippocampus Head (mm^3)	1486.83 (212.22)
Left Hippocampus Body (mm^3)	1080.63 (129.95)
Left Hippocampus Tail (mm^3)	330.63 (100.59)
Right Hippocampus Head (mm^3)	1614.19 (262.33)
Right Hippocampus Body (mm^3)	1021.42 (130.00)
Right Hippocampus Tail (mm^3)	321.65 (131.27)

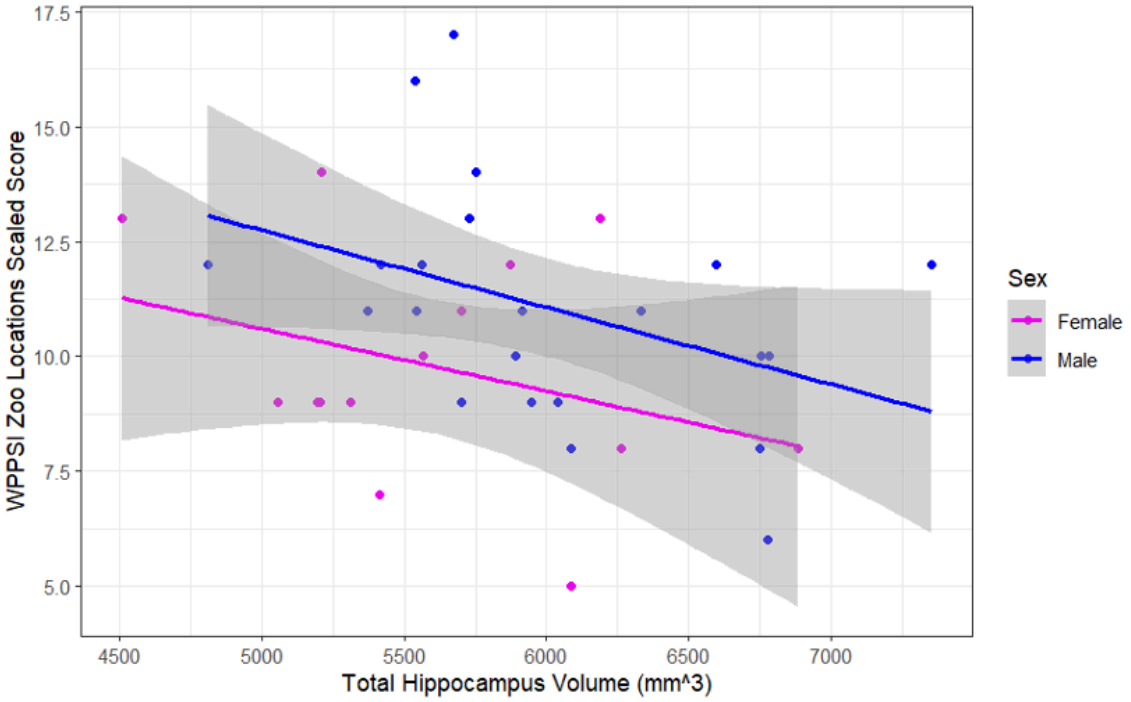


Figure 1: Relationship between total hippocampal volume and WPPSI Zoo Location Scaled Score separated by sex assigned at birth.

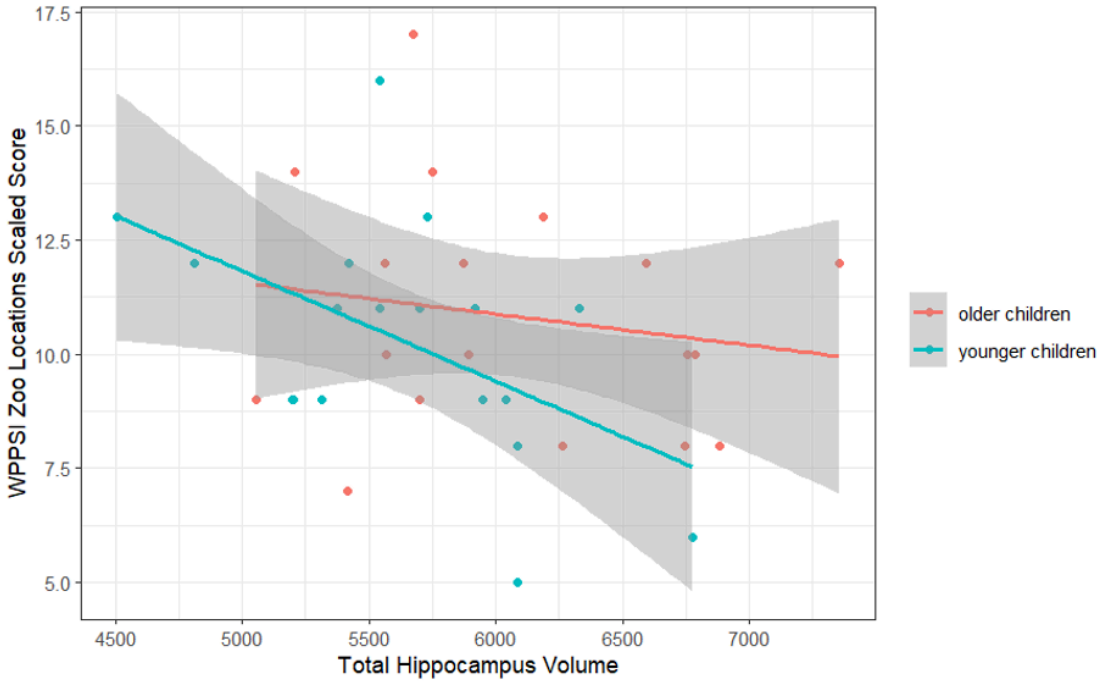


Figure 2: Relationship between total hippocampal volume and WPPSI Zoo Location Scaled Score separated by older children and younger children. Older children were children above the mean of the sample of 17.44 months. Younger children were below the mean of the sample, 17.44 months.

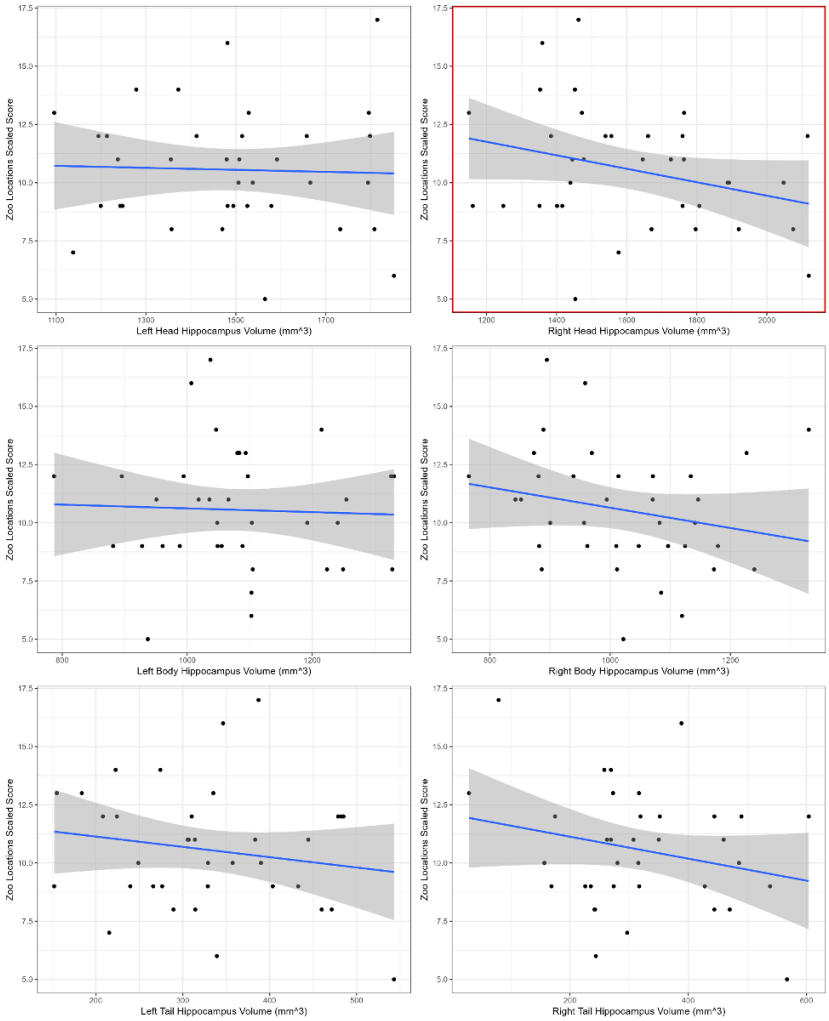
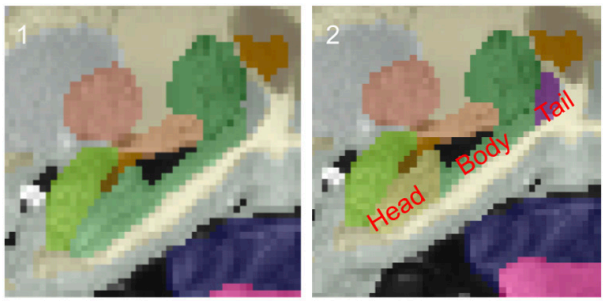


Figure 3: Correlations between hippocampal subregions and WPPSI Zoo Location Task Scaled Score. Among all subregions analyzed, only the right hippocampal head (highlighted in red) was statistically significant at $p = 0.05$. See Table 2 for statistical significance for each of the subregions.

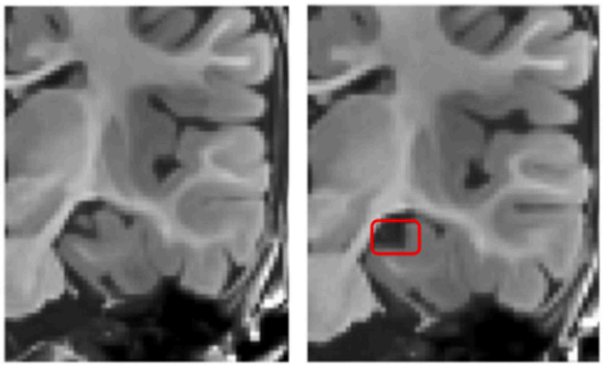
	Estimate	**p value**
Total Hippocampus	-0.0019147	0.0150*
Left Hippocampus Head	-0.001801	0.4472
Left Hippocampus Body	-0.001777	0.6290
Left Hippocampus Tail	-0.004240	0.3388
Right Hippocampus Head	-0.006486	0.0013*
Right Hippocampus Body	-0.004274	0.2109
Right Hippocampus Tail	-0.005170	0.1244

Table 2: Statistical Significance of Hippocampal Region Correlations Between Hippocampal Size and WPPSI Zoo Location Scaled Score. * = statistically significant at a p value of 0.05

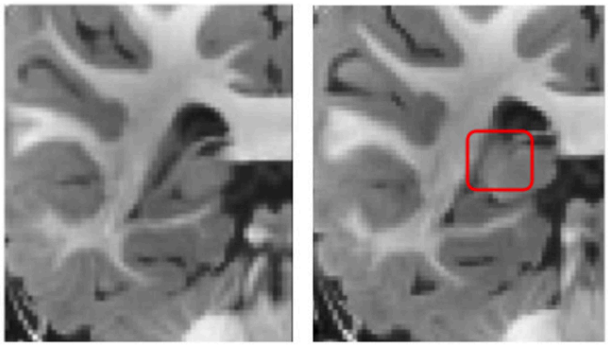
Appendices



Appendix A: Picture on the left (A1) shows the sample output after MRI segmentation is run through the BIBSnet program. Picture on the right (A2) shows the sample output after the hippocampus is manually adjusted for the head, body, and tail of the hippocampus.



Appendix B: The uncal apex is folded over on the left figure. On the right figure highlighted in the red box, the uncal apex retracts and is no longer visible. (Images from Stoyell unpublished dissertation)



Appendix C: The line of fornix is not intersected in the left figure. In the right figure, highlighted in the red box, the line of fornix is intersected by the thalamus. (Images from Stoyell unpublished dissertation)

Acknowledgements

I would like to thank Dr. Meghan Swanson and Dr. Jed Elison of the Cognition and Neurodevelopmental Studies Lab for helping me complete my thesis. They have provided me with constant encouragement and support throughout the process. I am grateful for their insight and dedication. I would also like to thank Dr. Sally Stoyell who helped guide me through data analysis. She lent me so much time in completing the thesis, and I appreciate her contributions. I would also like to thank Dr. Antony Dean and Dr. Daniel Berry for serving as my thesis committee members. They took time out of their busy schedules to read and provide feedback for my thesis. Their revision suggestions were helpful in improving the overall quality of my paper, and their expertise was invaluable. Lastly, I would like to extend my gratitude to the professors and staff at the College of Biological Sciences and the University Honors Program at the University of Minnesota - Twin Cities for all of their help throughout the completion of my neuroscience degree.

References

Anand, K., & Dhikav, V. (2012). Hippocampus in health and disease: An overview. *Annals of Indian Academy of Neurology, 15*(4), 239–246. https://doi.org/10.4103/0972-2327.104323

Ashbrook, D. G., Williams, R. W., Lu, L., Stein, J. L., Hibar, D. P., Nichols, T. E., Medland, S. E., Thompson, P. M., & Hager, R. (2014). Joint genetic analysis of hippocampal size in mouse and human identifies a novel gene linked to neurodegenerative disease. *BMC Genomics, 15*(1), 850–850. https://doi.org/10.1186/1471-2164-15-850

Barrós-Loscertales, A., Meseguer, V., Sanjuán, A., Belloch, V., Parcet, M.A., Torrubia, R., Avila, C. (2006). Behavioral Inhibition System activity is associated with increased amygdala and hippocampal gray matter volume: A voxel-based morphometry study. *NeuroImage (Orlando, Fla.), 33*(3), 1011–1015. https://doi.org/10.1016/j.neuroimage.2006.07.025

Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The Human Hippocampus and Spatial and Episodic Memory. *Neuron, 35*(4), 625–641. https://doi.org/10.1016/S0896-6273(02)00830-9

Cowan N. (2021). Differentiation of Two Working Memory Tasks Normed on a Large U.S. Sample of Children 2-7 Years Old. *Child Development, 92*(6), 2268–2283. https://doi.org/10.1111/cdev.13562

Ezzati, A., Katz, M. J., Zammit, A. R., Lipton, M. L., Zimmerman, M. E., Sliwinski, M. J., & Lipton, R. B. (2016). Differential association of left and right hippocampal volumes with verbal episodic and spatial memory in older adults. *Neuropsychologia, 93*(Pt B), 380–385. https://doi.org/10.1016/j.neuropsychologia.2016.08.016

Fields, R. D. (2008). White matter in learning, cognition and psychiatric disorders. *Trends in Neurosciences, 31*(7), 361–370. https://doi.org/10.1016/j.tins.2008.04.001

Glover G. H. (2011). Overview of functional magnetic resonance imaging. *Neurosurgery Clinics of North America, 22*(2), 133–vii. https://doi.org/10.1016/j.nec.2010.11.001

Guadalupe, T. , Mathias, S. R. , vanErp, T. G. M. , Whelan, C. D. , Zwiers, M. P. , Abe, Y. , … Francks, C. (2017). Human subcortical brain asymmetries in 15,847 people worldwide reveal effects of age and sex. *Brain Imaging and Behavior, 11*(5), 1497–1514.

Hannula, D. E., & Duff, M. C. (Eds.). (2017). *The hippocampus from cells to systems: Structure, connectivity, and functional contributions to memory and flexible cognition*. Springer. https://doi.org/10.1007/978-3-319-50406-3

Howell, B. R., Styner, M. A., Gao, W., Yap, P.-T., Wang, L., Baluyot, K., Yacoub, E., Chen, G., Potts, T., Salzwedel, A., Li, G., Gilmore, J. H., Piven, J., Smith, J. K., Shen, D., Ugurbil, K., Zhu, H., Lin, W., & Elison, J. T. (2019). The UNC/UMN Baby Connectome Project (BCP): An overview of the study design and protocol development. *NeuroImage (Orlando, Fla.), 185,* 891–905. https://doi.org/10.1016/j.neuroimage.2018.03.049

Immordino-Yang, M. H., & Singh, V. (2013). Hippocampal contributions to the processing of social emotions. *Human Brain Mapping, 34*(4), 945–955. https://doi.org/10.1002/hbm.21485

Kong, X. Z., Postema, M. C., Guadalupe, T., de Kovel, C., Boedhoe, P. S. W., Hoogman, M., Mathias, S. R., van Rooij, D., Schijven, D., Glahn, D. C., Medland, S. E., Jahanshad, N., Thomopoulos, S. I., Turner, J. A., Buitelaar, J., van Erp, T. G. M., Franke, B., Fisher, S. E., van den Heuvel, O. A., Schmaal, L., … Francks, C. (2022). Mapping brain asymmetry in health and disease through the ENIGMA consortium. *Human Brain Mapping, 43*(1), 167–181. https://doi.org/10.1002/hbm.25033

Kostakos, K., Pliakopanou, A., Meimaridis, V., Galanou, O. O., Anagnostou, A. A., Sertidou, D., Katis, P., Anastasiou, P., Katsoulidis, K., Lykogiorgos, Y., Mytilinaios, D., Katsenos, A. P., Simos, Y. V., Bellos, S., Konitsiotis, S., Peschos, D., & Tsamis, K. I. (2024). Development of

spatial memory: A behavioral study. *NeuroSci, 5*(4), 713–728. https://doi.org/10.3390/neurosci5040050

Knickmeyer, R. C., Gouttard, S., Kang, C., Evans, D., Wilber, K., Smith, J. K., Hamer, R. M., Lin, W., Gerig, G., & Gilmore, J. H. (2008). A Structural MRI Study of Human Brain Development from Birth to 2 Years. *The Journal of Neuroscience, 28*(47), 12176–12182. https://doi.org/10.1523/JNEUROSCI.3479-08.2008

Massoud, T. F. (2022). Neuroimaging Anatomy, Part 1: Brain and Skull. *Neuroimaging Clinics of North America, 32*(3), i-. https://doi.org/10.1016/S1052-5149(22)00047-8

Newcombe, N., Huttenlocher, J., Drummey, A. B., & Wiley, J. G. (1998). The development of spatial location coding: Place learning and dead reckoning in the second and third years. *Cognitive Development, 13*(2), 185–200. https://doi.org/10.1016/S0885-2014(98)90038-7

Newcombe, N. S. (2019). Navigation and the developing brain. *Journal of Experimental Biology, 222*(Suppl_1). https://doi.org/10.1242/jeb.186460

Nichols, E. S., Grace, M., Correa, S., de Vrijer, B., Eagleson, R., McKenzie, C. A., de Ribaupierre, S., & Duerden, E. G. (2024). Sex- and age-based differences in fetal and early childhood hippocampus maturation: a cross-sectional and longitudinal analysis. *Cerebral Cortex, 34*(1). https://doi.org/10.1093/cercor/bhad421

Oberauer K, Lewandowsky S, Awh E, Brown GDA, Conway A, Cowan N, … Ward G (2018). Benchmarks for models of working memory. *Psychological Bulletin, 144,* 885–958. 10.1037/bul0000153

O'Shea, A., Cohen, R. A., Porges, E. C., Nissim, N. R., & Woods, A. J. (2016). Cognitive Aging and the Hippocampus in Older Adults. *Frontiers in Aging Neuroscience, 8,* 298–298. https://doi.org/10.3389/fnagi.2016.00298

Rosenbloom, M. J., & Pfefferbaum, A. (2008). Magnetic resonance imaging of the living brain: Evidence for brain degeneration among alcoholics and recovery with abstinence. *Alcohol Research & Health: The Journal of the National Institute on Alcohol Abuse and Alcoholism, 31*(4), 362–376.

Shrager, Y., Bayley, P. J., Bontempi, B., Hopkins, R. O., & Squire, L. R. (2007). Spatial memory and the human hippocampus. *Proceedings of the National Academy of Sciences of the United States of America, 104*(8), 2961–2966. https://doi.org/10.1073/pnas.0611233104

Wechsler, D. (2012). *WPPSI–IV, Wechsler Preschool and Primary Scale of Intelligence—Fourth Edition: Administration and scoring manual.* San Antonio, TX: NCS Pearson.

Wheeler, S. M., Willoughby, K. A., McAndrews, M. P., & Rovet, J. F. (2011). Hippocampal Size and Memory Functioning in Children and Adolescents with Congenital Hypothyroidism. *The Journal of Clinical Endocrinology and Metabolism, 96*(9), E1427–E1434. https://doi.org/10.1210/jc.2011-0119

Winocur, G., & Moscovitch, M. (2011). Memory Transformation and Systems Consolidation. *Journal of the International Neuropsychological Society, 17*(5), 766–780. https://doi.org/10.1017/S1355617711000683