Children show adult-like hippocampal pattern similarity for familiar but not novel events

Susan L. Benear*[1], Elizabeth A. Horwath*[1], Emily Cowan[1], M. Catalina Camacho[2], Chi T. Ngo[3], Nora S. Newcombe[1], Ingrid R. Olson[1], Susan B. Perlman[2], Vishnu P. Murty[1]

*equal contribution

[1] Department of Psychology, Temple University, Philadelphia, USA

[2.] Department of Psychiatry, Washington University of St. Louis, St. Louis, USA

[3] Max Planck Institute for Human Development, Berlin, Germany

Address correspondence to:

Vishnu P. Murty
Department of Psychology
Temple University
1701 N. 13thStreet
Philadelphia, PA 19122
email: Vishnu.murty@temple.edu

Abstract

The ability to detect differences among similar events in our lives is a crucial aspect of successful episodic memory performance, which develops across early childhood. The neural substrate of this ability is supported by operations in the medial temporal lobe (MTL). Here, we used representational similarity analysis (RSA) to compare neural pattern similarity in hippocampus and in parahippocampal cortex for 4- to 10-year-old children and adults during naturalistic viewing of clips from the same movie or from different movies. Further, we assessed familiarity with individual movie clips that varied across participants. Neural pattern similarity was lower for clips from the same movies, suggesting that related content activates differentiation processes. However, children showed differentiation only for movies with which they were familiar, whereas adults showed the effect for both familiar and unfamiliar movies. These data suggest that children require extended exposure to stimuli to reach maturity of MTL functioning in differentiating similar events.

Keywords: representational similarity analysis, differentiation, hippocampus, cognitive development, episodic memory

Introduction

Young children do not remember events that they have experienced as well as adults do. Emerging research suggests that the lack of refined memory processes results from immaturity in the physical structures supporting episodic memory. The key brain region supporting episodic memory is the medial temporal lobe (MTL), which can be further divided into functional subregions. Prominent models propose that the hippocampus (HPC) and surrounding parahippocampal cortex (PHC) support contextual representations that can help differentiate highly similar events (Davachi, 2006; Eichenbaum et al., 2012), collectively allowing for the formation and retrieval of richly detailed episodic memories. However, retention of distinct episodic memories must overcome the problem of differentiating related information across episodes, as when two events share the same context. This kind of overlap necessitates keeping highly similar memories from interfering with one another. MTL regions, specifically the hippocampus, contribute to this process (Kirwan & Stark, 2007).

Research on the development of episodic memory has shown that MTL structure and activation during encoding often differ between children and adults (reviewed in Ghetti & Bunge, 2012), and hippocampal subfields supporting episodic specificity show relatively late maturational profiles in both humans (e.g., Riggins et al., 2018; Keresztes et al., 2017) and nonhuman primates (Lavenex & Banta Lavenex, 2013). Due to the protracted maturation of MTL structures, which underly memory processes, one would predict that these memory processes are not able to function maturely in early childhood, although they may begin to approach adult-like levels by middle or late childhood.

One important feature that may drive differences in MTL function across age groups is familiarity. In adults, increased familiarity with stimuli improves memory performance (Poppenk

et al., 2010). In children, repeated exposures to information enhances vocabulary learning and improves retention (Horst et al., 2011; Koenig et al., 2020). Familiarity can be thought of as multi-leveled. In children, repeated exposure may help them to comprehend their experiences, as they have less schematic knowledge that helps them predict what will happen next and which items are conceptually similar. In adults, repetition may primarily assist in the encoding of details that were missed the first time. Thus, familiarity with stimuli likely affects memory performance, especially in children, and this may be reflected in how the brain encodes information that is familiar versus information that is novel.

In the present study, we reanalyzed the KidVid dataset, which was designed to study temperament, affect, and neurodevelopment by using child-friendly naturalistic movie stimuli (Camacho et al., 2019; Karim & Perlman, 2017). We used it to investigate neural processes in the MTL in children as compared to adults. Children ages 4-10 and adults viewed video clips from popular family-friendly movies, with two clips coming from each movie, which enabled the comparison of idiosyncratic experiences that were drawn from the same context (i.e., within movie) or different contexts (i.e., across movies; Larocque et al., 2013). While we know much about age-related structural differences in the hippocampus across development (Canada et al., 2020; Gogtay et al., 2006; Krogsrud et al., 2014; Lavenex & Banta Lavenex, 2013), understanding children's functional activation while viewing naturalistic stimuli could inform how their MTL regions interact when encoding real-world events, which are often much richer and more complex than stimuli employed in traditional memory tasks.

We used representational similarity analysis (RSA) to examine age-related differences in patterns of activation in two MTL regions—the HPC and PHC—during viewing of movies for memoranda within versus across movies, thus allowing us to investigate how these regions may

differentiate between memoranda drawing from the same versus different contexts. RSA is a technique in which the multivoxel pattern responses of stimuli—obtained using similar methods to classification-based multivoxel pattern analysis (MVPA)—are compared to one another to provide a higher-order representation of the stimuli (Popal, Wang, & Olson, 2020). Simply stated, RSA helps to characterize how particular stimuli are represented in the brain. Studies using RSA of related and unrelated stimuli (e.g., Chanales et al., 2017; Favila et al., 2016) demonstrate that multivariate neuroimaging analyses can give insight into operations in the MTL that serve to differentiate similar stimuli. We operationalized an augmentation in pattern dissimilarity for related experiences compared to unrelated experiences as a proxy for differentiation in representations for more similar versus less similar events. Further, given prior evidence that differentiation is particularly engaged for well-studied items (e.g., Chanales et al., 2017; Favila et al., 2016), we assessed the role of familiarity in these processes.

The goal of this study was to arbitrate between two competing hypotheses. One hypothesis is that children will show dissimilar activation patterns compared to adults because immature MTL structures do not yet support mature mnemonic processing. This hypothesis would further suggest a relationship between age and neural pattern similarity within our child sample, as our age range spans a developmental window in which critical hippocampal changes and behavioral memory improvements are both taking place. The second and competing hypothesis is that children will show similar patterns to adults only when they are familiar with the stimuli. This hypothesis rests on prior findings showing increased memory performance in children when they are given increased exposure to memoranda (Horst et al., 2011; Koenig et al., 2020). In our study, this would be demonstrated by finding differences in pattern similarity for

children that mirror those found in adults—but only for movies which they have previously viewed.

Methods

Participants

Fifty-seven participants (21 adults and 36 children) with no history of psychiatric diagnosis were recruited from the University of Pittsburgh. After removing participants for excess head motion (see Methods: MRI data acquisition and pre-processing), our final sample consisted of 20 adults (9 female, 11 male; age 20-44, M_{age} = 26.65) and 25 children (14 female, 11 male; age 4-10, M_{age} = 7.36). Our child sample was distributed unevenly across the age range (see Figure 1), with few children under the age of 6 represented. This is important to keep in mind since the early childhood years represent a critical developmental window for memory—we address this in the following analyses by evaluating the relationship of reported effects by age within our child sample. Before participation began, adult participants and children's parents/guardians provided written consent and children provided assent.

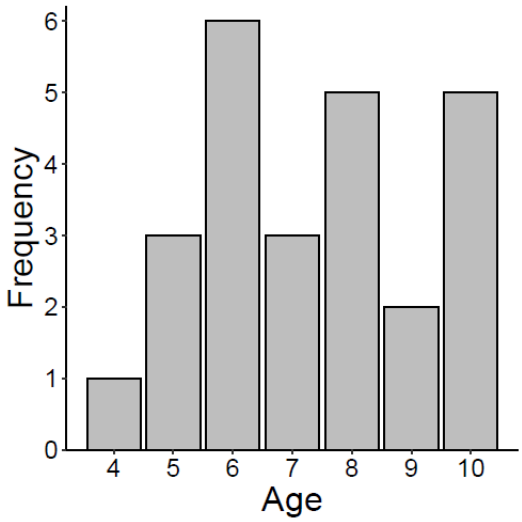

Figure 1 Distribution of children's ages.

Movie-viewing task

Participants watched 24 movie clips (see Figure 2A) while undergoing functional magnetic resonance imaging (fMRI). This task is explained in further detail in Karim & Perlman (2017) and Camacho, Karim, & Perlman (2019). In brief, clips ranged in length from 19-46 seconds (M = 31.1 seconds) with a jittered inter-stimulus interval (ISI) of 6-12 seconds, totaling 17 minutes of viewing time. The 24 clips were of positive, negative, or neutral affective valence (eight each). The positive and negative clips were taken from eight popular, child-friendly movies (e.g., *Lion King*, *Up*, etc.), with one positive and one negative clip taken from each movie; the neutral clips were taken from nature documentaries. Each clip was rated on a second-by-second basis for the valence of positive or negative affective content by an independent rater. Critically, there was no difference between positive and negative clips in duration ($t(14) = -.67$, $p = .51$) or absolute value of emotional valence ($t(14) = 1.38$, $p = .19$; Karim & Perlman, 2017). For the purpose of the current work, we only looked at positive and negative clips, as they were the only stimuli for which there were two clips drawn from the same movie. The order of clips was randomized across three versions, which were randomly assigned to participants. Participants were simply instructed to lay in the scanner without moving while "[watching] the movies as they normally would" (Karim & Perlman, 2017). To ensure that participants were adequately attending to the task, a 16-question quiz was given following the scanning session in which participants were asked whether still frame images were taken from the clips they had watched—accuracy was near ceiling in both children and adults (Karim & Perlman, 2017). Additionally, adult participants and children's parents reported on their/their child's familiarity with each movie on a scale of "never seen it", "seen only parts", "has seen it once or twice", or "watches often". Parents could ask their children if they were unsure. Importantly, the movies used in this study were all older films that were not recently released, therefore increasing the

likelihood that adults and children would have equivalent exposure to the films, and decreasing the influence on familiarity of toys, games, etc. that tend to accompany newly-released movies. Adults and children did not differ in average familiarity with the movies ($t(43) = -.40$, $p = .69$). For our analyses, we binned familiarity into low ("never seen it" and "seen only parts") and high ("has seen it once or twice" and "watches often"). There was no difference in the number of movies that were rated high ($M = 4.32$, $SD = 2.04$) versus low on familiarity ($M = 3.68$, $SD = 2.04$) in children ($t(24) = -.79$, $p = .44$). In adults, there was also no difference between high ($M = 4.25$, $SD = 1.16$) versus low ($M = 3.75$, $SD = 1.16$) familiarity ratings ($t(19) = -.96$, $p = .35$).

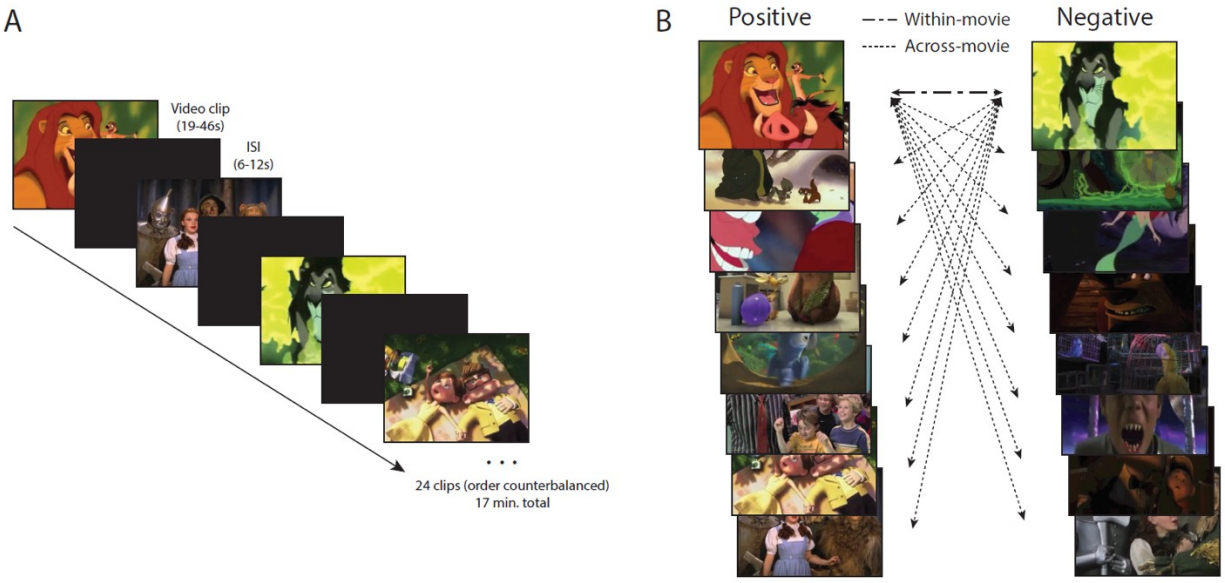

Figure *2* (A) Task schematic. Participants viewed movie clips while undergoing fMRI. (B) Depiction of within- and across-movie correlations to calculate pattern similarity for related and unrelated stimuli.

MRI data acquisition and pre-processing

MRI data was collected using a 3T Siemens Trio scanner with a 12-channel parallel transmit-receive head coil. Functional whole brain blood oxygen-level dependent (BOLD) images were collected in a sagittal acquisition (excluding part of the middle/superior temporal cortex from both hemispheres; TR = 2,000 ms, TE = 30 ms, flip angle = 90°, FOV = 256 mm, matrix size 64 x 64, voxel size 4 x 4 x 4 mm). Five hundred and ten brain volumes were collected during this gradient echo EPI (echo-planar imaging) sequence, lasting 17 minutes and 6 seconds, collected in a single run.

We preprocessed our data in a manner that would minimize the effects of head motion. This included preprocessing using FEAT (fMRI Expert Analysis Tool) with high-pass filtering, and skull stripping using BET (Brain Extraction Tool) in FSL version 5.0 (FMRIB Software Library; Jenkinson et al., 2012). Functional data were then registered to the anatomical images and nonlinearly warped to MNI space. Head motion and noise-related factors were identified by

calculating and thresholding metric values of how motion-affected each time point was using timeseries extracted from white matter and CSF, six head motion parameters, and their first derivatives. In addition to the listed nuisance regressors, we identified and regressed out individual TRs based on excessive head motion if greater than 15% of TRs were considered outliers, or if head motion values for any of the three rotations were greater than 1.5mm.

Analyses

To investigate neural pattern similarity, for each participant we first estimated voxel-wise activation in response to each movie clip. We constructed a GLM with each individual movie clip modeled separately, including neutral clips not used in the current analyses, using a double-gamma hemodynamic response function (HRF) with the duration of the movie clip (19-46 sec). From these single-clip activation maps, we extracted the activation of each individual voxel from our regions of interest (ROI). The hippocampal ROI was taken from the Harvard-Oxford subcortical atlas and thresholded at 50%. The PHC ROI was created from manually-segmented T1 images and thresholded at 50% (Ritchey, Montchal, Yonelinas, & Ranganath, 2015). All ROIs were defined at the group level in MNI space and transformed into subject native space using non-linear estimation (FNIRT) and visually inspected for accuracy.

We used representational similarity analysis (RSA) to compare pattern similarity within and across movie clips (Figure 2B). Within-movie correlations were defined as the correlation between the *t*-statistics across individual voxels within a region of interest for two clips from the same movie (e.g., *Lion King* positive-valence to *Lion King* negative-valence). We Fisher-transformed each correlation and then took the average of all eight correlations to yield one within-movie similarity value per participant. Across-movie correlations were the average of correlations between the *t*-statistics across individual voxels within a region of interest in

response to each negative clip to every other positive clip—critically excluding the clip from the same movie—and each positive clip to every other negative clip. This was done to reflect the same type of across-valence comparisons that were inherent in the within-movie correlations. We then Fisher-transformed each correlation coefficient and then took the average of the 28 values to yield one across-movie correlation value for each participant.

We wanted to ensure that there was no effect of valence in the across-movie correlations. It is mathematically the case that combining correlations from each negative clip to all other positive clips and each positive clip to all other negative clips results in the same pattern similarity. Due to the nature of capturing all possible correlations in the across-movie comparisons in RSA, there is no effect of valence on our results. For further clarification, see Figure S1. There is also naturally a larger number of correlations being computed for the across-movie comparisons (7 + 7) than for the within-movie comparisons (1) for each movie, leading to wider and more variable within-movie distributions. Rather than sampling a subset of across-movie correlations to match the availability of within-movie data, we opted to use all of the data available to provide a more accurate depiction and reduce the variability in this metric.

Finally, for our main analyses aimed at determining the differences in pattern similarity within and across movies, we wanted to ensure that our results were not due to differences in univariate activation. To mirror the correlations we obtained for similarity, we calculated univariate activation within and across movies separately. For within-movie univariate activation, we took the mean signal between the two clips from each movie (e.g., *Lion King* positive-valence and *Lion King* negative-valence). To calculate across-movie univariate activation for each clip, we took the mean signal of all clips excluding the target clip. We then ran a model comparison between the base model that contained the fixed effect of interest (e.g.,

within versus across correlation) and the same model that also included univariate activation for that region on a movie-level basis, to evaluate whether any effects of pattern similarity we found were due in part to univariate activation. In cases where the model comparison is significant, we cautiously interpret the similarity effects given that we cannot be fully sure that the patterns are not due to differences in mean activity level.

Results

Before conducting our main analysis of interest, we determined if there were any effects of laterality within each ROI (i.e., HPC, PHC, and V1) and age group (children, adults). Specifically, we ruled out laterality effects by separately running a two-way analysis of variance (ANOVAs) in children and adults with pattern similarity predicted by correlation type (within-movie versus across-movie) and laterality. No significant laterality differences were seen in any of these regions (all p's > .07). Thus, laterality was only included as a control term for relevant analyses.

Hippocampus (HPC)

To determine if correlation type significantly influenced pattern similarity, we submitted our RSA values for HPC to a mixed effects model in which subject and video identity were defined as random effects and laterality as a control term. To determine significance, we ran model comparisons in which one model contained the fixed effect of interest (e.g., within- versus across-movie correlation) and the other model excluded that effect with everything else remaining. Using these mixed effects models, we asked whether adults and children, separately, show different levels of hippocampal pattern similarity when viewing clips from the same

compared to different movies. In adults, we found a significant effect of correlation type (i.e., within- versus across-movie), such that within-movie comparisons showed lower pattern similarity than across-movie comparisons ($\chi^2 = 14.95$, $p < .001$; Figure 3A). Like adults, children showed the same pattern of lower similarity within-movies ($\chi^2 = 5.07$, $p = .02$; Figure 3A).

Next, we asked if there was a difference in pattern similarity across correlation type between children and adults by calculating a difference score (within – across) for each participant. A two-samples *t*-test revealed no significant difference between the age groups ($t(40.14) = -1.03$, $p = .31$, $BF_{01} = 2.20$; Figure 3B). Because our sample included children spanning ages 4-10 years, we predicted that there might be variation in similarity patterns within the child group, as substantial neural development takes place across this age range. Thus, to examine whether children's pattern similarity profile would more closely resemble that of adults with increasing age, we tested whether age was related to the within-across difference score in children only, and found no significant relationship ($r^2 = 2 \times 10^{-5}$, $F(1,23) = .0006$, $p = .98$, $BF_{01} = 2.72$; Figure 3C).

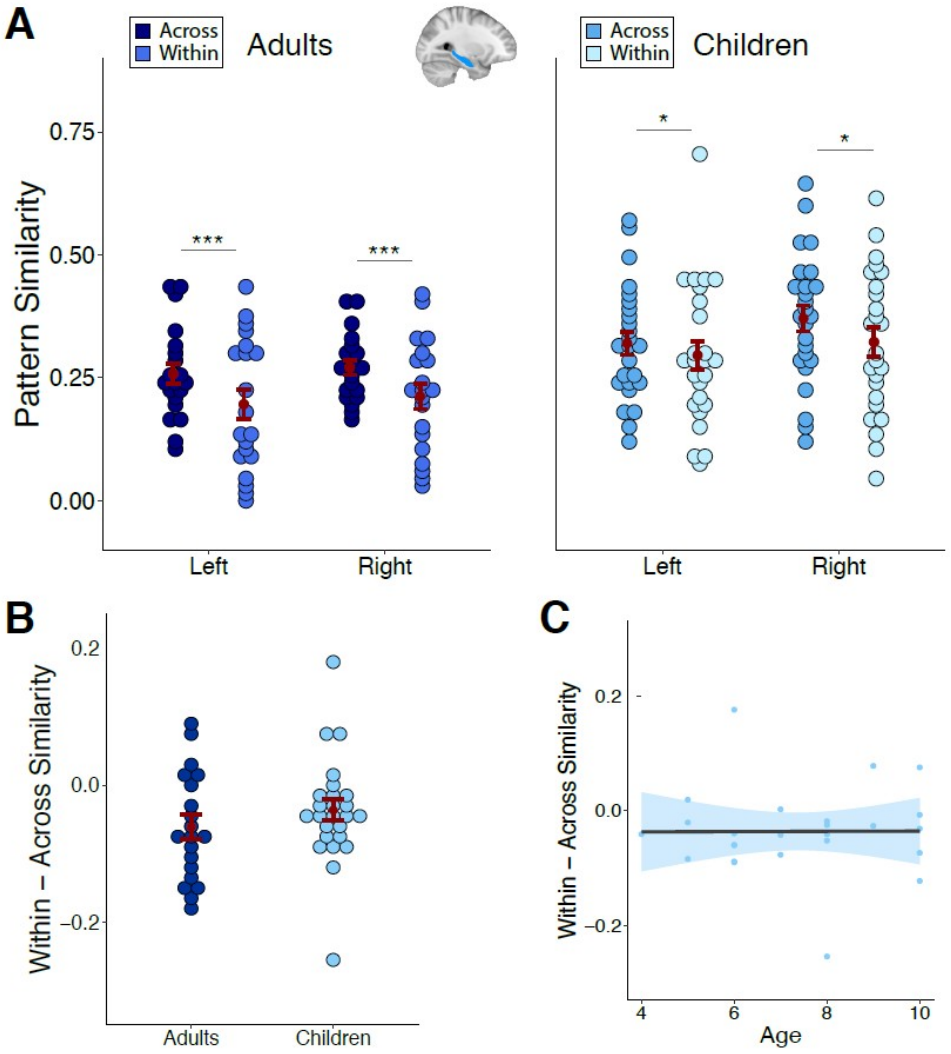

Figure 3. RSA effects in hippocampus. (A) Mixed-effect models conducted separately for adults and children including correlation type (within vs. across) and laterality. (B) Comparison of adults and children by within – across similarity score. (C) Regression of within – across pattern similarity on age in children. Error bars represent standard error of the mean. ***$p < .001$, *$p < .05$

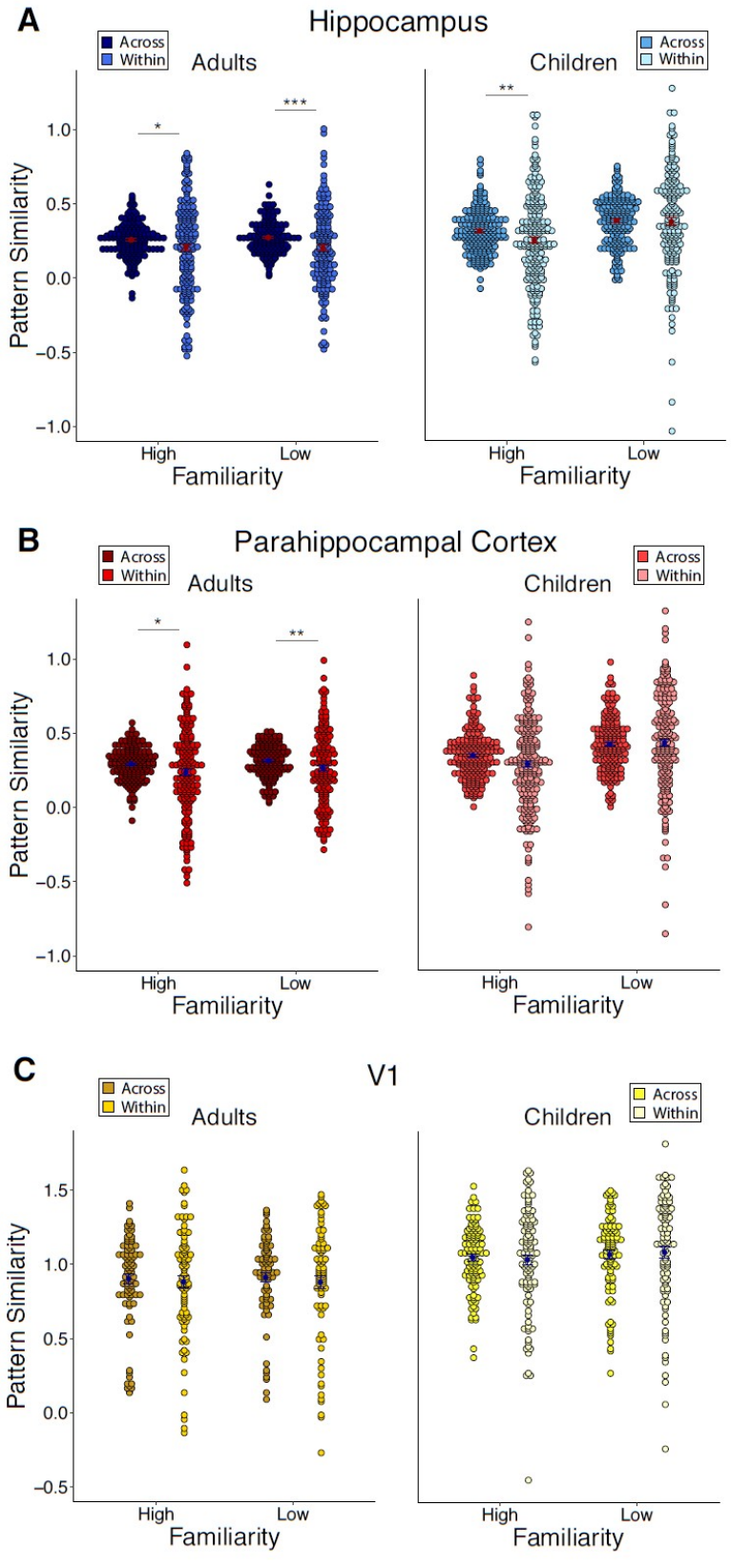

Figure 4. Planned t-tests for differences in within- versus across-movie comparisons by high and low familiarity in (A) HPC, (B) PHC, and (C) V1, each run separately for adults and children. Error bars represent standard error of the mean. ***p < .001, **p < .01 *p < .05

Finally, we tested whether the participants' familiarity with the movies would explain any differences in neural similarity between the within- and across-movie correlations. Bonferroni-corrected planned t-tests revealed that adults had lower hippocampal pattern similarity for within-movie comparisons than across-movie comparisons both when they were highly familiar ($t(169) = 2.39$, $p = .04$; Figure 4A) and when they were less familiar ($t(149) = 3.88$, $p < .001$) with the movie. Interestingly, this pattern was only evident in children when they were highly familiar with the movie ($t(215) = 3.32$, $p = .002$), but not

when they had low familiarity with the movie ($t(183) = .25$, $p = .80$; Figure 4A). We then asked if, among the low familiarity clips, there was an interaction between age group and within/across comparisons. We saw a significant interaction between a model including only main effects of age group and correlation type and a model with their interaction term ($\chi^2 = 4.28$, $p = .04$)—a *t*-test revealed that adult pattern similarity within movie is significantly lower than that for children for low familiarity clips ($t(331.8) = -5.16$, $p < .001$). All aforementioned significant effects hold in a model comparison including movie-level univariate activation (see Supplemental Table 1).

Parahippocampal Cortex (PHC)

We then tested whether, similar to HPC, adults and children show different levels of pattern similarity in PHC to clips from the same versus different movies. We submitted our PHC RSA values to a mixed effects model with subject and video identity again defined as random effects, and laterality as a control term. We compared a model including within- versus across-movie correlations—our fixed effect of interest—to a model without these correlations included. Adults again showed significantly lower pattern similarity for within-movie comparisons than across-movie comparisons ($\chi^2 = 12.89$, $p < .001$; Figure 5A). This effect was trending towards significance in children ($\chi^2 = 3.38$, $p = .07$; Figure 5A); however, a significant result when comparing this model to one with univariate activation included ($\chi^2 = 10.21$, $p < .01$) suggests that mean activation for a participant might guide similarity differences across conditions (see "Methods"). Again, a two-samples *t*-test for a within – across difference score showed no significant difference in pattern similarity between children and adults ($t(35.39) = -1.05$, $p = .30$, $BF_{01} = 2.12$; Figure 5B). We again asked whether there was a change in pattern similarity with age in children, and found that age was not a significant predictor in explaining within- versus

across-movie differences (r^2 = .006, $F(1,23)$ = .14, p = .71, BF_{01} = 2.59; Figure 5C). Finally, when using Bonferroni-corrected t-tests to ask whether pattern similarity differed by familiarity with the movies, adults showed the same pattern in PHC as in HPC: lower similarity within movies than across movies, both when they were highly familiar ($t(169) = 2.64$, p = .02) and when they were less familiar ($t(149) = 2.93$, p = .008) with the movies (see Figure 4B). Children showed an interaction between within- and across-movie similarity and familiarity, with lower within-movie pattern similarity only for movies with which they were familiar ($\chi^2 = 5.09$, p = .02). However, when comparing this model to one with univariate activation included, there was a significant difference between the models ($\chi^2 = 10.88$, $p < .001$), indicating that the similarity difference by familiarity in children might have been driven by individual differences in univariate activation.

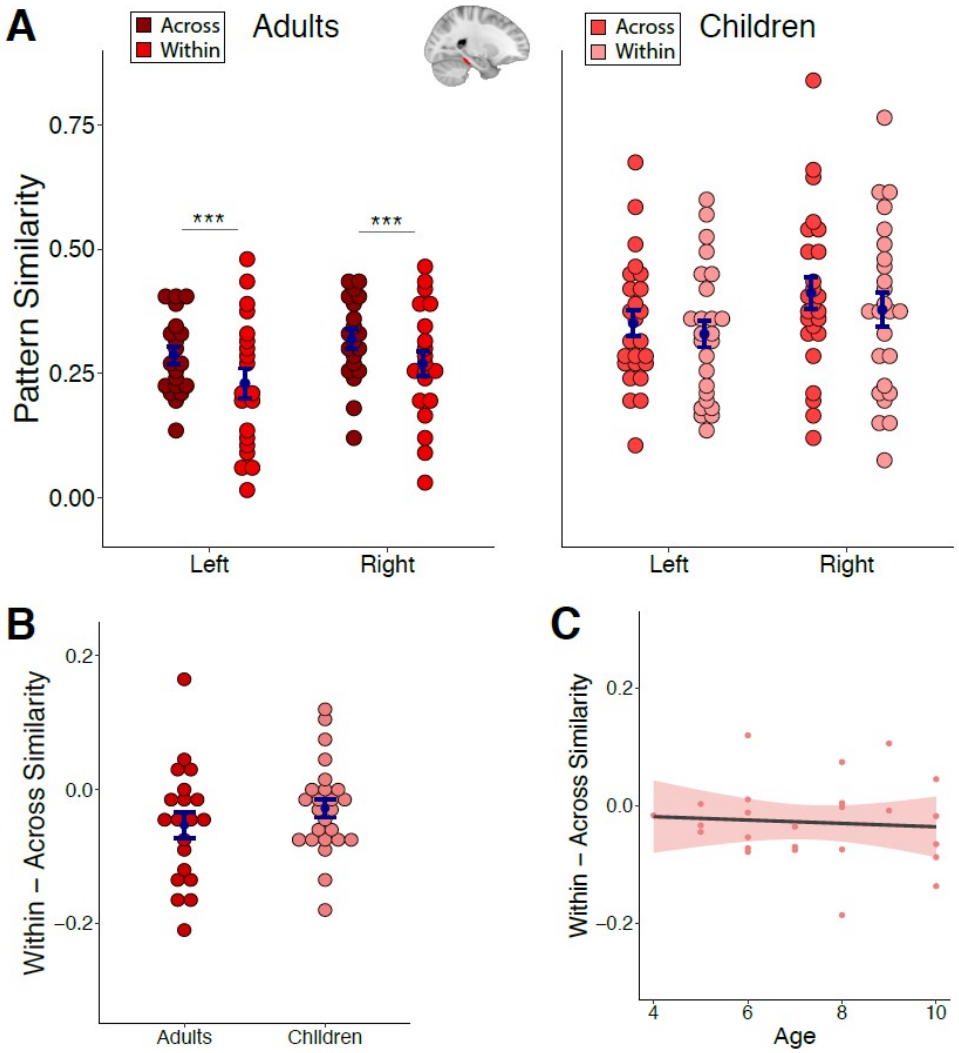

Figure 5 RSA effects in parahippocampal cortex. (A) Mixed-effect models conducted separately for adults and children, including correlation type (within vs. across) and laterality. (B) Comparison of adults and children by within – across similarity score. (C) Regression of pattern similarity on age in children. Error bars represent standard error of the mean. ***$p < .001$

Visual Cortex (V1)

As a control, we conducted the same analyses as above in V1, to ensure that our findings were specific to MTL regions, and not purely driven by perceptual differences in the clips. Here, paired samples *t*-tests for each age group separately showed that neither adults ($t(19) = 1.70$, $p = .10$; Figure 6A) nor children ($t(24) = .13$, $p = .89$; Figure 6A) showed a significant difference in pattern similarity between the across- and within-movie comparisons. A two-samples *t*-test revealed that there was no difference between the age groups in the within—across difference

score ($t(35.67) = -1.31$, $p = .20$; Figure 6B). Further, pattern similarity for within- and across-movie comparisons did not differ between high ($t(84) = .90$, $p = .37$) or low ($t(74) = 1.53$, $p = .13$) levels of familiarity for adults. Similarly, there were no significant differences in within- and across-movie similarity in children when they were highly familiar ($t(107) = .67$, $p = .50$) compared to less familiar ($t(91) = -.69$, $p = .49$) with the movies.

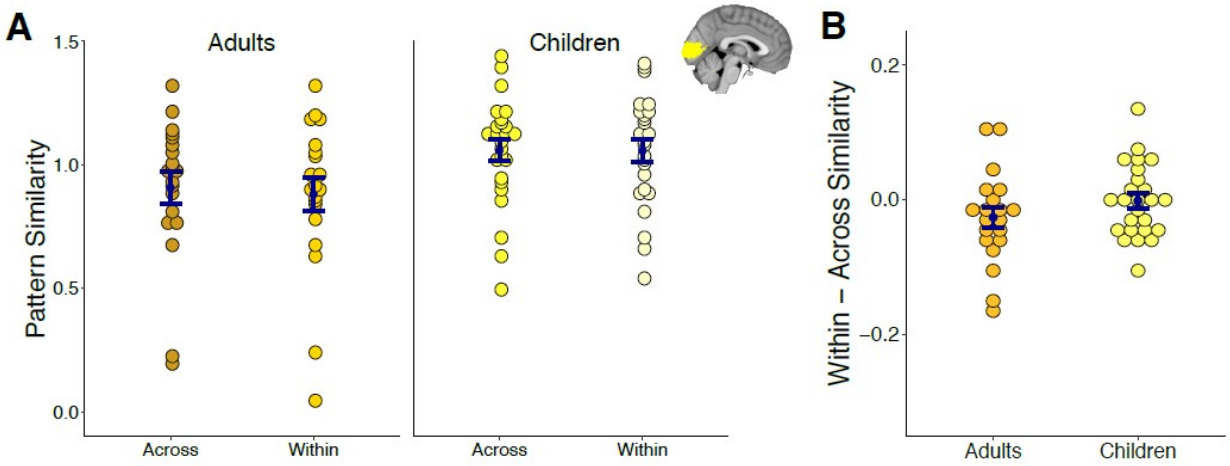

Figure 6. RSA effects in V1. (A) Mixed-effect models conducted separately for adults and children, including correlation type (within vs. across) and laterality. (B) Comparison of adults and children by within – across similarity score. Error bars represent standard error of the mean.

Discussion

The goal of this study was to investigate the neural development of processes that allow one to differentiate between events that share the same versus different contexts. Our results demonstrate that both children and adults showed lower pattern similarity for related compared to unrelated video clips in HPC, akin to previously reported processes which highlight a role for the HPC in the differentiation of similar memory representations. In the PHC, this effect was present only in adults. Further, in children, the difference in within versus across movie similarity showed an interaction with familiarity in HPC; that is, neural processes subserving differentiation of similar stimuli were only present for movies with which children were familiar,

whereas adults showed this effect regardless of familiarity with the movies, suggesting that familiarity may boost mnemonic differentiation processes in early childhood.

Although research on non-human primates suggests HPC continues to develop across childhood (Lavenex & Banta Lavenex, 2013) and prior behavioral work has demonstrated that the ability to retain specific aspects of episodes is worse in children compared to adults (e.g. Keresztes et al., 2017; Ngo et al., 2018; Ngo, Newcombe, et al., 2019; Rollins & Cloude, 2018), we found that the neural patterns in HPC that subserve differentiation between related representations of encoded information are similar across age groups. These results may seem at odds, especially since the movies contained many related elements across contexts, but dovetail well with prior literatures when considering the moderating effects of familiarity in children, but not adults. Additionally, although young children are not able to remember components of events with related elements as effectively as older children, they still perform above chance on these tasks (Benear, Ngo, Olson, & Newcombe, 2020 PREPRINT; Keresztes et al., 2017; Ngo et al., 2018; Ngo, Lin, et al., 2019). The familiarity effect we found for children suggests that increased exposure to stimuli is necessary for children to differentiate representations in HPC (Chanales et al., 2017; Favila et al., 2016). Although participants' level of exposure to the stimuli was not manipulated in our study, prior familiarity with the movies serves as a proxy for level of exposure. Children may need more exposures than adults to build up schematic knowledge that will allow them to successfully differentiate representations in HPC. Indeed, young children often require multiple repetitions and exposures to retain information (Horst et al., 2011). Overall, while behavioral investigations show that complex mnemonic abilities such as context binding are not at adult-like levels in children before age 6 or 7, our results suggest the

underlying neural machinery for these abilities exists and can be bolstered by schematic knowledge.

Additionally, we saw differentiation effects in PHC only for adults, suggesting this region may become relevant to differentiation processes later in development. PHC is a region important to the encoding of contextual details (Davachi, 2006; Eichenbaum et al., 2012), which young children are often not yet skilled at detecting (e.g., Ngo, Lin, Newcombe, & Olson, 2019). The fact that we found effects for adults in PHC as well as in HPC—the structure most commonly associated with differentiation among competing representations—was surprising given prior literature and may be due to the nature of our experimental design. Specifically, differentiation of scenes drawn from the same movies emphasizes picking up on contextual details to distinguish between clips. Rather than encoding explicit images to later be recalled in a behavioral memory task (Chanales et al., 2017; Favila et al., 2016), participants in our study were simply passively watching movie clips. PHC has been shown to be sensitive to recollection effects (Diana, Yonelinas, & Ranganath, 2012), so it is not necessarily surprising that we found similar results in PHC as we did in HPC, since both regions are often engaged during encoding of contextually rich stimuli. Future work should address what is driving the differentiation of patterns in PHC for related versus unrelated content in adults, which would provide great insight into interpreting the ramifications for child development.

Further, our findings extend work in adults showing that familiarity enhances differentiation in HPC by showing the same phenomenon occurs in children with dynamic, naturalistic stimuli, which may better reflect real-world memoranda than previously used stimuli. Memorization of static images is a commonly used paradigm in neuroimaging studies of human memory, but the dynamically-unfolding video scenes used in our study more closely resembles

how one experiences events in daily life. Our study did not include a memory task that encouraged retention of the movie content for later recollection. However, the way the movie clips proceed naturalistically is reminiscent of daily experiences in which we do not expect to later be tested on what we experience, but in which it is nevertheless adaptive to be able to distinguish one experienced event from another. Research looking at pattern differentiation for naturalistic stimuli in children that later tests their memory is needed to determine the nature of both differentiation and familiarity effects in children and how they relate to memory performance.

Although we provide evidence that children as young as 4 years old show adult-like neural activation patterns in HPC, the younger children in our study were under-sampled. Thus, the absence of an age effect within our child group may be due to under-representation of the younger ages, which is particularly relevant given the developmental gains in mnemonic processes that occur between the ages of 4 and 6 (Benear et al., 2020 PREPRINT; Newcombe, Lloyd, & Ratliff, 2007; Ngo et al., 2018). Since many of the children in our sample were 6 years old or older, perhaps their memory systems were more mature, allowing for neural activation patterns that more closely resembled those of adults. However, the non-significant pattern similarity differences in HPC as a function of age within our child sample (see Figures 3 & 5C) suggests that children's neural differentiation processes mirror adults' regardless of age. There is also a notion that young children's mnemonic systems may favor generalization across episodes over recall of specific episodic details, especially before the age of 6 (discussed in Keresztes et al., 2018), perhaps explaining why children's mnemonic discrimination performance is not as sophisticated as adults' when tested behaviorally. Future work should examine pattern similarity during encoding of stimuli for which task demands later require generalization versus mnemonic

discrimination (e.g., Ngo, Benear, et al., 2020 PREPRINT) to compare whether hippocampal pattern similarity is differentially associated with success in each mnemonic function.

The present work demonstrates that children indeed show neural patterns in HPC in response to encoding of naturalistic stimuli that are similar to those of adults, although patterns in PHC demonstrate differences across the age groups, with effects present only in adults. Familiarity with the stimuli influences the level of pattern similarity differences in HPC for shared versus distinct content in children, demonstrating that while adults may be able to orthogonalize related mnemonic representations after a single encounter with a set of stimuli, children may require multiple exposures in order to show adequate neural signatures of differentiation between similar representations. This work sets the foundation for indicating how structural integrity of the MTL may not completely predict the functional operations of these systems and highlights the need to integrate across multiple levels of analysis to better understand the development of episodic memory.

Acknowledgements

This work was supported in part by National Institute of Health grants to V. Murty [R21 DA043568, K01 MH111991], S. Perlman [K01 MH094467, R01 MH107540], I. Olson [R01 MH091113] and I. Olson and N. Newcombe [R21 HD098509; R01 HD099165], and by a National Science Foundation Graduate Research Fellowship to M.C. Camacho [DGE-1745038]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

Benear, S. L., Ngo, C. T., Newcombe, N. S., & Olson, I. R. Understanding relational binding in early childhood: Interacting effects of overlap and delay. PsyArxiv. [**Preprint**]. November 2020. Available from: https://doi.org/10.31234/osf.io/48wv5

Camacho, M. C., Karim, H. T., & Perlman, S. B. (2019). Neural architecture supporting active emotion processing in children: A multivariate approach. *NeuroImage*, *188*(August 2018), 171–180. https://doi.org/10.1016/j.neuroimage.2018.12.013

Canada, K. L., Botdorf, M., & Riggins, T. (2020). Longitudinal development of hippocampal subregions from early- to mid-childhood. *Hippocampus*, 1–14. https://doi.org/10.1002/hipo.23218

Canada, K. L., Ngo, C. T., Newcombe, N. S., Geng, F., & Riggins, T. (2019). It's all in the details: Relations between young children's developing pattern separation abilities and hippocampal subfield volumes. *Cerebral Cortex*, *29*(8), 3427–3433. https://doi.org/10.1093/cercor/bhy211

Chanales, A. J. H., Oza, A., Favila, S. E., & Kuhl, B. A. (2017). Overlap among spatial memories triggers repulsion of hippocampal representations. *Current Biology*, *27*(15), 2307-2317.e5. https://doi.org/10.1016/j.cub.2017.06.057

Davachi, L. (2006). Item, context and relational episodic encoding in humans. *Current Opinion in Neurobiology*, *16*(6), 693–700. https://doi.org/10.1016/j.conb.2006.10.012

Diana, R. A., Yonelinas, A. P., & Ranganath, C. (2012). Adaptation to cognitive context and item information in the medial temporal lobes. *Neuropsychologia, 50*(13), 3062–3069. https://doi.org/10.1016/j.neuropsychologia.2012.07.035

Eichenbaum, H., Sauvage, M., Fortin, N., Komorowski, R., & Lipton, P. (2012). Towards a

functional organization of episodic memory in the medial temporal lobe. *Neuroscience and Biobehavioral Reviews*, *36*(7), 1597–1608. https://doi.org/10.1016/j.neubiorev.2011.07.006

Favila, S. E., Chanales, A. J. H., & Kuhl, B. A. (2016). Experience-dependent hippocampal pattern differentiation prevents interference during subsequent learning. *Nature Communications*, *7*. https://doi.org/10.1038/ncomms11066

Ghetti, S., & Bunge, S. A. (2012). Neural changes underlying the development of episodic memory during middle childhood. *Developmental Cognitive Neuroscience*, *2*(4), 381–395. https://doi.org/10.1016/j.dcn.2012.05.002

Gogtay, N., Hugent, T. F., Herman, D. H., Ordonez, A., Greenstein, D., Hayashi, K. M., Clasen, L., Toga, A. W., Giedd, J. N., Rapoport, J. L., & Thompson, P. M. (2006). Dynamic mapping of normal human hippocampal development. *Hippocampus*, *16*, 664–672. https://doi.org/10.1002/hipo

Horst, J. S., Parsons, K. L., & Bryan, N. M. (2011). Get the story straight: Contextual repetition promotes word learning from storybooks. *Frontiers in Psychology*, *2*(FEB), 1–11. https://doi.org/10.3389/fpsyg.2011.00017

Hunsaker, M. R., & Kesner, R. P. (2013). The operation of pattern separation and pattern completion processes associated with different attributes or domains of memory. *Neuroscience and Biobehavioral Reviews*, *37*(1), 36–58. https://doi.org/10.1016/j.neubiorev.2012.09.014

Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., & Smith, S. M. (2012). Fsl. *Neuroimage*, *62*(2), 782–790.

Karim, H. T., & Perlman, S. B. (2017). Neurodevelopmental maturation as a function of irritable temperament: Insights from a naturalistic emotional video viewing paradigm. *Human Brain*

Mapping, *38*(10), 5307–5321. https://doi.org/10.1002/hbm.23742

Keresztes, A., Bender, A. R., Bodammer, N. C., Lindenberger, U., Shing, Y. L., & Werkle-Bergner, M. (2017). Hippocampal maturity promotes memory distinctiveness in childhood and adolescence. *PNAS, 114*(34), 9212–9217. https://doi.org/10.1073/pnas.1710654114

Keresztes, A., Ngo, C. T., Lindenberger, U., Werkle-Bergner, M., & Newcombe, N. S. (2018). Hippocampal maturation drives memory from generalization to specificity. *Trends in Cognitive Sciences*, *22*(8), 676–686. https://doi.org/10.1016/j.tics.2018.05.004

Kirwan, C. B., & Stark, C. E. L. (2007). Overcoming interference: An fMRI investigation of pattern separation in the medial temporal lobe. *Learning and Memory, 14*(9), 625–633. https://doi.org/10.1101/lm.663507

Koenig, L., Wimmer, M. C., & Trippas, D. (2020). Item repetition and response deadline affect familiarity and recollection differently across childhood. *Memory*. https://doi.org/10.1080/09658211.2020.1790612

Krogsrud, S. K., Tamnes, C. K., Fjell, A. M., Amlien, I., Grydeland, H., Sulutvedt, U., Due-Tønnessen, P., Bjørnerud, A., Sølsnes, A. E., Håberg, A. K., Skrane, J., & Walhovd, K. B. (2014). Development of hippocampal subfield volumes from 4 to 22 years. *Human Brain Mapping*, *35*(11), 5646–5657. https://doi.org/10.1002/hbm.22576

Larocque, K. F., Smith, M. E., Carr, V. A., Witthoft, N., Grill-Spector, K., & Wagner, A. D. (2013). Global similarity and pattern separation in the human medial temporal lobe predict subsequent memory. *Journal of Neuroscience*, *33*(13), 5466–5474. https://doi.org/10.1523/JNEUROSCI.4293-12.2013

Lavenex, P., & Banta Lavenex, P. (2013). Building hippocampal circuits to learn and remember: Insights into the development of human memory. *Behavioural Brain Research*, *254*, 8–21.

https://doi.org/10.1016/j.bbr.2013.02.007

Newcombe, N. S., Lloyd, M. E., & Ratliff, K. R. (2007). Development of episodic and autobiographical memory: a cognitive neuroscience perspective. In *Advances in Child Development and Behavior* (Vol. 35). Elsevier Inc. https://doi.org/10.1016/B978-0-12-009735-7.50007-4

Ngo, C.T., Benear, S.L., Popal, H., Olson, I.R., Newcombe, N.S. Contingency of semantic generalization on episodic specificity: Variations across development. OSF Preprints. [**Preprint**]. November 2020. Available from: https://osf.io/rcz7w

Ngo, C. T., Lin, Y., Newcombe, N. S., & Olson, I. R. (2019). Building up and wearing down episodic memory: mnemonic discrimination and relational binding. *Journal of Experimental Psychology: General.* https://doi.org/10.1037/xge0000583

Ngo, C. T., Newcombe, N. S., & Olson, I. R. (2018). The ontogeny of relational memory and pattern separation. *Developmental Science*, *21*(2), 1–11. https://doi.org/10.1111/desc.12556

Ngo, C. T., Newcombe, N. S., & Olson, I. R. (2019). Gain-loss framing enhances mnemonic discrimination in preschoolers. *Child Development*, *90*(5), 1569–1578. https://doi.org/10.1111/cdev.13297

Popal, H., Wang, Y., & Olson, I. R. (2020). A guide to representational similarity analysis for social neuroscience, 1243–1253. https://doi.org/10.1093/scan/nsz099

Poppenk, J., Köhler, S., & Moscovitch, M. (2010). Revisiting the novelty effect: When familiarity, not novelty, enhances memory. *Journal of Experimental Psychology: Learning Memory and Cognition*, *36*(5), 1321–1330. https://doi.org/10.1037/a0019900

Riggins, T., Geng, F., Botdorf, M., Canada, K., Cox, L., & Hancock, G. R. (2018). Protracted hippocampal development is associated with age-related improvements in memory during

early childhood. *NeuroImage*, *174*(January), 127–137. https://doi.org/10.1016/j.neuroimage.2018.03.009

Ritchey, M., Montchal, M. E., Yonelinas, A. P., & Ranganath, C. (2015). Delay-dependent contributions of medial temporal lobe regions to episodic memory retrieval. *ELife, 2015(4),* 1–19. https://doi.org/10.7554/eLife.05025

Rollins, L., & Cloude, E. B. (2018). Development of mnemonic discrimination during childhood. *Learning and Memory*, *25*(6), 294–297. https://doi.org/10.1101/lm.047142.117