# Longitudinal investigation of task-free hippocampal functional connectivity and episodic memory in early childhood

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## Introduction

- The hippocampus is an important neural substrate for memory in adults (e.g., Xue, 2018) and children (Ghetti, DeMaster, Yonelinas, & Bunge, 2010).
- Developmental studies have suggested that development of the hippocampus and it's associated cortical regions might underlie the significant development of memory abilities between the age of 4 and 8 years (Riggins, 2014).
- Specifically, previous studies suggested that during early childhood, there were age- and memory-related differences in hippocampal functional connectivity during task-free state (e.g., Riggins, Geng, Blankenship, & Redcay, 2016; Blankenship, Redcay, Dougherty, & Riggins, 2017).
- However, these investigations have used cross-sectional study design, which may involve confounding variables hard to control.
- Therefore, the current study **used longitudinal data to investigate the age- and memory-related differences in hippocampal functional connectivity during task-free state between the age of 4 and 8 years.**
- We predicted both age- and memory-related differences in hippocampal functional connectivity would be observed during task-free state.

## Method

### Participants

A cohort-sequential design was utilized. At Wave 1, 4-, 5-, 6-, 7- and 8-year-old children participated. Both the 4- and 6-year-old children were followed longitudinally for two years (Waves 2 & 3).

| Age (years) | Wave 1 (*n*) | Wave 2 (*n*) | Wave 3 (*n*) |
|---|---|---|---|
| **4** | **36** | | |
| **5** | 23 | **39** | |
| **6** | **36** | | **40** |
| **7** | 29 | **30** | |
| **8** | 29 | | **31** |

Table 1. The number of subjects for each age group and each wave. The highlighted numbers represent the number of children included in longitudinal study.

### Memory Assessment

During encoding, fMRI data were collected while children viewed and were instructed to remember 120 stimuli and cartoon characters they were paired with. Outside the scanner, children were asked to make item and source memory judgments on 160 stimuli during retrieval (120 old, 40 new). Source memory was computed as the proportion of characters accurately recalled among the recognized items.

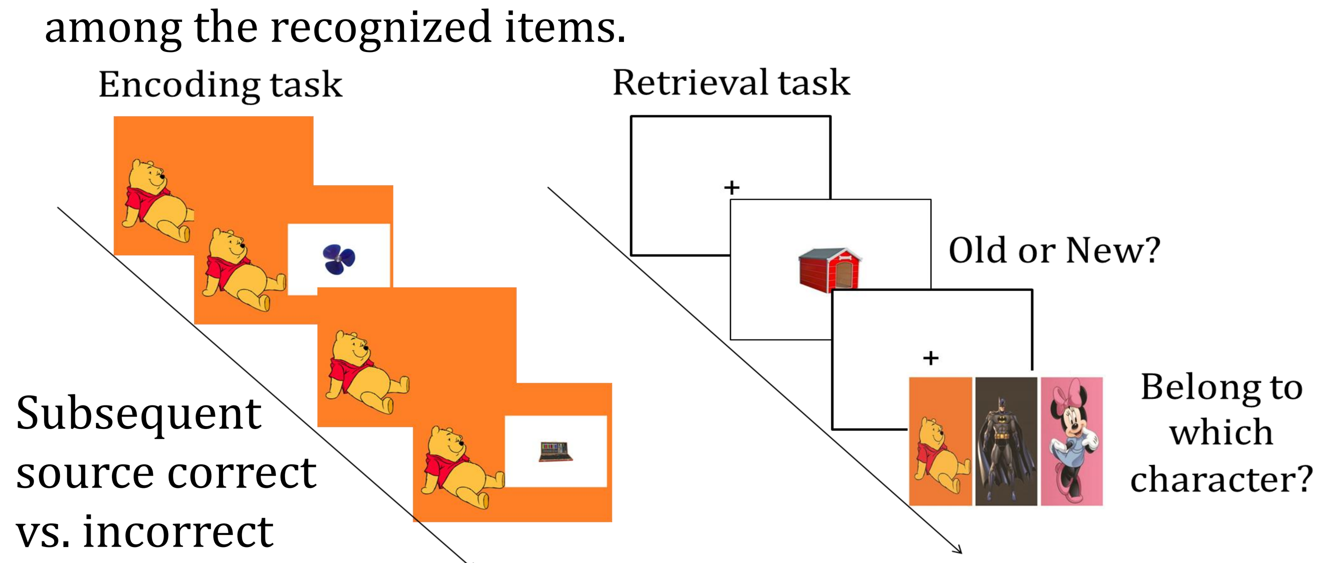


Figure 1. Illustration of encoding and retrieval tasks

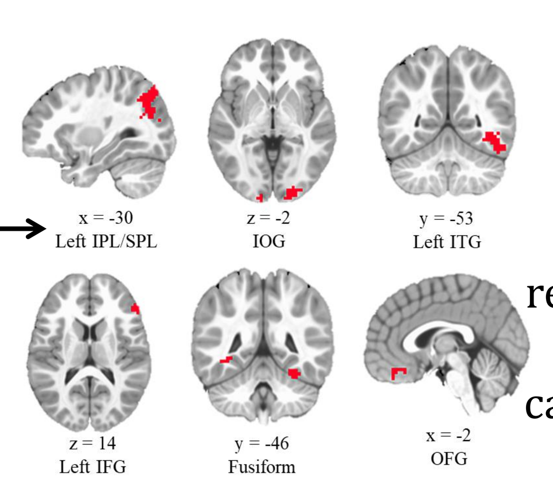


Figure 2. These regions showed significant activation during the encoding of source information that could be subsequently retrieved. These regions were later treated as ROI regions for calculating hippocampal functional connectivity.

## MRI Data Collection and Analyses

- MRI data were collected at the Maryland Neuroimaging Center using a 32-channel coil in a Siemen's 3T scanner.
- During the task-free scan, children were instructed to lie as still as possible with eyes open **watching Inscapes**, a movie designed for collecting fMRI data to reduce potential head motion (Vanderwal, Kelly, Eilbott, Mayes, & Castellanos, 2015).
- Preprocessing steps included: slice timing correction, motion correction, smoothing, brain extraction, and normalization.
  - Individual anterior and posterior hippocampus (Figure 3) were derived from Freesurfer 5.1 and edited using Freesurfer v5.1 (Fischl, 2012) and Automatic Segmentation Adapter Tool (ASAT, Wang et al., 2011).
  - **We calculated the connectivity from anterior and posterior hippocampus to the brain regions shown in Figure 2.**

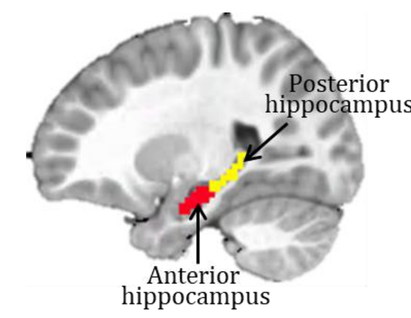


Figure 3. Hippocampal subregions

- Linear mixed effect models were used to examine how age and hippocampal functional connectivity predicted source memory performance. If interactions were detected, follow-up analyses were carried out on Younger vs. Older age groups defined according to mean age (mean age = 6.64 years, SD = 1.37).

## Behavioral Results

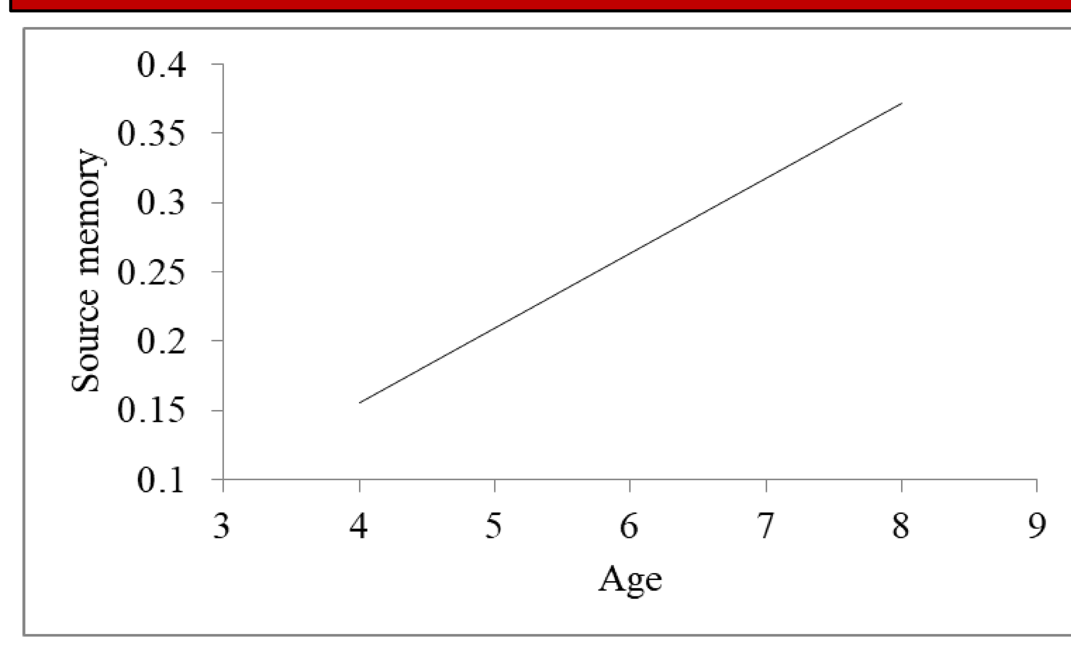


Figure 4. Age was positively related to source memory performance, $F$ (1, 207) = 50.66, $p < .001$.

## Task-free Functional Connectivity Results

Analyses revealed 4 regions, including fusiform, inferior frontal gyrus (IFG), inferior temporal gyrus (ITG), and superior parietal lobe (SPL), showing an interaction between age and functional connectivity in predicting source memory. In each case, there was a significant positive correlation in the Older group, but Not in the Younger group.

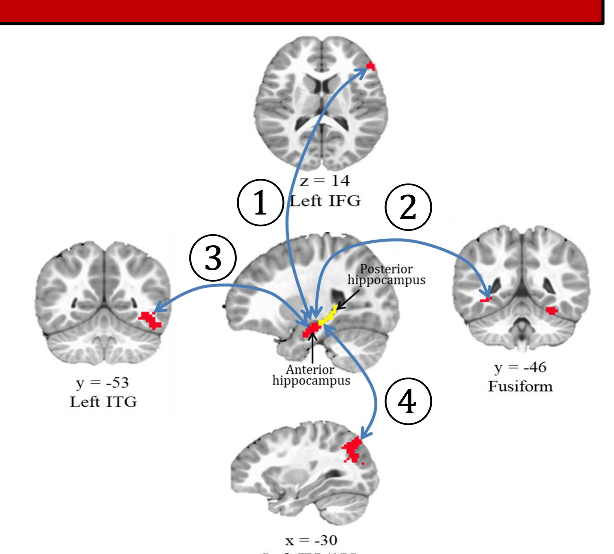


Figure 5. Brain regions showing significant interaction

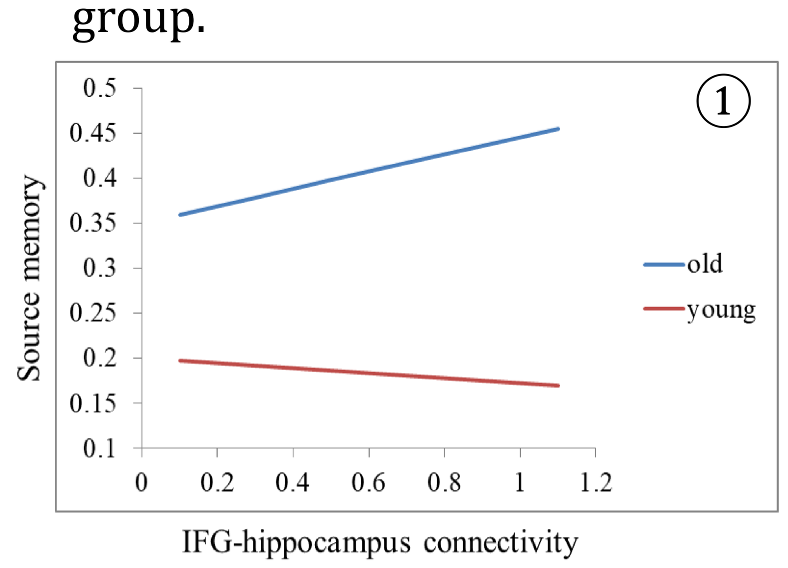


Figure 6. There was a significant positive correlation in the Older group ($F$ (1, 240) = 5.26, $p$ = .02), but not in the Younger group ($F$ (1, 284) = .125, $p$ = .72).

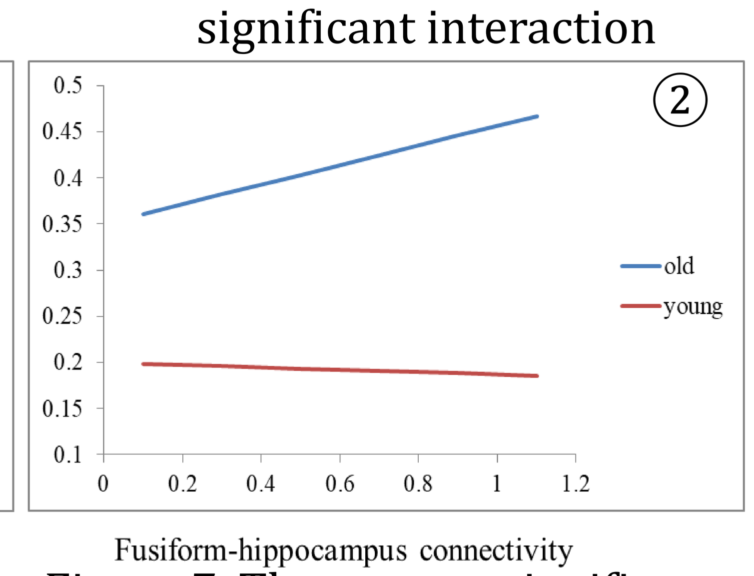


Figure 7. There was a significant positive correlation in the Older group ($F$ (1, 218) = 8.34, $p$ = .004), but not in the Younger group ($F$ (1, 272) = .097, $p$ = .76).

## Task-free Functional Connectivity Results

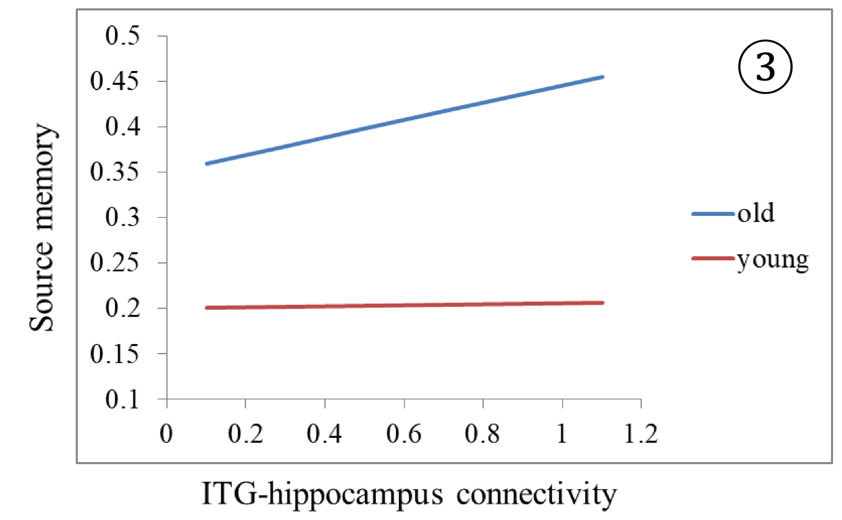


Figure 8. There was significant correlation in the Old group ($F$ (1, 225) = 5.52, $p$ = .02), but not significant in the Young group ($F$ (1, 280) = .09, $p$ = .764).

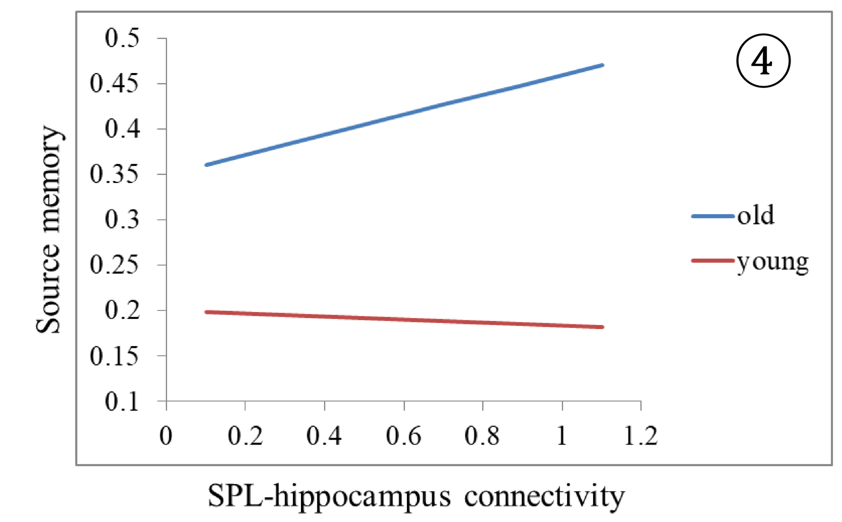


Figure 9. There was significant correlation in the Old group ($F$ (1, 222) = 7.302, $p$ = .007), but not significant in the Young group ($F$ (1, 279) = .04, $p$ = .839).

## Discussion

- These findings suggest that, during early childhood, there are age-related differences in task-free hippocampal functional connectivity and performance on a source memory task.
  - Specifically, in older children, greater connectivity from hippocampus to IFG, ITG, fusiform, and SPL, was related to better behavioral performance.
- These results are consistent with the component process model (Moscovitch, Cabeza, Winocur, & Nadel, 2016), which suggests that hippocampus and its interaction with other cortical regions (e.g., prefrontal cortex, PFC) are the neural networks supporting episodic memory.
- These results are also consistent with previous studies suggesting positive associations between task-free hippocampal connectivity and memory performance in 6-year-old children (Riggins, Geng, Blankenship, & Redcay, 2016).
- For future research, we will test whether young children's hippocampal functional connectivity can predict their episodic memory ability later.

## References

Blankenship, S. L., Redcay, E., Dougherty, L. R., & Riggins, T. (2017). Development of hippocampal functional connectivity during childhood. *Human Brain Mapping, 38*(1), 182-201. doi:10.1002/hbm.23353

Fischl, B. (2012). FreeSurfer. *NeuroImage, 62*(2), 774-781. doi:https://doi.org/10.1016/j.neuroimage.2012.01.021

Ghetti, S., DeMaster, D. M., Yonelinas, A. P., & Bunge, S. A. (2010). Developmental differences in medial temporal lobe function during memory encoding. *The Journal of Neuroscience, 30*(28), 9548-9556.

Moscovitch, M., Cabeza, R., Winocur, G., & Nadel, L. (2016). Episodic Memory and Beyond: The Hippocampus and Neocortex in Transformation. *Annual Review of Psychology, 67*(1), 105-134. doi:10.1146/annurev-psych-113011-143733

Riggins, T. (2014). Longitudinal investigation of source memory reveals different developmental trajectories for item memory and binding. *Developmental Psychology, 50*(2), 449-459. doi:10.1037/a0033622

Riggins, T., Geng, F., Blankenship, S. L., & Redcay, E. (2016). Hippocampal functional connectivity and episodic memory in early childhood. *Developmental Cognitive Neuroscience, 19*, 58-69. doi:http://dx.doi.org/10.1016/j.dcn.2016.02.002

Vanderwal, T., Kelly, C., Eilbott, J., Mayes, L. C., & Castellanos, F. X. (2015). Inscapes: A movie paradigm to improve compliance in functional magnetic resonance imaging. *NeuroImage, 122*, 222-232. doi:https://doi.org/10.1016/j.neuroimage.2015.07.069

Wang, H., Das, S. R., Suh, J. W., Altinay, M., Pluta, J., Craige, C., . . . Yushkevich, P. A. (2011). A learning-based wrapper method to correct systematic errors in automatic image segmentation: Consistently improved performance in hippocampus, cortex and brain segmentation. *NeuroImage, 55*(3), 968-985. doi:https://doi.org/10.1016/j.neuroimage.2011.01.006

Xue, G. (2018). The Neural Representations Underlying Human Episodic Memory. *Trends in Cognitive Sciences*. doi:https://doi.org/10.1016/j.tics.2018.03.004

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