Examining the role of the hippocampus in the episodic memory network in young children: A graph theoretical analysis

Morgan Botdorf, Fengji Geng, & Tracy Riggins
University of Maryland, College Park

Introduction

- Episodic memory improves across early childhood (Bauer, 2007).
- Research has identified a network of brain regions important for episodic memory in adults (Vincent et al., 2016).
- Recently, this network was identified in young children (Riggins et al., 2016); however, it's unclear how its organization may differ across development to support improvements in memory.
- *Interactive specialization* (Johnson, 2001) suggests that brain and cognitive development occurs through changes in the connections between regions of the brain, including increased *integration* (increased within-network connections) and *segregation* (decreased between-network connections).
- **The present study aims to investigate the functional integration of the hippocampus within the episodic memory network and segregation of the hippocampus from other networks (e.g., frontoparietal network) in the brain using a graph theoretical approach.**

Methods

Participants

- 137 healthy children aged 4-8 years (M= 6.50, SD = 1.48 years) provided usable data for analyses.
- Participants were part of a larger study examining the development of episodic memory in early childhood.

MRI Data

- T1-weighted high resolution ($1mm^3$) anatomical images were acquired from a Siemens 3T scanner with a 32-channel coil at the Maryland Neuroimaging Center using a standard structural MRI scan sequence.
- Resting state data was also collected via a 7 min resting state fMRI scan during which children viewed *Inscapes*, a video of abstract shapes (Vanderwal et al., 2016).
- Functional and structural data were preprocessed using the DPARSF-A toolbox (v3.1, Yan & Zang, 2010).

Methods: Defining Nodes

- Regions (nodes) were defined on an MNI child template using a 4mm sphere.

Regions "within" the episodic memory network

- Hippocampal regions were defined using coordinates from previous functional and anatomical research (Chen et al., 2016).
- Other regions were defined using coordinates from meta-analyses of regions activated during retrieval (Spaniol et al., 2009)

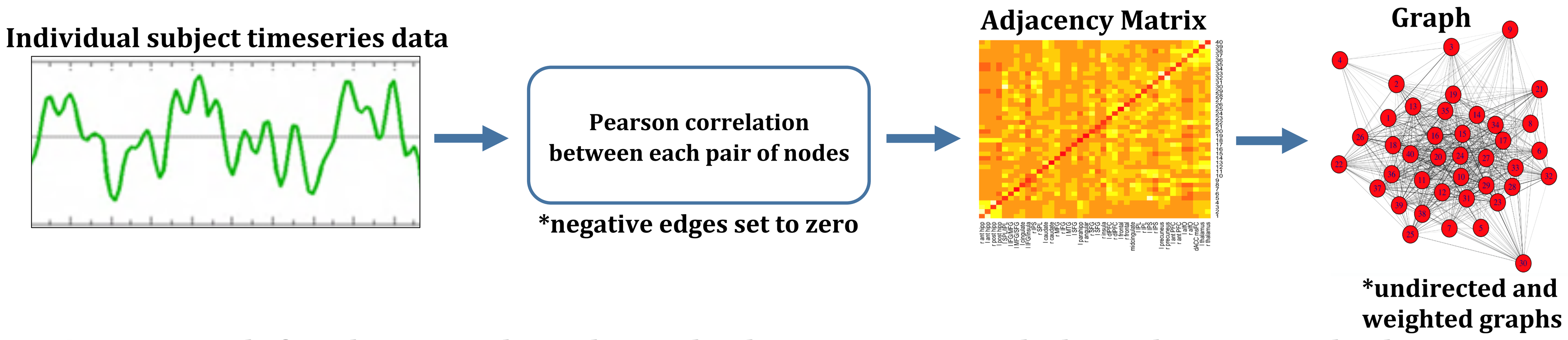
	Hemisphere	Region
1	R	Anterior Hippocampus
2	L	Anterior Hippocampus
3	R	Posterior Hippocampus
4	L	Posterior Hippocampus
5	L	Superior Parietal Lobule, Precuneus, Inferior Parietal Lobule
6	L	Inferior Frontal Gyrus, Middle Frontal Gyrus, Precentral Gyrus
7	L	Middle Frontal Gyrus, Anterior Cingulate, Superior Frontal Gyrus
8	L	Cingulate Gyrus
9	L	Inferior Frontal Gyrus, Insula
10	R	Inferior Parietal Sulcus
11	R	Superior Parietal Lobule
12	L	Caudate
13	R	Caudate
14	R	Middle Frontal Gyrus
15	R	Inferior Frontal Gyrus
16	L	Middle Temporal Gyrus
17	L	Superior Frontal Gyrus
18	L	Parahippocampal Gyrus
19	R	Angular Gyrus
20	R	Superior Frontal Gyrus
21	L	Superior Frontal Gyrus
22	R	Insula

Regions "outside" the episodic memory network

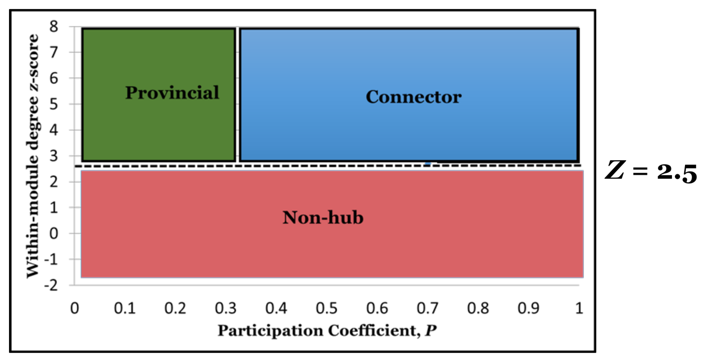
- Regions within the frontoparietal and cingulo-opercular networks
- Defined using coordinates from prior research (Fair et al., 2009)

	Hemisphere	Region
1	L	Dorsolateral Prefrontal Cortex
2	R	Dorsolateral Prefrontal Cortex
3	L	Frontal
4	R	Frontal
5		Midcingulate Cortex
6	L	Inferior Parietal Lobule
7	R	Inferior Parietal Lobule
8	L	Intraparietal Sulcus
9	R	Intraparietal Sulcus
10	L	Precuneus
11	R	Precuneus
12	L	Anterior Prefrontal Cortex
13	R	Anterior Prefrontal Cortex
14	L	Anterior Insula, Frontal Operculum
15	R	Anterior Insula, Frontal Operculum
16	L	Dorsal Anterior Cingulate, Medial Superior Frontal Cortex
17	L	Thalamus
18	R	Thalamus

Methods: Network Construction and Analysis



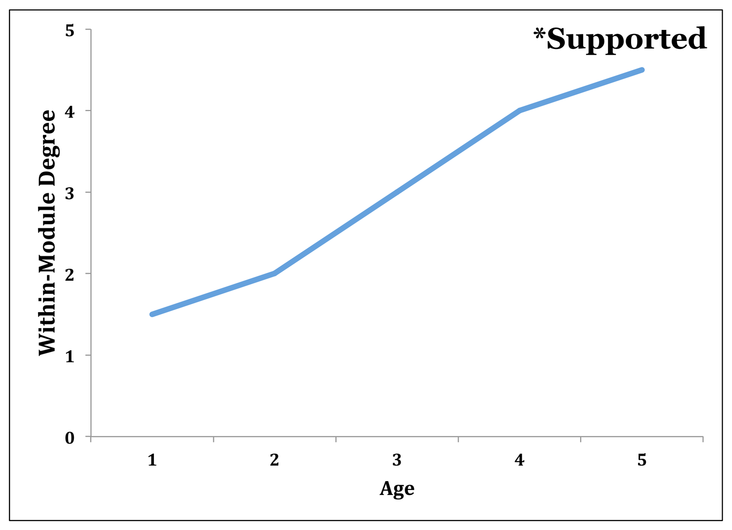
- **Community assignment**: defined a priori based on whether regions resided inside or outside the memory network
- **Nodes of interest:** right/left anterior and posterior hippocampus
- **Metrics of interest**: two metrics were used to characterized integration and segregation of the hippocampus across the specified age range:
  - ***within-module degree (Z)-*** used to assess the within-network connections of the hippocampus.
    - ↑ Z → ↑ within-network connections → ↑ integration of the hippocampus
  - ***participation coefficient (P)-*** used to assess between-network connections of the hippocampus relative to other networks in the brain.
    - ↓ P → ↓ between-network connections → ↑ segregation of the hippocampus

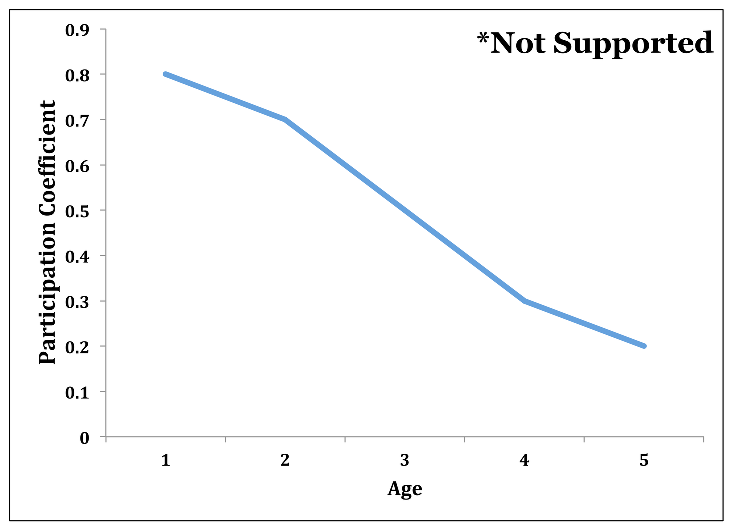


Results: Network Organization

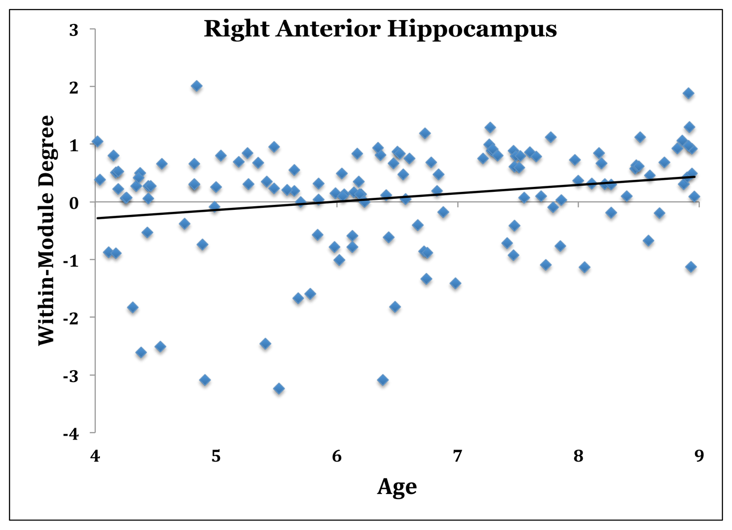
- **Results of bivariate correlations with age:**
  - Significant positive association between age and the within-module degree Z score associated with right anterior hippocampus (r = 0.23, p = .008)
  - Significant positive association between age and the participation coefficient associated with left anterior hippocampus (r = 0.18, p=.038)
  - No significant associations including posterior hippocampus
- **Results of linear regressions controlling for mean framewise displacement:**
  - Associations between the within-module degree Z score and age (b=0.15, SE=0.05, p=.008) and the participation coefficient and age (b=0.009, SE=0.004, p=0.03) held after controlling for mean framewise displacement.

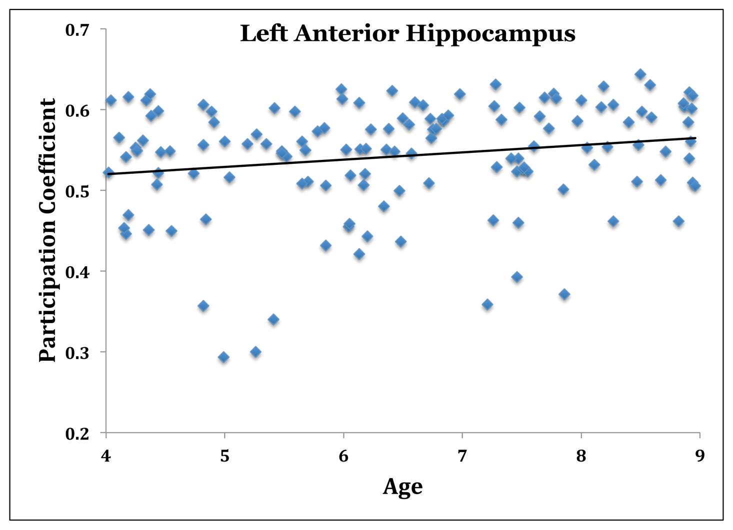
Predicted Results





Actual Results





Discussion & Future Directions

- Results indicated an increase in within-network connections between the right anterior hippocampus and regions within the episodic memory network between the ages of 4 and 8.
  - These results suggest that this region becomes functionally integrated with the memory network in early childhood, which likely supports improvements in memory observed during this period of time.
  - The right anterior hippocampus did not have a within-module degree of 2.5 or higher over the age range assessed so this region cannot be considered a hub. However, it may reach the status of a hub in older children.
- Results suggest that there is also an increase in between-network connections of the left anterior hippocampus to regions outside the memory network.
  - It is possible that there is a general increase in connections between the hippocampus and regions distributed throughout the brain in this age range.
  - It is also possible that our selection of nodes and a priori community assignment impacted the present results.
- Future research will investigate the relation between these metrics and behavioral differences in episodic memory.

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For questions or comments, please contact mbotdorf@terpmail.umd.edu