Development of hippocampal resting-state networks during childhood

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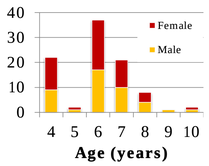
Introduction

- The ability to remember details of life events relies on a network of brain regions including the hippocampus, prefrontal, and parietal cortices in both school-age children and adults.
  - The majority of evidence for this memory network comes from task-based fMRI studies in individuals 8 years of age and older (see Ghetti & Bunge, 2012 for review).
- Investigations examining hippocampally-mediated memory networks earlier in life have been limited due to the demands of the testing environment.
  - This is unfortunate, as behavioral studies suggest important changes in memory development prior to 8 years of age (e.g., Drummey & Newcombe, 2002; Riggins, 2014).
- To overcome these challenges, we utilized a method in which the hippocampal memory network was examined in the absence of a task via "resting-state functional connectivity" MRI (or rs-fcMRI)
  - In adults, this approach has been shown to reveal the full distribution of the hippocampal memory network (Vincent et al., 2006) and connectivity within this network during rest is predictive of memory performance (Wang et al., 2010a, b).
- Results from both age-independent and age-dependent analyses are reported.
  - Both anterior and posterior regions of the hippocampus were explored, given known developmental (e.g., DeMaster et al., 2013) and functional (Poppenek et al., 2013) differences along the longitudinal (anterior to posterior) axis.

Methods

Participants

- A total of 93 children aged 4 to 10 years are included in the present analyses (out of 180 tested).
  - Mean age =6.57 years (*SD* = 1.45 years), range=4.02-10.81)

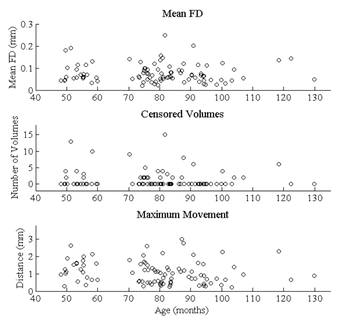


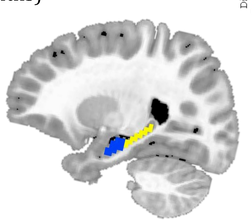
MRI Data Collection

- Functional and anatomical data were collected at the Maryland Neuroimaging Center using a 12-channel coil in a Siemen's 3T scanner. Participants watched a video of abstract patterns/shapes (like a screen saver) during a 6-minute acquisition of resting-state functional data.

MRI Data Processing & Analysis

- All functional analyses were conducted using AFNI (Cox, 1996).
- BOLD signal from white matter and CSF masks and continuous motion regressors from 6 directions (roll, pitch, yaw, x, y, z) and their temporal derivatives were included as noise covariates. (Global signal regression was not used.)
- Data were band-pass filtered at .009<f<.08.
- Motion control:
  - < 1 voxel (3mm) from reference
  - Framewise displacements >1mm were censored
  - < 5.5 minutes of resting-state after censoring
  - Mean FD entered as a covariate in all analyses
- Age-controlled connectivity
  - Controlling for age (in months) & mean FD
  - Testing against 0
- Age-dependent connectivity
  - Controlling for mean FD
  - Testing against age (in months)
- Bilateral hippocampal seeds
  - Whole hippocampus
  - Anterior
  - Posterior



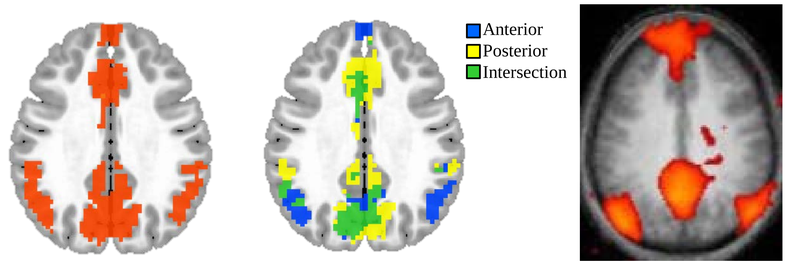


Results: Age-Controlled Connectivity

Whole Hippocampus

Anterior/Posterior Hippocampus

Adults (Vincet et al., 2006)



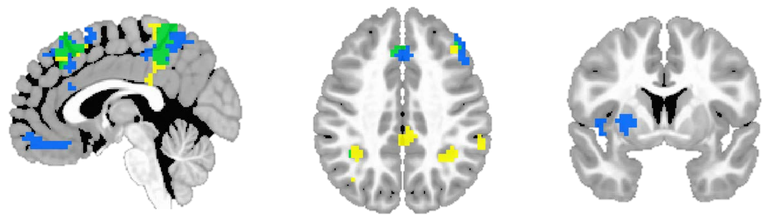
z=32, p=10^{-15}

Results: Age-Dependent Connectivity

Whole Hippocampus

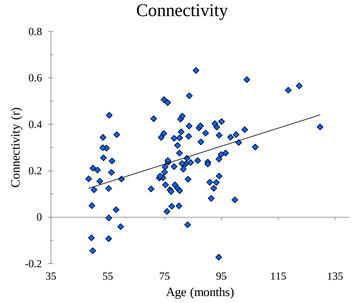
Anterior/Posterior Hippocampus

Anterior Posterior Intersection

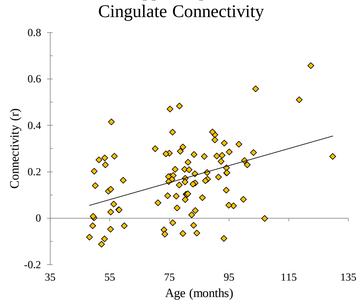


[2,2, 37], p.=05 corrected

Anterior Hippocampus - vmPFC Connectivity



Posterior Hippocampus – Posterior Cingulate Connectivity



Discussion

- The major components of mature hippocampal network were evident by 4 years of age (i.e., medial prefrontal cortex, anterior and posterior cingulate, precuneus, and lateral parietal regions).
- Anterior and posterior hippocampus appear functionally distinct, even during early childhood.
  - Anterior seed shows connectivity with the medial prefrontal and more posterior parietal regions
  - Posterior seed shows connectivity with anterior and posterior cingulate and more anterior parietal regions
  - Significant overlap in precuneus
- Age-related increases in connectivity were observed between 4-10 years in ventromedial prefrontal, dorsomedial prefrontal, precuneus, dorsolateral prefrontal, inferior parietal sulcus, left insula.
  - Anterior seed shows unique age-related increases in connectivity with ventromedial prefrontal cortex, anterior cingulate, dorsolateral prefrontal cortex, left putamen, and left insula
  - Posterior seed shows unique age-related increases in connectivity with posterior cingulate, and bilateral inferior parietal sulcus
  - Significant overlap in connectivity with dorsomedial prefrontal and precuneus.
- Future directions include examining relations between memory performance and hippocampal connectivity.
- On a methodological note, the whole hippocampal seed may not be the most appropriate, depending on the question of interest as it does obscure some unique age-related changes (e.g,. posterior seed shows age-related increases in connectivity with the posterior cingulate, whereas the anterior seed shows age-related increases in connectivity with the left putamen, which are both absent from the whole hippocampus results.)

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