Influence of Hippocampal Volume and Connectivity with the Prefrontal Cortex on Memory Ability in Early Childhood

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Introduction

Memory, particularly the ability to recall details associated with an event, dramatically improves between 4 to 6 years of age (e.g., Drummey & Newcombe, 2002).

Few studies have investigated the neural mechanisms driving these changes, largely due to methodological challenges of acquiring neuroimaging data from young children.

Recent fMRI studies in school-aged children have revealed the importance of medial temporal lobe (MTL) structures, such as the hippocampus, and prefrontal cortex (PFC) for memory ability (Ghetti & Bunge, 2012).

These regions undergo developmental change between 4 and 6 years:

- Synaptic connectivity within the hippocampus is not mature until 5 years of age (Serres, 2001), and the relative volume of anterior and posterior regions changes between 4-25 years (Gogtay et al., 2006).
- PFC shows protracted development through 25 years of age (Giedd, 2004).

The present study aimed to address this gap by examining associations between 4- and 6-year-old children's ability to recall previously seen pictures and 1) hippocampal volume and 2) functional connectivity between the hippocampus and other neural regions at rest.

- Measures of resting-state functional connectivity (rs-fcMRI) were used because they place few demands on participants. In adults rs-fcMRI 1) reveals the full distribution of memory-related regions (Vincent et al., 2006), 2) is predictive of memory performance (Wang et al., 2010a,b), and 3) shows variation in atypical populations before memory impairments (suggesting it is casual, Roosendaal et al., 2010).

Methods

Participants*

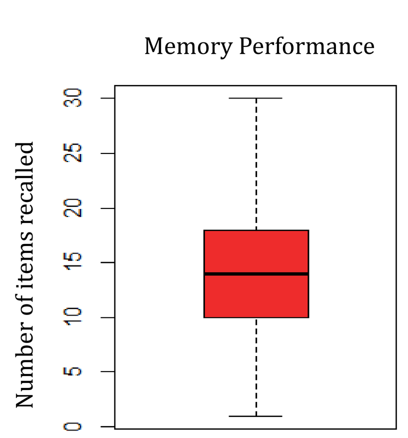
27 6-year-old children (14 female, mean age = 6.63 years ± .26)
17 4-year-old children (9 female, mean age = 4.44 years ±.24)

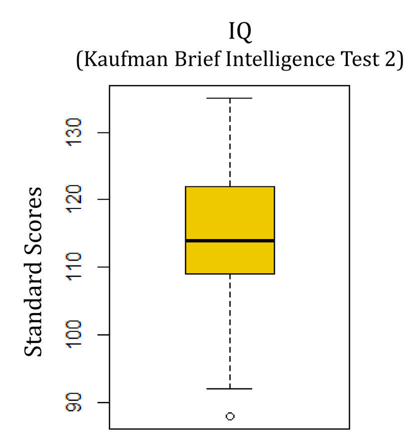
* 5 6yos, and 5 4yos were excluded from connectivity analyses and 2 6yos, and 5 4yos were excluded from volumetric analyses due to excessive motion or noncompliance.

Behavioral Assessments

(1) Memory: Participants completed a picture recall task (modified from Wang et al., 2010a, 2010b). Children viewed 12 Snodgrass and Vanderwart line drawings and indicated whether each item was living or not living using a button press. Immediately following a 15s distractor task, participants had 60s to freely recall all items on the list. Memory scores were calculated as the sum of items recalled across all lists. Children completed 5 lists for a maximum score of 60.

(2) IQ: Participants completed the Kaufman Brief Intelligence Test 2.





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 during acquisition of functional data.

Data Processing

- Structural analyses were conducted using Freesurfer (Fischl et al, 2002) to obtain hippocampal volumes for each participant.
- All analyses were conducted using SPM8 and the conn functional connectivity toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2002).
- BOLD signal from white matter and CSF masks as well as continuous motion regressors from 6 directions of movement (roll, pitch, yaw, x, y, z) and outlier timepoints were included as noise covariates.
- Data were band-pass filtered at $.01<f<.08$.
- Correlation coefficients were computed between bilateral hippocampal regions of interest (Freesurfer) and the rest of the voxels in the brain using memory performance as a covariate.
- AlphaSim (AFNI) was used to calculate cluster-corrected p-values to maintain an alpha of $p<.05$ ($p<.001$, 26 voxels or $p<.005$, 38 voxels)

Right Hippocampal Connectivity (N=34)

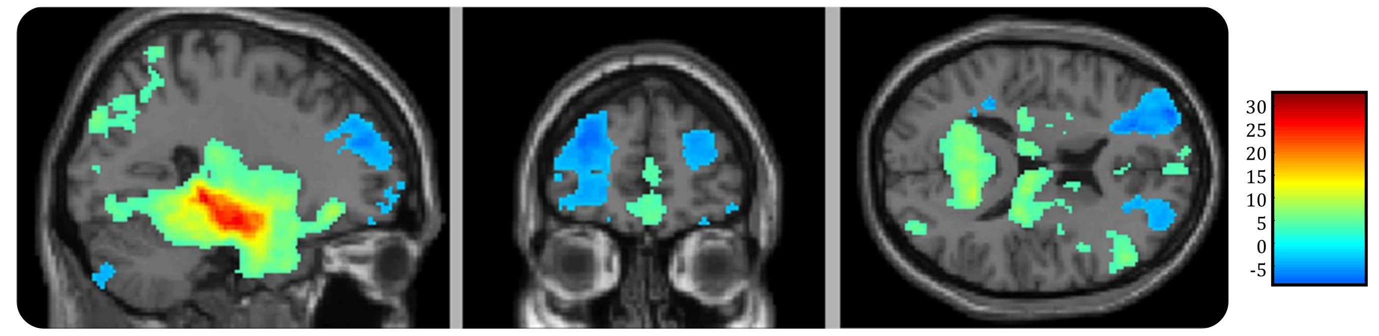


Figure 1: Right hippocampal resting network ,*p*<.05 corrected

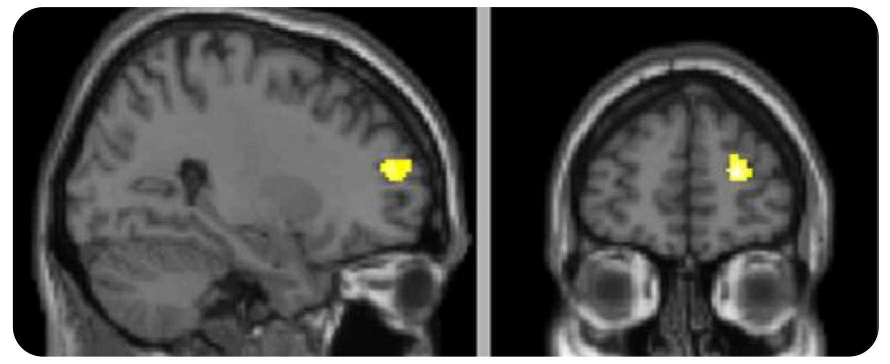


Figure 2: Right Hippocampus to BA10 (Middle Frontal Gyrus). [28 54 15] 152 voxels, *p*<.05 corrected

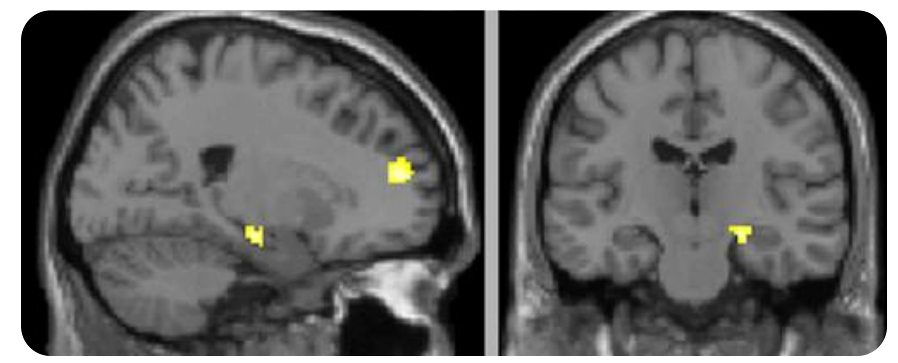
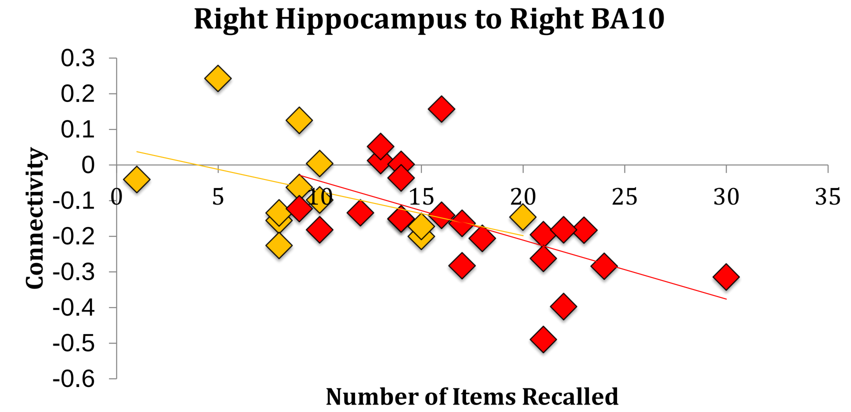
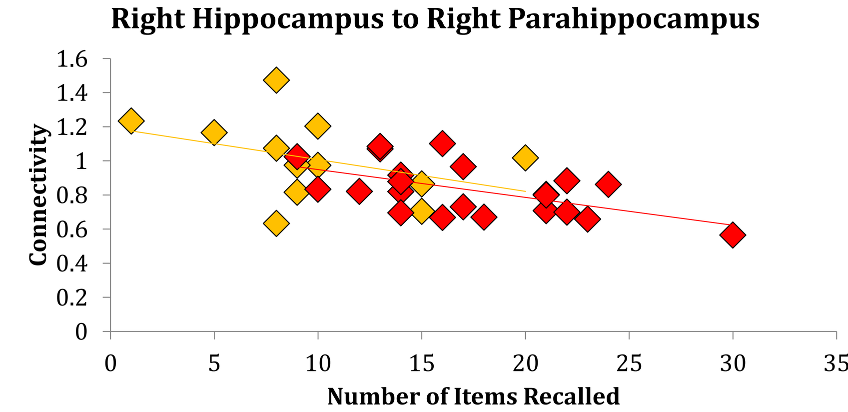


Figure 3: Right hippocampus to right parahippocampal gyrus. [22 18 13] 49 voxels, *p*<.05 corrected



- Greater *negative* connectivity between right hippocampus and right BA10 is associated with *better* memory performance.



- Greater *positive* connectivity between right hippocampus and right parahippocampus is associated with *poorer* memory performance.

Left Hippocampal Connectivity (N=34)

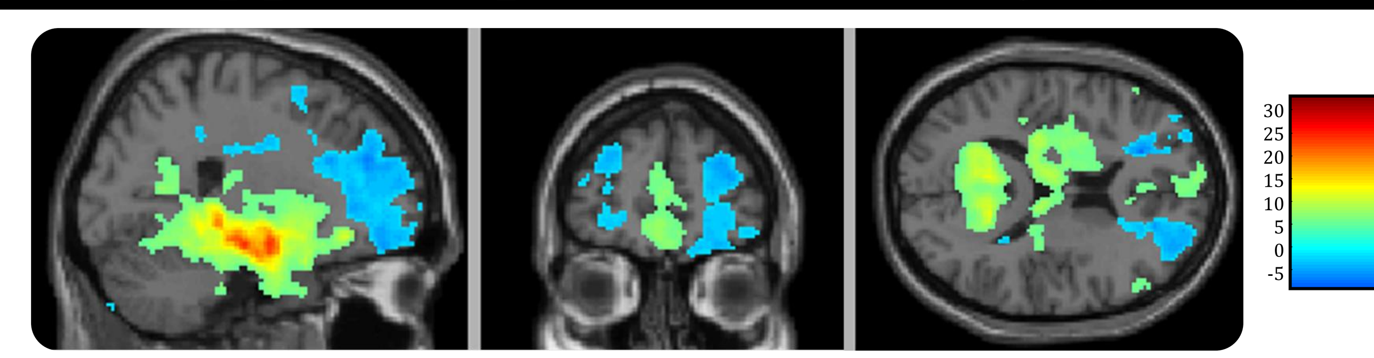


Figure 4: Left hippocampal resting network, *p*<.05 corrected

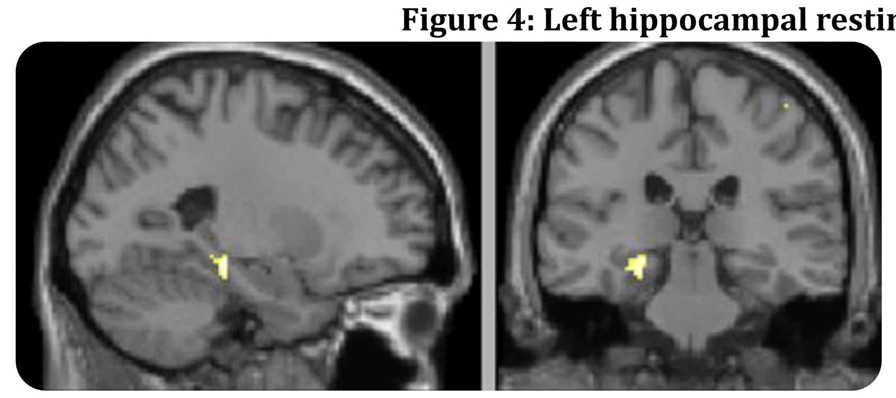


Figure 5: Left hippocampus to right BA10 (Middle Frontal Gyrus). [24 54 16] 134 voxels, *p*<.05 corrected

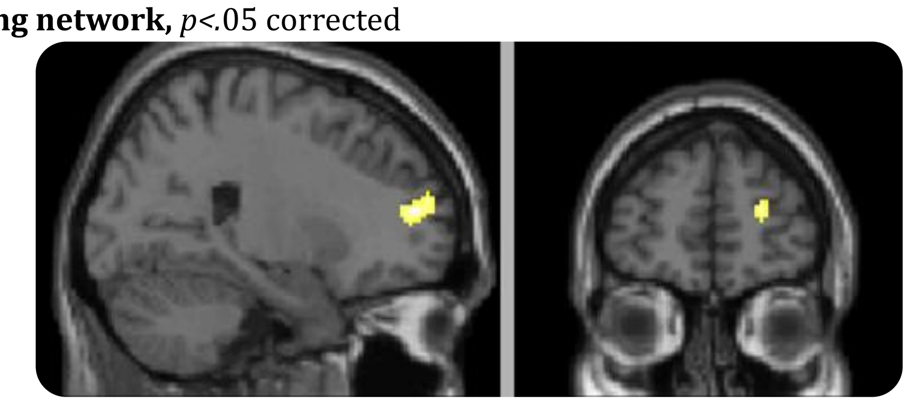
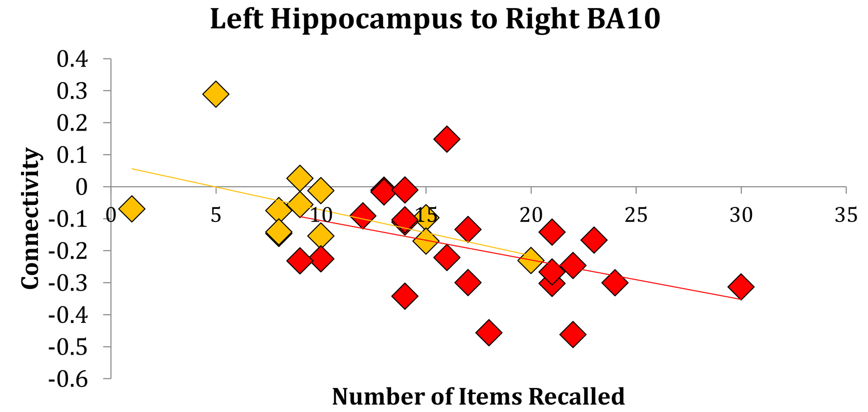
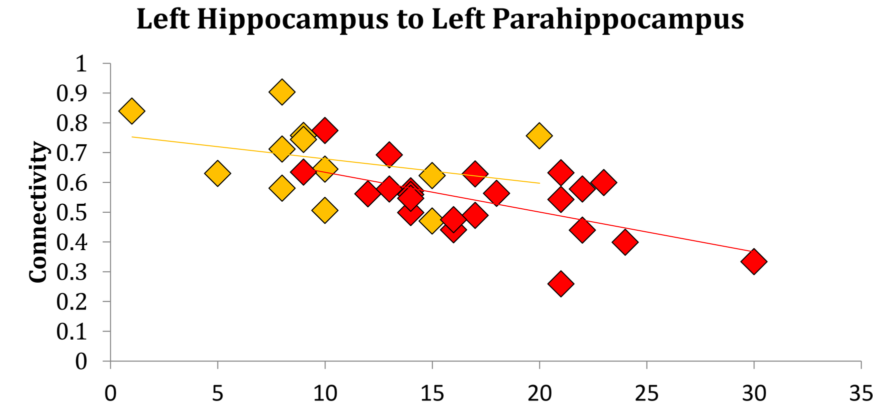


Figure 6: Left hippocampus to left parahippocampal gyrus. [24 28 14] 38 voxels, *p*<.05 corrected

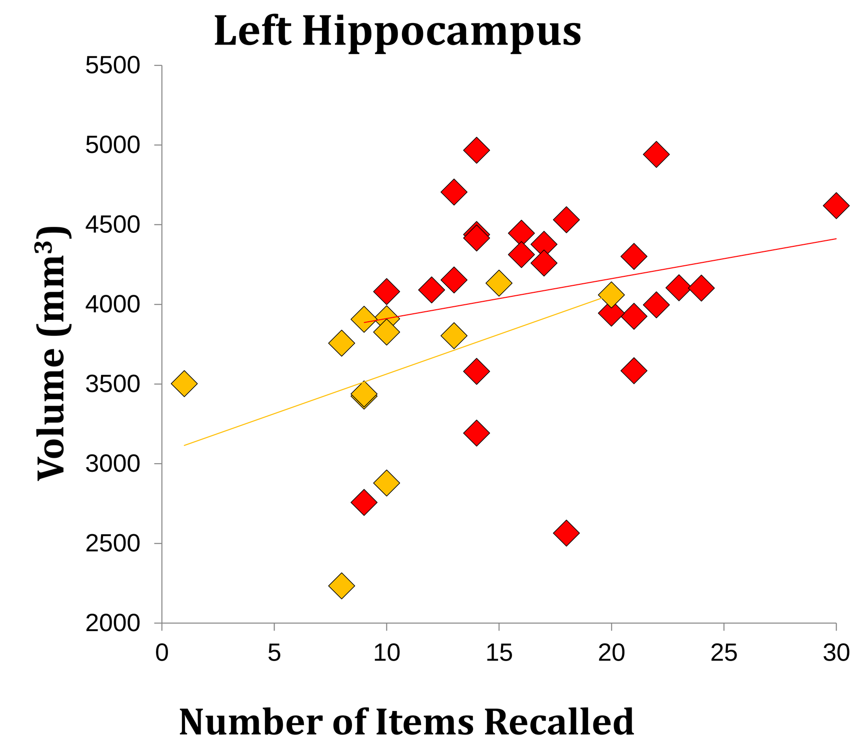


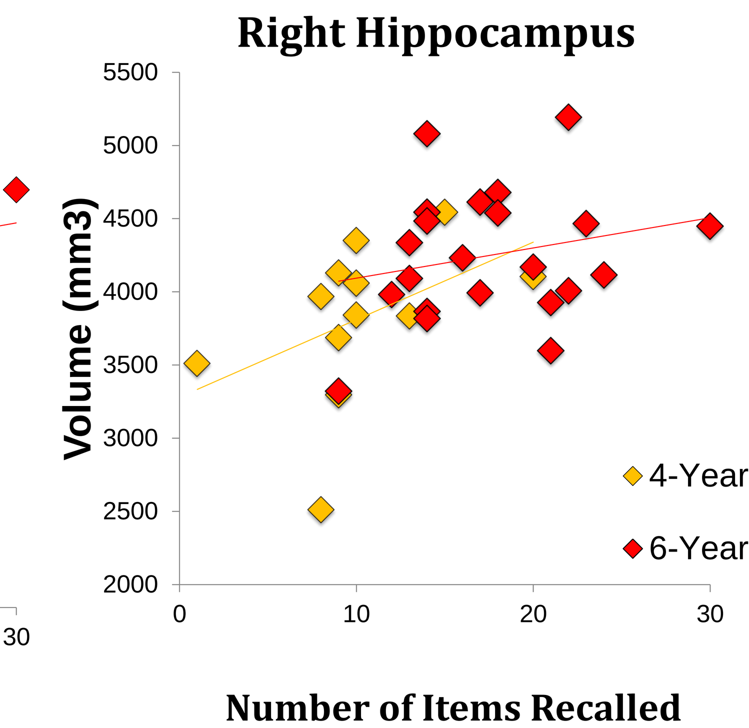
- Greater *negative* connectivity between left hippocampus and right BA10 is associated with *better* memory performance.



- Greater *positive* connectivity between left hippocampus and left parahippocampus is associated with *poorer* memory performance.

Volumetric Results (N=37)





- Left and right hippocampal volumes were significantly correlated with performance on picture recall, $r(35)=.43$, $p<.01$ and $r(35)=.46$, $p<.01$, respectively.
- The correlation remained marginally significant after controlling for total gray matter volume, IQ, and age in the right hippocampus: $r(35)=.306$, $p=.08$ (Left hippocampus: $r(35)=.258$, $p=.140$)
- Picture recall was not significantly correlated with either left or right amygdala volume $r(35)=.22$, $p=.20$ and $r(35)=.15$, $p=.38$, respectively.

Discussion

- These data suggest memory ability during early childhood is associated with individual differences in the hippocampus.
  - Specifically, in 4- to 6-year-old children, hippocampal volume was significantly associated with performance on our memory task, even after controlling for age, IQ, and gray matter.
  - Connectivity between the hippocampus and 1) parahippocampal gyrus and 2) middle frontal gyrus was associated with better memory performance.
    - Negative associations between connectivity and performance were unexpected.
- Future directions include comparison with an adult sample and examining differences between 4- and 6-year-old groups.

Acknowledgements

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References

Drummey, A.B., Newcombe, N.S. (2002). Developmental changes in source memory. *Developmental Science,* 5*(4)*, 502-513.
Ghetti, S., Bunge., S.A. (2012). Neural changes underlying the development of episodic memory during middle childhood. *Developmental Cognitive Neuroscience,* 2*(4),* 381-395.
Giedd. J.N. (2004). Structural magnetic imaging of the adolescent brain. *Ann NY Acad Sci,* 1021, 77-85.
Gogtay, N., Nugent, 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(8), 664-672.
Fischl, B., Salat, D.H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., van der Kouwe, A., Killiany, R., Kennedy, D., Klaveness, S., Montillo, A., Makris, N., Rosen, B., Dale, A.M., (2002). Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. *Neuron,*33, 341-355.
Menon, V., Boyett-Anderson, J.M., Reiss, A.L. (2005). Maturation of medial temporal lobe response and connectivity during memory encoding. *Cognitive Brain Research,* 25, 379-385.
Serres, L. (2001). Morphological changes of the human hippocampal formation from midgestation to early childhood. In C.A. Nelson & M. Luciana (Eds.), *Handbook of developmental cognitive neuroscience* (pp. 45-58). Cambridge, MA: MIT Press.
Wang, L., Negreira, Al, LaViolette, P., Bakkour, A., Sperling, R.A., Dickerson, B.C. (2010a). Intrinsic interhemispheric hippocampal functional connectivity predicts individual differences in memeory performance ability. *Hippocampus,* 20*(3)*, 345-351.
Wang, L., LaViolette, P., O'Keefe, K., Putcha, D., Bakkour, A., Van Dijk, K.R.A., Pihlajamaki, M., Dickerson, B.C., Sperling, R.A. (2010b). Intrinsic connectivity between the hippocampus and posteromedial cortex predicts memory performance in cognitively intact older individuals. *NeuroImage,* 51*(2)*, 910-917.
Whitfield-Gabrieli, S., Nieto-Castanon, A. (2012). Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connect.,* 2*(3),* 125-141.

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