Age-related differences in functional connectivity patterns along the hippocampal long axis.

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Background

- The hippocampus supports memory, and its structural and functional integrity tends to decline in older age.[1]
- Studies in young adults have shown functional differentiation along the hippocampal long axis[2], including different patterns of cortical connections.[3]
- Functional differentiation along the long axis of the hippocampus in older adults is less clear.

How is the distinctiveness of functional connectivity networks along the hippocampal longitudinal axis influenced by older age?

Adult Lifespan Sample

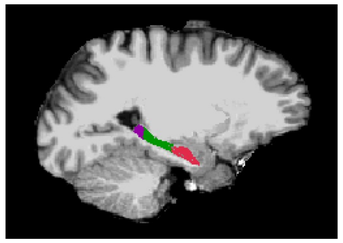
Cambridge Center for Aging and Neuroscience Data[4]

- 650 participants ages 18-88
- 413 included in analyses following exclusions for motion.
- Used the resting state functional scan

Age Group	N Included	% Female	MMSE Score
18-29	61	61%	29.2 (29.3)
30-39	79	47%	28.9 (28.8)
40-49	86	50%	29.1 (29.1)
50-59	57	56%	29.4 (29.2)
60-69	61	43%	28.8 (28.8)
70-79	46	46%	27.7 (27.9)
80+	23	48%	28.3 (28.0)
Total	413	50%	28.9 (28.7)

Resting State Functional Connectivity

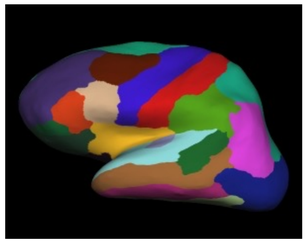
Hippocampal seed regions



Freesurfer hippocampal segmentation[5].

- Tail = most posterior, Head = most anterior
- Separate right, left hemisphere seeds

Whole-brain target regions



Cortical regions from Desikan-Killiany parcellation + subcortical regions

- Separate right, left hemisphere seeds
- 84 targets in all

Following pre-processing, computed partial correlations between time courses for each seed-target pair, removing timepoints with excessive motion and including motion covariates.

References

1. Leal & Yass (2015). *Trends in Neurosciences*.
2. Brunec et al., (2018). *Current Biology.*
3. Frank, Bowman & Zeithamova (2019). *Journal of Cognitive Neuroscience.*
4. Shafto, et al., (2014). *BMC Neurology.*
5. Iglesias, et al., (2015). *NeuroImage*.

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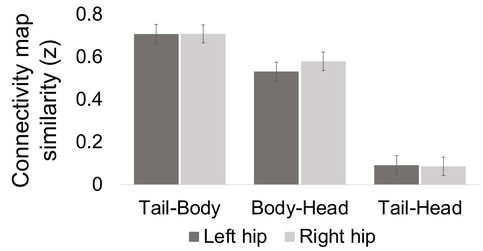
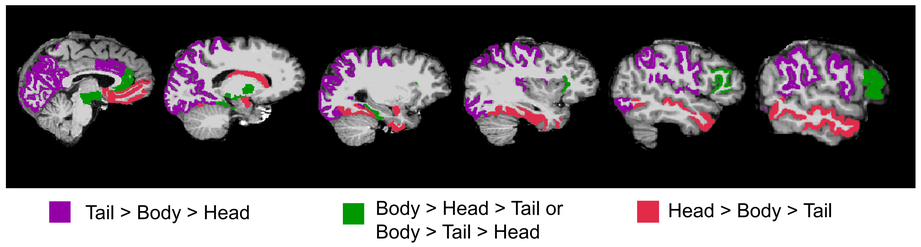
Are there differences in long-axis hippocampal connectivity across the adult lifespan?

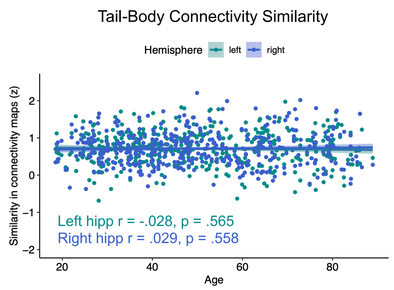


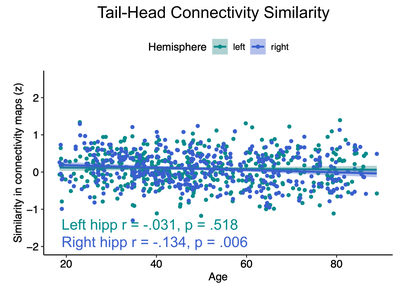


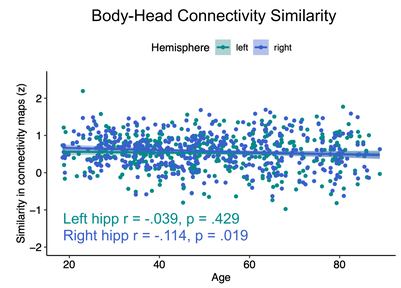
- Hippocampal tail and body have most similar pattern of connectivity, but head and body also have substantial overlap.

- Tail to head connectivity gradient for occipital and parietal regions.
- Head to tail connectivity gradient for medial PFC and temporal regions.
- Body connectivity strongest for portions of lateral PFC, ACC, and entorhinal cortex.

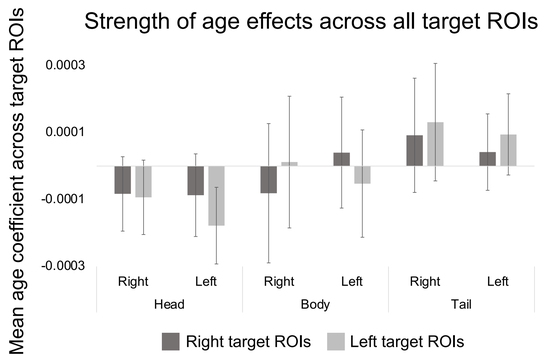
How do patterns of hippocampal connectivity differ across the adult lifespan?





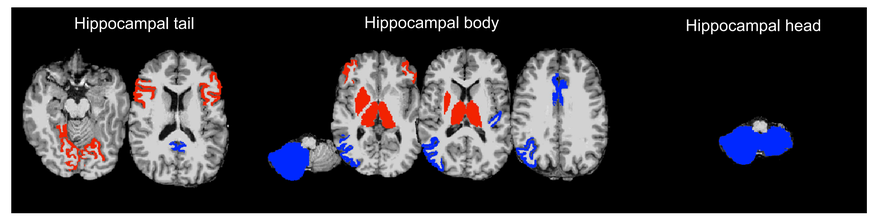


- Overall, hippocampal connectivity maps becoming *less similar* to one another in older age.
- Effect strongest and significant for right head compared to right tail and body.



With age,

- …connectivity decreases for the head.
- …a mix of increases and decreases for the body.
- …connectivity increases for the tail.



- Tail: age-related increases in connectivity with posterior cingulate and bilateral inferior frontal gyrus (BA44 & 45); decrease with lingual gyrus.
- Body: age-related increases in connectivity with thalamus, inferior frontal gyrus (BA 47), right putamen and pallidum; decreases with mid cingulate, right cerebellum, insula, and inferior parietal.
- Head: age-related decreases in connectivity with cerebellum.

Summary & Future Directions

- Functional connectivity differences along the long axis of the hippocampus in a lifespan sample.
- Patterns of functional connectivity across hippocampal regions become *more distinct* in older age, with the right head becoming especially distinct from the right tail and body.
- Overall gradient in age-related differences: tail connections tend to increase, body connections are mixed, and head connections tend to decrease with older age.
- Future direction: link connectivity patterns to cognitive abilities.