Age-related changes in hippocampal-neocortical connectivity during successful associative retrieval

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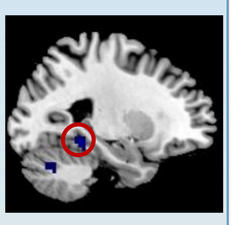
Background

- **Successful associative retrieval** critically depends on the hippocampus[1].

- **Hippocampal activity in older adults** varies across studies, either showing *hyper*[2]- or *hypo-activation*[3] during memory tasks, despite comparable task performance with young adults.



- **Functional connectivity measures** of the hippocampus with other cortical regions can provide a window into the underlying neuronal compensation mechanisms in the aging brain.

- **Compensatory mechanisms** in older adults are often reflected by increased frontal coupling[4]. However, as task demand increases, older adults reach a resource ceiling[5], showing reduced flexibility in functional coupling to meet demands.

Predictions

- **Successful associative retrieval was expected to lead to:**

1) increased hippocampal coupling with frontal regions in older *vs.* young adults, even when memory load was low.

2) undifferentiated coupling in older adults from the low to the high memory load condition due to deficient resource allocation.

Methods

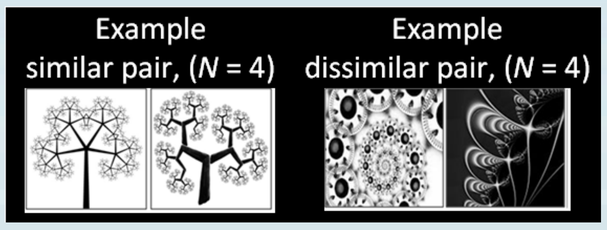
Participants

- 19 young adults (21-32 years; M = 24.06)
- 19 older adults (59-81 years; M = 66.21)

Tasks:

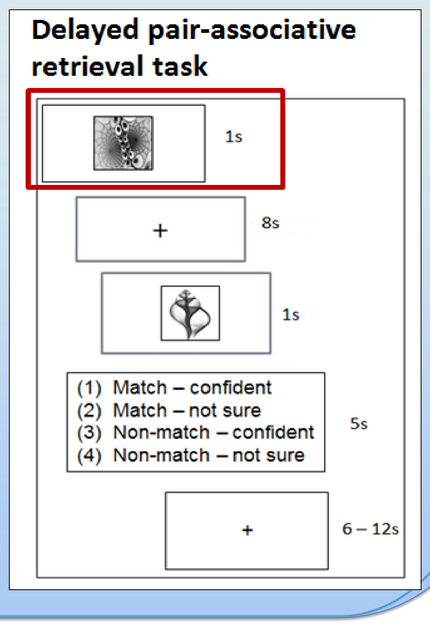
1. Self-paced learning (pre-scanning session)

- Participants learned 8 fractal pair-associates to 87% correct performance criterion on a computer outside the scanner. Memory load was manipulated by visual similarity.



2. Memory retrieval (scanning session)

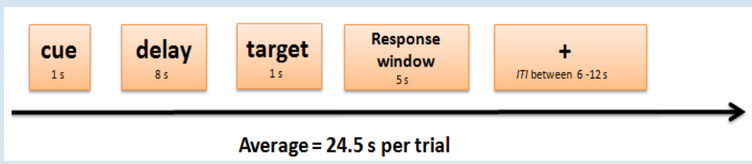
-Memory was tested in the scanner using a delayed pair-associative retrieval task.



fMRI protocol & Analyses

Event-related design, including 32 similar and 32 dissimilar pair trials

Trial structure:



Data acquisition parameters:
Data were collected on a 1.5 T Siemens Magnetom Avanto MRI Scanner with a 32-channel head coil. 644 volumes were obtained using a T2* weighted EPI sequence; TR=2.62s, TE=42ms, flip angle=90 degrees

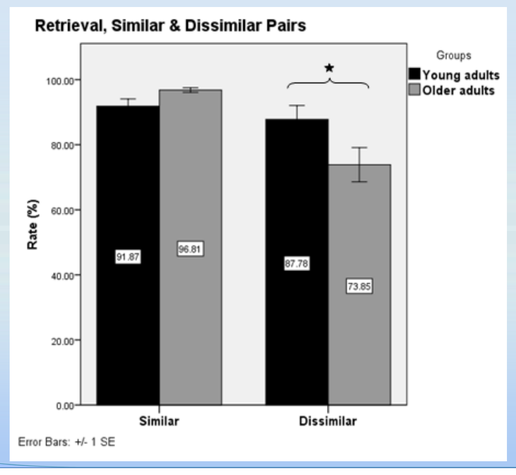
Univariate analyses

- Pre-processing: All functional images were slice-time and motion corrected, unwarped, coregistered to participants' individual structural volume, and spatially normalised.
- Hits & Correct rejections of similar & dissimilar pairs were analysed using the GLM. Events were convolved with a canonical HDR function, time-locked to cue onset with a 1s duration (modelling cue-period).
- Contrast images were computed for the *Similar* and *Dissimilar* conditions. Results were subjected to a group analysis (2-level random effects analyses). A conjunction analysis was performed with trials averaged across similarity. This yielded activity in the left (L) hippocampus.

Functional connectivity

- Region of interest (ROI): an anatomical seed region of the entire L hippocampus was created.
- Temporal pre-processing: spurious effects of white matter, cerebrospinal fluid, head motion and task conditions were removed; a band-pass filter was set at 0.008Hz < f < 0.09Hz.
- Seed-to-voxel analysis: Using the CONN fMRI connectivity toolbox in SPM8 (v13o, 2011, *http://www.nitrc.org/projects/conn*), the mean BOLD time-series of the ROI was regressed with all other voxels in the brain.

Behavioural Results



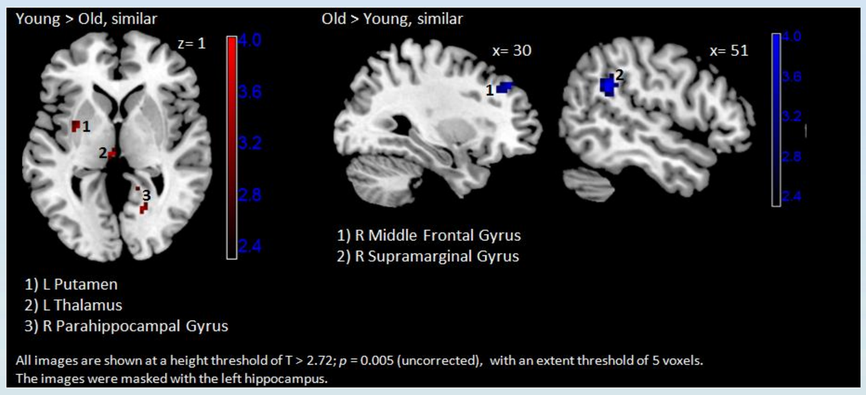
Results summary

-We found a significant interaction between young and older adults and the number of successfully retrieved trials:

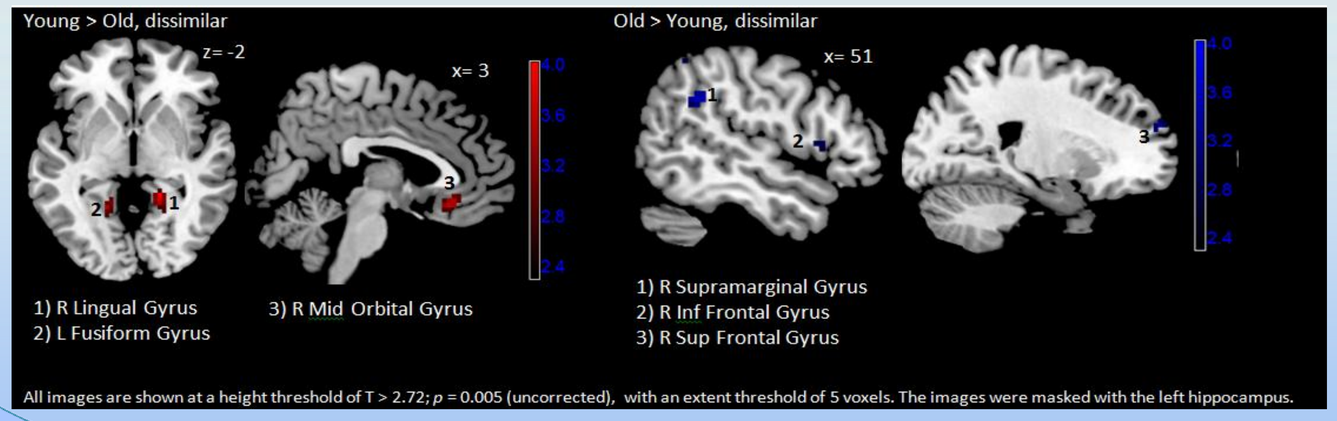
- Young and older adults showed a comparable number of retrieved similar pair-associates (low memory load) but older adults retrieved significantly fewer trials of the dissimilar pair-associates than young adults.

fMRI Results

Condition: Similar



Condition: Dissimilar



Results summary

-**In the low memory load condition**, young adults show hippocampal coupling with the basal ganglia & parahipp. gyrus, while older adults recruit a frontal-parietal network.

-**In the high memory load condition**, young adults show hippocampal coupling with medial occ.-temp. regions & the orbitofrontal cortex, while older adults continue to recruit a frontal-parietal network.

Conclusions

- Our results demonstrate that in healthy aging, associative retrieval involves hippocampal coupling with frontal-parietal brain regions, even when memory load is low. The memory network in older adults remains largely invariant to changing memory load.
- By contrast, younger adults show more automatic retrieval mechanisms during low memory load, supported by subcortical brain structures. They flexibly switch to visual and orbitofrontal brain regions with increasing memory load to aid associative retrieval.
- Our results support the account of a deficient resource allocation in aging.

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