Age-related differences in hippocampal activation during implicit sequence learning

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INTRODUCTION

While there are known differences between older and younger adults in implicit associative learning, the neural bases underlying the differences have not been well characterized. Generally, hippocampal activity during early training has been reported, as has greater reliance on medial temporal regions in older adults.

AIM: The current study examines age-related differences in hippocampus (HC) and parahippocampal gyrus (PHC) activity during a Triplets Learning Task (TLT), as well as the relationship between task-related activity and task performance.

METHODS

Experimental Paradigm

- Healthy older adults (n=11) and younger adults (n=11) performed the Triplets Learning Task (TLT; Howard, J. H., et al., 2008)
- Viewed a sequence of three visual stimuli and responded to third (target) with button press (see Figure 1 below)

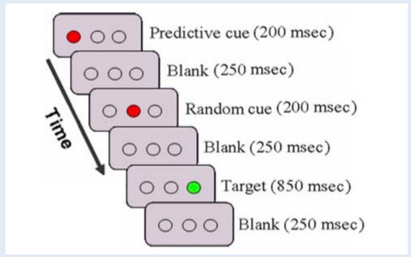

Figure 1. Visual of one triplet of TLT, with timings. Additionally, a jitter of 0-6 s was placed between trials.

- Participants underwent three event-related fMRI sessions of 135 trials (triplets) each-- representing early, middle, and late learning, respectively

Imaging Parameters: 3T Siemens Trio Scanner

- Anatomical: T1-weighted MPRAGE sequence: TR=2300ms, TE=2.94ms, FoV=256mm, FA=90°; number of slices=160, thickness= 1mm; 1.0mm^3 isotropic resolution; TA=7:23.
- Functional: T2*-weighted EPI sequence: TR=2500ms, TE=30ms, FoV=256mm, FA=90°; number of slices=42, thickness= 3.7mm; voxel size= 4x4x3.7mm; TA=6:30.

Imaging Analysis: AFNI (http://afni.nimh.nih.gov/afni/)

- Preprocessing: slice timings correction, motion correction, brain-only mask, spatial smoothing (5mm FWHM kernel).
- Signal regression using trial timings convolved with HRF as ideal reference waveform; β-coefficients were shown in statistical parametric maps after warping to common (Talairach) space
- Correction for multiple comparisons was performed using AlphaSim
- Region-of-interest (ROI) masks were derived from the anatomical Talairach atlas

RESULTS

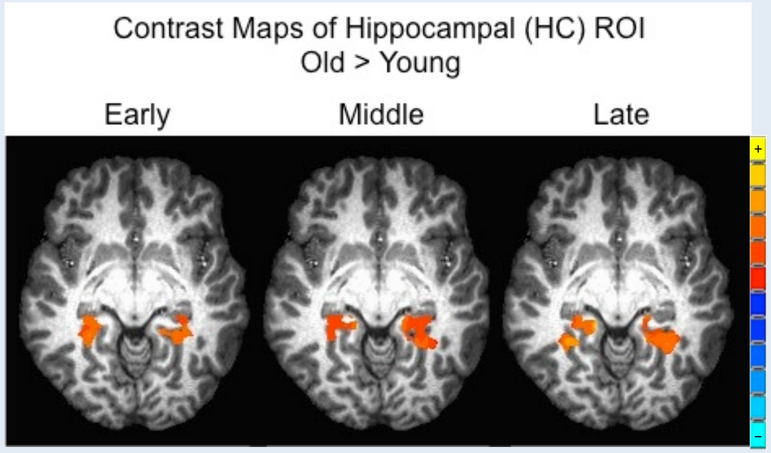

Figure 2. Axial slices of HC region showing greater bilateral activation in Older group as compared to Young at all learning sessions; z=60, corrected p<0.05.

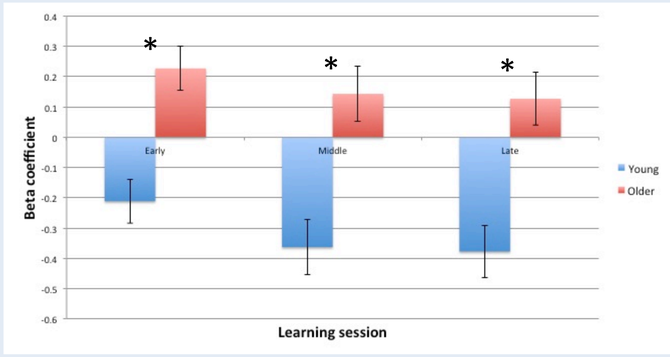

Figure 4. Triplet activation in HC region by learning session. Beta coefficient from regression analysis; bars represent mean±SEM; *denotes significantly higher activation in Older group as compared to Young (2-tailed t-test; p<0.005).

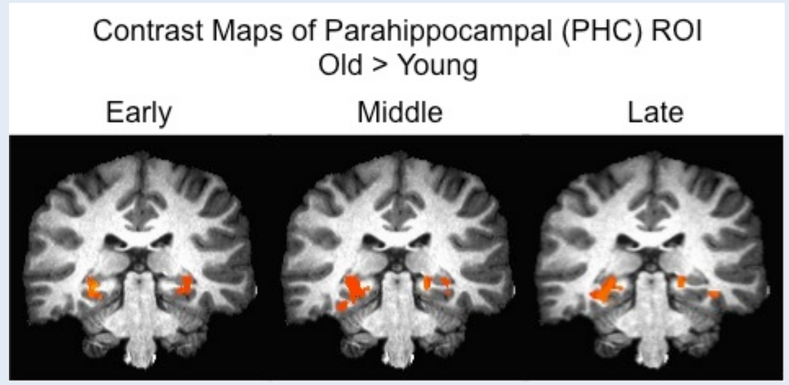

Figure 3. Coronal slices of PHC region showing greater bilateral activation in Older group as compared to Young at all learning sessions; y=111, corrected p<0.05.

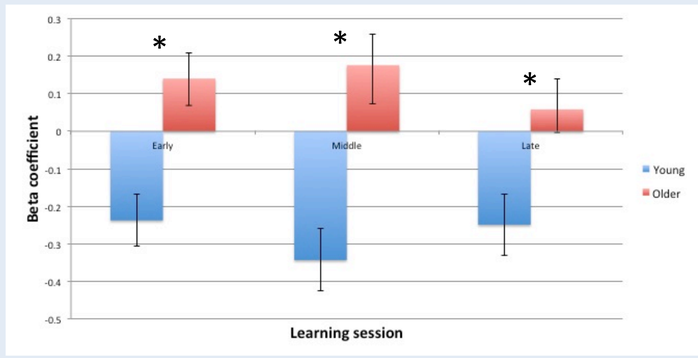

Figure 5. Triplet activation in PHC region by learning session. Beta coefficient from regression analysis; bars represent mean±SEM; *denotes significantly higher activation in Older group as compared to Young (2-tailed t-test; p<0.05).

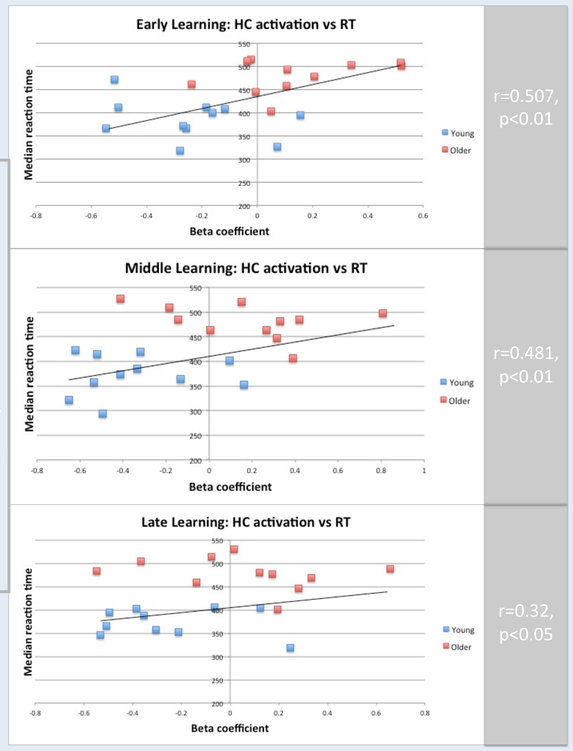

Figure 6. Scatter plots of activation in HC vs median reaction time (MedRT) on TLT. MedRT was significantly lower in older adults (p<0.001) in all learning sessions. Significant positive correlation was also seen between MedRT and PHC activation (not shown; r>0.3, p<0.05 for all sessions).

DISCUSSION

The findings in this study suggest that older adults rely more on the hippocampal regions during training in the TLT, and that this activity may be related to their overall reaction time. A previous analysis of these data (Simon, J. R., et al., 2011) had found a significant HC response to predictability of the target location for both age groups early in training, whereas late in training HC response to predictability correlated with the amount of sequence learning in the older, but not the younger group. Given this result, it is possible HC activity is needed as a baseline for older adults to perform the task, regardless of predictability. This would explain the older group's higher reliance on HC activity throughout all learning sessions. Other regions with task-related activation, including cingulate gyrus, medial frontal gyrus, and caudate, did not show differences in older vs young individuals; further study is needed to examine the role of these regions in differential task performance between age groups.

ACKNOWLEDGEMENTS

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