NEURAL BASIS OF PROBABILISTIC SEQUENCE LEARNING IN AGING: An fMRI Study

Jessica R. Simon[1], Kelly Anne Barnes[1], Chandan J. Vaidya[1,2] , James H. Howard, Jr.[1,3,4] & Darlene V. Howard[1]

[1]Department of Psychology, Georgetown University; [2]Children's National Medical Center, Washington DC;
[3]Department of Psychology, The Catholic University of America; [4]Department of Neurology, Georgetown University Medical Center

AIM

• To identify neural basis of sequence learning in healthy old adults and determine age-related differences in brain activation associated with learning on a probabilistic sequence learning task

INTRODUCTION

PROBABILISTIC SEQUENCE LEARNING involves gaining sensitivity to the typical order of events, making it possible to anticipate, predict and process future events more effectively

TRIPLETS LEARNING TASK is a recently developed probabilistic 2nd order sequence learning paradigm without strong motor demands (Howard et al., 2008)

AGE DEFICITS are reported in complex 2nd order sequencing tasks, especially with extended practice, despite learning in both young and old adults (Howard et al., 2004; Howard et al,, 2008)

GRAY MATTER SUBSTRATES: In similar tasks, young adults reveal activations in frontal, medial temporal, and striatal regions (e.g., Aizenstein et al., 2004; Reiss et al., 05; Schendan et al., 2003)

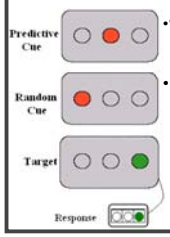
OLD ADULTS show age-related brain differences in above regions (e.g. volume declines and neurotransmitter disruption) (Hedden & Gabrieli, 2005; Kennedy & Raz, 2005; Raz, 2000; Raz et al., 2005)

METHOD

PARTICIPANTS

Group	Sample Size (# female)	Age (SD)	MMSE (SD)	Digit Span (SD)
Young	10 (5 female)	18.8 (.6)	30.0 (0.0)	20.2 (4.7)
Old	11 (8 female)	67.6 (3.3)	29.3 (.8)	21.2 (3.9)

EVENT-RELATED TRIPLETS LEARNING TASK



- 'Triplets': series of discrete, 3-event sequences
  - 2 cues (predictive, then random) and 1 target
  - Respond to target location with right hand
- 2nd order structure: Location of 1st cue probabilistically predicts target location
  - In one location on 80% of trials (High Probability (HP) Condition)
  - In another location on 20% of trials (Low Probability (LP) Condition)
  - Cue and Target location counterbalanced

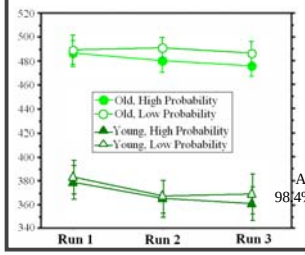
fMRI PARAMETERS

- 3T Seimens Magnet, T2* sensitive gradient EPI acquisition
- Three 6.5 minute runs
- 135 trials/run, 42 axial slices; voxel size = 4.0 x 4.0 x 3.7 mm
- TR = 2500 ms, TE = 30ms, 90˚ flip angle, FOV = 256
- Data Analysis in SPM5 (Realignment, Spatial Normalization to MPRAGE, Spatial Smoothing {8mm})
- Random-effects group averaging:
  - High Probability – Low Probability contrast: *Response to Predictability*
  - Low Probability – High Probability contrast: *Response to Novelty*
  - Correlational analyses
  - p < .01 uncorrected, extent 10 voxels

BEHAVIORAL RESULTS

Learning Across Sessions:

Mean Reaction Time (milliseconds)



AGE GROUP :
Young adults faster than old adults overall
F(1,19)=37.31, p < .0001

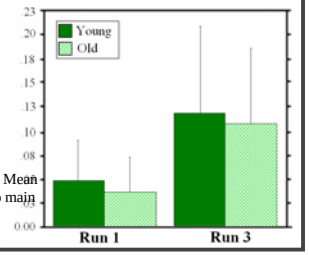
SKILL LEARNING:
Reaction time improved over time
F(2,38)=2.98, p= .063

TRIPLET LEARNING:
Faster reaction time for HP vs. LP triplets
F(1,19)=10.02, p=.005

ACCURACY:
98.4% (SD=.03)
No main effect or interactions

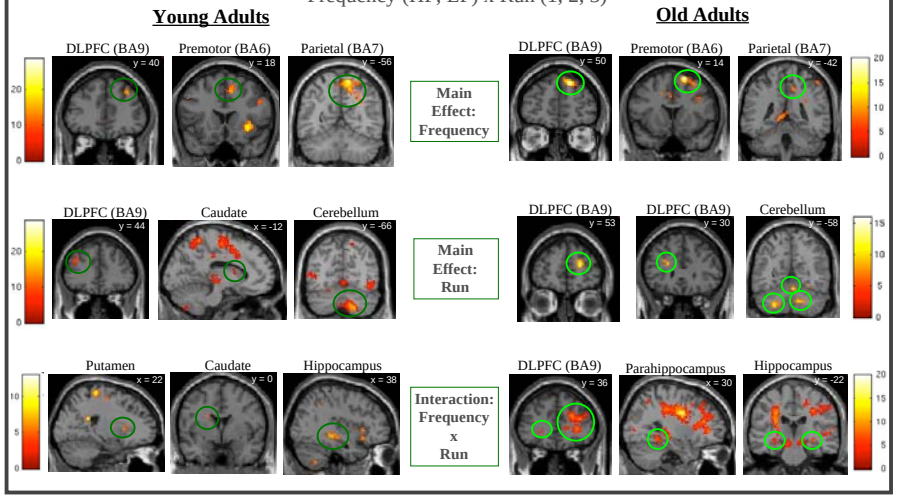
Triplet Learning Measure:

Mean Correlation -1 * (Triplet Probability x Mean Reaction Time)



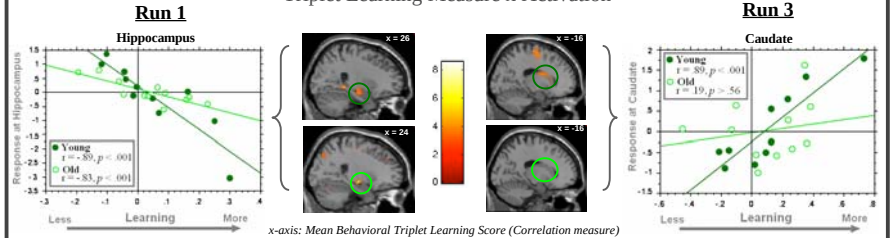
WITHIN-SUBJECTS ANOVA

Frequency (HP, LP) x Run (1, 2, 3)



CORRELATIONS

Triplet Learning Measure x Activation



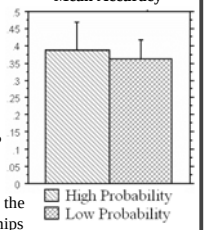
x-axis: Mean Behavioral Triplet Learning Score (Correlation measure)
y-axis: Activation from HP - LP contrast

NO EXPLICIT AWARENESS

FOLLOW-UP STUDY
- 9 young adults
- Significant skill (p < .004) and triplet learning (p < .0007)

RECOGNITION MEASURES
- Recognition paradigm:
  - Equal recognition of HP and LP triplets (p > .78)
- Post-experiment interview:
  - No subject accurately described the regularity or predictable relationships

Mean Accuracy



ADDITIONAL fMRI RESULTS

HIGH vs. LOW PROBABILITY CONTRASTS
- Run 1: Greater response to predictability (most often repeated sequences) in both young and old adults
- Run 3: Greater response to novelty (least often repeated sequences) in both young and old adults

p = .005; k = 15	RUN 1 ACTIVATIONS		RUN 3 ACTIVATIONS	
	Response to Predictability *HP > LP*	Response to Novelty *LP > HP*	Response to Predictability *HP > LP*	Response to Novelty *LP > HP*
Young Adults	• Hippocampus • Parahippocampal Gyrus (BA 35) • Medial Temporal Gyrus (BA 21) • Cerebellum	• Postcentral Gyrus (BA 7)	None	• DLPFC (BA 46) • Superior Parietal Lobule (BA 37) • Inferior Frontal Gyrus (BA 47) • Medial Temporal Gyrus (BA 21)
Old Adults	• Hippocampus • DLPFC (BA 9) • Inferior Frontal Gyrus (BA 47) • Inferior Parietal Lobule (BA 40) • Cerebellum	•DLPFC (BA 9)	• Medial Frontal Gyrus (BA 10)	• Cingulate (BA 32) • Medial Temporal Gyrus (BA 21)

DISCUSSION

- Similar levels of implicit learning were supported by different regional recruitment in young and old adults
- Both groups showed cerebellar and DLPFC activation, though it was bilateral in old adults only
- Deficient striatal response in older adults
- Greater recruitment of frontal or MTL networks during learning in old adults might suggest compensation or greater reliance on top-down control processes during learning of sequential probabilistic information

Society for Neuroscience
38th Annual Meeting, November 2008
Washington, DC
Email: jrs92@georgetown.edu
Supported by NIH/NIA Grant R37AG15450 and GCRC NIH/ NCRR Grant M01 RR023942-01