# WHITE MATTER INTEGRITY AND IMPLICIT SEQUENCE LEARNING IN YOUNGER AND OLDER ADULTS

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## INTRODUCTION

IMPLICIT SEQUENCE LEARNING describes non-conscious sensitivity to sequential regularities

GRAY MATTER SUBSTRATES include frontal cortex (DLPFC, premotor, supplementary motor), striatum (caudate, putamen), and cerebellum (Jenkins et al., 1994; Pascual-Leone et al., 1996; Rauch et al., 1997)

OLDER ADULTS often show smaller implicit sequence learning effects than younger adults (Curran, 1997; Howard, et al., 2004)

- May reflect age differences in underlying brain regions (e.g. volume decline in gray matter substrates; frontal-striatal neurotransmitter disruption) (Hedden & Gabrieli, 2005; Kennedy & Raz, 2005; Raz, 2000; Raz et al., 2005)

WHITE MATTER SUBSTRATES of implicit sequence learning are unknown

- Implications for aging because of robust age-related differences in white matter (Pfefferbaum et al., 2005; Raz & Rodrigue, 2006; Sullivan & Pfefferbaum, 2006)

PRESENT STUDY ASSESSED:

- White matter correlates of implicit sequence learning
- Age differences in white matter integrity-implicit sequence learning relationships

## METHOD

PARTICIPANTS

- 14 younger adults (18.9 ± 0.7 years; 9 female)
- 13 older adults (67.8 ± 3.2 years; 10 female)

GENERAL PROCEDURE

- DAY 1: Diffusion Tensor Imaging (DTI)
- DAY 2: Alternating Serial Reaction Time (ASRT)

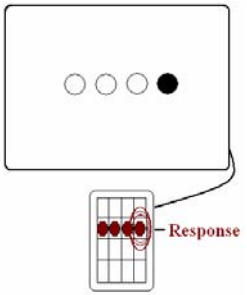
DTI METHODS

- 3T Siemens Trio
- One EPI sequence acquired per participant
  - Diffusion weighted gradients b=0 and b=1000 s/mm$^2$ applied in 35 orthogonal directions
  - 55 axial interleaved slices
  - 2.5 mm$^3$ spatial resolution
  - TR/TE=7700/100ms
  - FOV=240x240 mm
- FMRIB's diffusion toolbox (Behrens, 2003; Smith et al., 2004)
  - Eddycorrect: corrected eddy current distortion
  - BET binary brain mask: limited tensor fitting to brain space
  - DTIfit: independently fit diffusion tensors to each voxel
  - Fractional Anisotropy (FA) maps derived from eigenvalues of the diffusion tensor
- Voxel-wise statistics using Tract-Based Spatial Statistics (t value threshold set to p < .05) (Smith et al., 2006)
  - Within-group correlations
    - FA x ASRT last epoch learning scores
    - FA x ASRT overall reaction time
  - Between-group t-test

## SEQUENCE LEARNING

ASRT TASK:

- Respond to stimuli at 1 of 4 locations with right hand



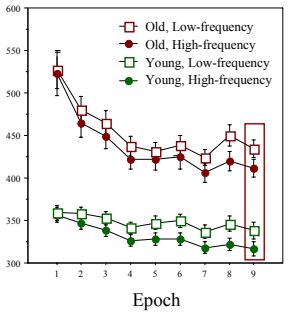

2nd ORDER SEQUENCE STRUCTURE:

- e.g. 1r2r3r4r
- 1, 2, 3, 4 = target location follows a repeating pattern
- r = target location is randomly determined

BEHAVIORAL ANALYSIS:

- Last trial of High-frequency (e.g. 112) and Low-frequency (e.g. 113) triplets compared across 9 Epochs
- Learning (i.e. significant Triplet Type and Triplet Type x Epoch effects) for reaction time and accuracy measures did not differ with Age Group

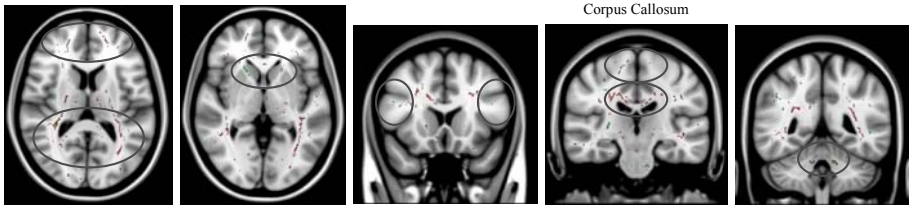
REACTION TIME (ms)
(mean of median)




## WHITE MATTER INTEGRITY-SEQUENCE LEARNING RELATIONSHIP

- Separate FA x ASRT last epoch learning voxel-wise positive correlations for Younger and Older adults

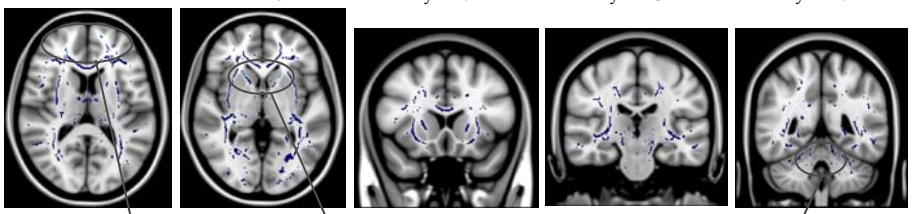
| z = 12 | z = 0 | y = 17 | y = -23 | y = -47 |
|---|---|---|---|---|
| Ant. Coronal Radiata and Post. Sup. Longitudinal Fas. | Ant. Limb of Int. Capsule b/t Caudate and Putamen | White matter near right DLPFC BA 9/45 | Right Corticospinal near Premotor BA 6 and Corpus Callosum | Superior Cerebellar Peduncle |

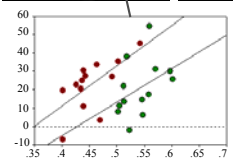


## AGE DIFFERENCES IN WHITE MATTER INTEGRITY

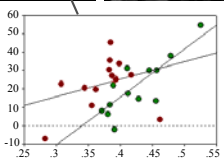
- T-test showing voxels where FA is higher in Younger versus Older adults (dark blue)
- Correlations from masked voxels (light blue) that have age differences in FA and that correlate with sequence learning

| z = 12 | z = 0 | y = 17 | y = -23 | y = -47 |
|---|---|---|---|---|



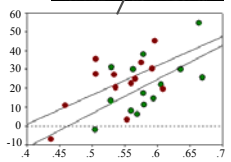



Younger adults: r = .45, ns
Older adults: r = .64, p < .02




Younger adults: r = .79, p < .001
Older adults: r = .31, ns

- Y-axis: ASRT last epoch learning (ms)
  - Reaction time difference between High- and Low-frequency triplets in epoch 9
- X-axis: Fractional anisotropy (FA)

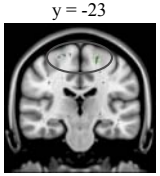



Younger adults: r = .60, p < .03
Older adults: r = .58, p < .04

## WHITE MATTER INTEGRITY-REACTION TIME RELATIONSHIP

- Separate FA x ASRT overall reaction time voxel-wise negative correlations for Younger and Older adults
- The only region that correlated with ASRT overall reaction time *and* ASRT last epoch learning was corticospinal tract near Premotor BA 6 in younger adults
  - May reflect motor demands of the ASRT, not sequence-specific learning

y = -23



## IMPLICITNESS

RECOGNITION TASK:

- Sort cards depicting all possible triplets as occurring "more often" versus "less often"
- Chi-square analyses for each participant revealed that no individual was able to discriminate between High-frequency and Low-frequency triplets

POST-EXPERIMENT INTERVIEW:

- No participant accurately described the regularity

## SUMMARY AND DISCUSSION

There are age differences in white matter correlates of implicit sequence learning

- In younger adults, superior learning in the ASRT task was related to higher white matter integrity in frontal regions (adjacent to the striatum; right dorsolateral prefrontal cortex, DLPFC; and right premotor cortex) and the cerebellum
  - Consistent with activation patterns from functional imaging studies of implicit sequence learning
- Older adults showed similar correlations in one frontal region (near premotor cortex) and the cerebellum
  - Plus additional regions (bilateral frontal coronal radiata, corpus callosum, bilateral posterior superior longitudinal fasciculus)

Results are reminiscent of age-related compensation seen in functional imaging studies

- No group differences in learning
- Age differences in white matter correlates of learning
- Age-related decline in underlying white matter integrity

| Region with greater FA in Younger versus Older adults | Correlate with ASRT learning | |
|---|---|---|
| | Younger adults | Older adults |
| Near striatum | Yes | No |
| Cerebellum | Yes | Yes |
| Prefrontal | No | Yes |

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