shift integral (MAPS-HBSI) - were calculated. The 264 patients in the ADNI1 study with BTB 1.5T MPRAGE MRIs at baseline, year 1 and year 3 were used. The BTB reproducibility of the atrophy rate of both the left and right hippocampus over 1 year and 3 years were compared with a simple statistical test based on the binomial sign test that handled outlying data points robustly. **Results:** The noise in the atrophy rate, as measured by the reproducibility in units of percentage points, showed no statistical difference between 1 and 3 years in 4 of the 5 methods. FSL/FIRST was slightly noisier in both hippocampi over 1 year than 3 years (p=0.002 & p=0.002). For example, the noise for the left hippocampus for FreeSurfer longitudinal was 2.0% over 1 year and 2.2% over 3 years while the corresponding atrophy rates were 1.9% and 5.2%. **Conclusions:** The noise of measuring hippocampal atrophy rates over 3 years was no worse than over 1 year for the 5 methods studied. Therefore, if the atrophy rate was stable over the 3 years, the 3 year study would be at least 3 times as sensitive as the 1 year study to changes in atrophy rate.

IC-P-134 DIFFERENTIATING PRECLINICAL ALZHEIMER'S DISEASE FROM NORMAL AGING: THE EFFECTS OF AGE AND AMYLOID ON COGNITIVE DECLINE OVER 3.5 YEARS

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Background: Autopsy and amyloid PET imaging studies have consistently demonstrated that amyloid pathology is present in many non-demented older adults. Consequently, it has become critical to differentiate normal age-related cognitive decline from decline due to AD pathology. To help disentangle these two processes, we examined the effects of age and amyloid deposition on 3.5-year longitudinal cognitive changes across multiple domains in healthy adults, using data from the Dallas Lifespan Brain Study. **Methods:** Participants (n=98, age=55-89) who completed amyloid imaging (f-18-Florbetapir) at baseline and cognitive assessments at baseline and 3.5-year follow-up were included. Linear Mixed Model analyses were performed with Age, Amyloid Status (positive or negative at baseline), and Time (Baseline or Follow-up) as independent variables and construct-based measures of processing speed, fluid reasoning, episodic memory, and crystallized knowledge as dependent variables, while controlling for sex, education, and APOE4 status. All interaction terms were also tested. **Results:** We found an Amyloid×Time interaction on episodic memory and crystallized knowledge, such that individuals who were amyloid positive at baseline showed significant decline on these measures over a 3.5-year interval, while amyloid negative individuals remained stable (Figure 1). Additionally, we did not detect an effect of age on decline in episodic memory or crystallized knowledge. In contrast, for processing speed and reasoning, we found greater rates of decline over the 3.5-year interval at older ages (Figure 2), regardless of amyloid status. **Conclusions:** Episodic memory declined in amyloid positive but not amyloid negative healthy older adults, showing specificity of decline to this behavioral hallmark of AD. Amyloid positive but not amyloid negative adults additionally declined in crystallized knowledge, while aging alone did not have this effect. These findings highlight the potential predictive power of declining crystallized knowledge as a marker of preclinical AD, as crystallized knowledge normally remains stable throughout the adult lifespan. In contrast, declining processing speed and reasoning were associated with old age but not baseline amyloid. This suggests that decline in processing speed and reasoning over a relatively short time span may be characteristic of normal aging rather than Alzheimer's disease, though further analyses are needed, particularly with longitudinal change in amyloid.

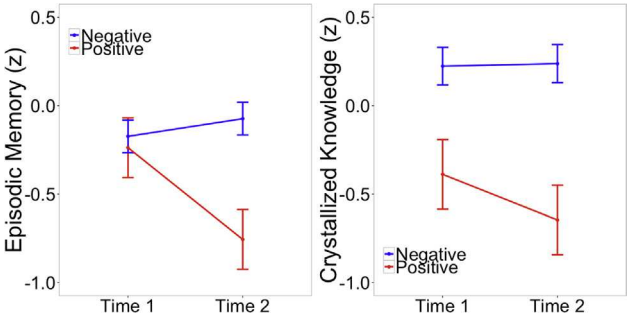

Figure 1. Episodic memory and crystallized knowledge decline over 3.5 years in initially amyloid positive subjects but remain stable in amyloid negative.

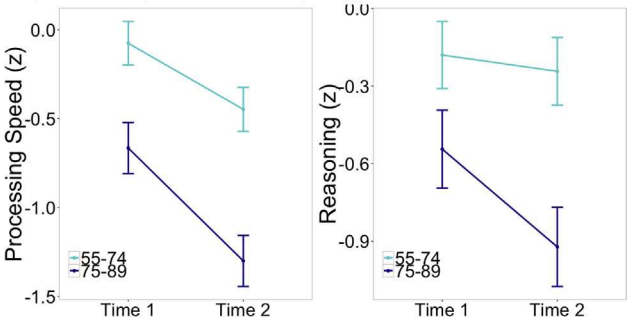

Figure 2. Processing speed and reasoning exhibit greater rates of decline over 3.5 years in 75-89 year olds than 55-74 year olds.

IC-P-135 BASELINE NORMAL APPEARING WHITE MATTER STRUCTURAL INTEGRITY AND CEREBRAL BLOOD FLOW CAN PREDICT WHITE MATTER HYPERINTENSITY EXPANSION OVER TIME: A VOXEL-WISE ANALYSIS

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Background: White matter hyperintensity (WMH) penumbra is the normal appearing white matter (NAWM) surrounding WMH that demonstrates decreased structural integrity and perfusion, and is vulnerable to becoming injured white matter. Previous longitudinal work has shown that baseline cerebral blood flow (CBF), DTI-FA, and FLAIR intensity can predict WMH expansion over time. However, none of the previous studies identified which signal can best predict the growth of WMH and none performed voxel-wise analysis. The aim of this study was to identify the sensitivity of CBF,

DTI and FLAIR signals in predicting WMH development. **Methods:** Fifty-two cognitively intact (CDR = 0) elderly volunteers (mean age 83.5 years old) underwent two scan visits with 3T MRI FLAIR, MPRAGE, PASL and DTI. The mean interscan interval was 16 months. For each individual dataset, baseline and follow-up WMH were aligned and subtracted from each other, creating a binary map containing 0s and 1s for persistent NAWM and new WMH voxels, respectively. We focused on the 5 mm area surrounding WMH where there was significant growth of WMHs. Baseline CBF map. DTI-FA, DTI-MD and FLAIR images were then registered to the binary map. Correlation analysis was performed between the binary map and CBF map, DTI and FLAIR images, individually. The predictive order was determined by comparing the group mean R^2 using paired t-test. **Results:** Increased FLAIR intensity had the strongest correlation with new WMH voxels, followed by increased DTI-MD, decreased DTI-FA and decreased CBF for both periventricular (PV) and deep WMH penumbras ($p<0.001$). Mean R^2, ordered from greatest to smallest associations, are 0.072, 0.014, 0.011, and 0.005 for PV WMHs, and are 0.025, 0.014, 0.004, and 0.001 for deep WMHs. **Conclusions:** Within the immediate WMH environment, baseline indicators of microstructural WM damage are more predictive of future WMH expansion than CBF. For future studies, investigating the contribution of CBF to future microstructural WM degeneration is needed.

IC-P-136 CARDIORESPIRATORY FITNESS IS ASSOCIATED WITH HIPPOCAMPAL VOLUME AND EPISODIC MEMORY IN A POPULATION AT RISK FOR ALZHEIMER'S DISEASE

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Background: Hippocampal volume (HV) and episodic memory (EM) decline with age and may indicate a preclinical stage of Alzheimer's disease (AD). Previous research indicates individuals with a familial or genetic risk for AD experience accelerated rates of hippocampal atrophy and episodic memory decline in older adulthood. Cardiorespiratory fitness (CRF) has been shown to be beneficial for brain health in older adults, however the evidence for a relationship between CRF and both HV and EM is less clear. CRF is a modifiable risk factor that could attenuate anticipated declines in HV and EM in individuals at-risk for developing AD. The objectives of this study were to determine the associations between (1) CRF and HV and (2) CRF and EM in a cohort of cognitively healthy older adults at-risk for AD. **Methods:** Eighty-six enrollees from the Wisconsin Registry for Alzheimer's Prevention (age=63.6±5.9 years, 61.6% female) participated in this study. Participants were classified as at-risk by either possessing the APOE-e4 allele (53.5%), having a parental family history (FH) of AD (91.9%), or were both APOE-e4 and FH positive (45.3%). All participants performed a graded maximal exercise test to volitional exhaustion, underwent a magnetic resonance imaging scan, and completed the Rey Auditory and Verbal Learning Test (RAVLT). Peak oxygen consumption during the exercise test (VO_2peak, ml/kg/min), assessed according to established criteria, was used to determine CRF. Freesurfer software was used to obtain hippocampal volumes from T1 weighted images. Performance on the RAVLT was used to measure episodic memory. Regression analyses, adjusted for covariates were conducted to determine whether CRF is associated with HV and EM for both male and female participants. **Results:** There was a significant positive association between CRF and HV for the female participants ($p = .018$). Additionally, significant positive associations were observed between CRF and both the RAVLT delayed recall score ($p = .026$), and the RAVLT composite memory score ($p = .049$) for the male participants. **Conclusions:** These results suggest that CRF is protective against both HV and EM decline in older adults at-risk for AD, but that the relationships may be gender-specific. Interventions aimed at improving or maintaining CRF in at-risk populations are warranted.

IC-P-137 APPLICATION OF BRAIN ATROPHY LESION INDEX (BALI) TO COMMON CLINICAL MRI SEQUENCES: EVALUATION OF WHOLE BRAIN STRUCTURAL CHANGES IN AGING AND DEMENTIA

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Background: Aging is associated with multiple structural brain changes, which occur heterogeneously in older adults and, combined, can affect general cognitive functioning. The MRI-based Brain Atrophy and Lesion Index (BALI) assesses age-related common brain changes, and has been validated to evaluate whole brain structural health in aging and dementia. Previous BALI research has shown significant sensitivity across both T1 and T2 weighted whole brain images. The present study expands this investigation to the use of BALI on additional routine clinical MRI examinations (e.g., T2-FLAIR and T2*GRE). **Methods:** We evaluated anatomical MRI data from three independent studies: The Alzheimer's Disease Neuroimaging Initiative (n=950; women=47.9%; age=72.7±7.4 yrs) consisted of participants with normal cognition, mild cognitive impairment, and Alzheimer disease; the National Alzheimer's Coordinating Centre (n=829; women=56.0%; age=70.0±12.9 yrs) contained multiple clinical and research protocols of the Alzheimer's Disease Centres on patients with different dementia subtypes; the Tianjin Medical University General Hospital dataset (n=142; women=43.7%; age=74.0±6.6 yrs) involved older outpatients who were diagnosed with no cognitive disorders. Brain images with T1WI, T2WI, T2-FLAIR, and T2*GRE were examined following BALI scheme. **Results:** Atrophic and lesion based changes were detected using each of the four sequences (Figure 1). A greater number of cases with cavernous malformation, patchy or lacunar malacia, meningioma, and normal pressure hydrocephalus were found in the clinical samples than in the research samples ($p<0.05$). Increased sensitivity from T2-FLAIR revealed lesions in the white matter, but missed identifying dilated perivascular spaces in subcortical, deep white matter, basal ganglia and surrounding regions, and cerebral peduncle. Lacunar malacia and dilated perivascular spaces were more clearly differentiated using T2-FLAIR.