cerebral small vessel health, were quantified by MRI. **Results:** After adjusting for age and cardiovascular risk factors, there was a significant negative association between Aβ burden and FMD ($p<0.01$), such that for each 0.1 increase in Aβ burden, FMD decreased by 0.8%. Decreased brachial artery FMD response was found in individuals with elevated Aβ compared with the non-elevated group ($p<0.01$). The optimal cut point of FMD predicting Aβ elevation was 5% (AUC=0.836, $p<0.01$, 95%CI: 0.742 - 0.930), with 81.8% sensitivity and 75.4% specificity. Higher PI was demonstrated in elevated Aβ individuals ($p=0.04$), but was not correlated with Aβ burden. WML were not associated with Aβ. **Conclusions:** Among cognitively normal older adults, poor central and peripheral vascular health is predictive of Aβ burden. FMD, specifically, has potential value as a vascular biomarker for neuropathologic changes associated with Alzheimer's disease.

P3-398 EARLY STAGE METABOLITE DIFFUSION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Background: Alzheimer's disease develops small neuronal alterations: axonal transport deficits and localized cell swelling, from the onset of amyloid plaque deposition and neurofibrillary tangles. It is significantly important to develop non-invasive biomarkers *in vivo* utilizing these early neuronal changes. Diffusion-weighted spectroscopy (DWS), which measures metabolite diffusion using MRI, has been providing useful information about tissue microstructure and function, and is expected to provide specific information about neuronal changes by probing diffusion properties of intra-neuronal specific metabolites. In the present study, we applied DWS to investigate metabolite diffusion of the early stages in an AD mouse model. **Methods:** This study was approved by the institutional IACUC. Twelve male 3xTg-AD transgenic mice (average age 25.6 weeks) and ten wild-type littermate controls (WT) (average age 19.1 weeks) were used. Diffusion-weighted spectra were measured by using DWS in a region (5x2x2 mm^3) containing both hippocampi on a 14-T MRI (Avance III, Bruker BioSpin Corp). Mean diffusivity (MD) of major metabolites (N-acetylaspartate (NAA), Creatine (Cr), Choline (Cho)) and water were estimated from the measured spectra by calculating signal attenuation due to diffusion-weighting. **Results:** MDs of water and metabolites were compared between WT and AD (Fig. 1). Student t-test was performed between WT and AD after outliers were excluded. Only NAA shows significantly higher MD in AD than in WT (38% in average, $P = 0.03$), but the other metabolites and water do not show significant differences in MD between AD and WT (Table 1). This result suggests that early small neuronal changes of AD can be detected by only NAA diffusion because NAA mostly exists in neurons; however, Cho and Cr exist also in glial cells, and water exists intra- and extracellular spaces. Further investigation is needed to clarify the mechanism associating MD change of NAA with neuronal changes, because axonal transport deficits and localized cell swelling have an opposite effect on NAA diffusion. **Conclusions:** Metabolite diffusion of a mouse model of AD was measured using DWS. Increased NAA diffusion demonstrates that DWS will be useful in investigating early neuronal changes in AD because DWS can provide focused information about intra-neuronal properties.

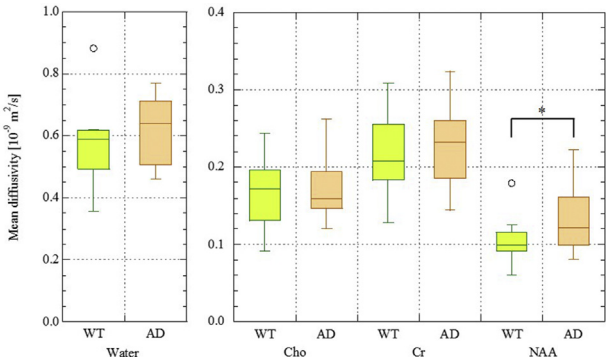

Fig. 1. Tukey boxplots show MD of water and metabolites compared between WT and AD mice. ° = outlier, * = statistically significance ($P < 0.05$).

Table 1
Average MD of water and metabolites, and group comparison between WT and AD mice.

	Water		Cho		Cr		NAA	
	WT	AD	WT	AD	WT	AD	WT	AD
Average MD [10^{-9} m^2/s]	0.536	0.616	0.168	0.173	0.215	0.223	0.095	0.132
P-va lue	0.099		0.831		0.731		0.031	

P3-399 ASSOCIATION BETWEEN CORTICAL THINNING AND TAU PATHOLOGY IN PRECLINICAL AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

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Background: Research has suggested that cortical thinning in key brain regions can be used to identify individuals at high risk for Alzheimer's disease (AD). We previously reported that unimpaired individuals with autosomal dominant Alzheimer's disease have cortical thinning in parietal regions, several years before their anticipated clinical onset (Quiroz et al., 2013). Here we compared brain imaging measurements of cortical thickness, amyloid and tau pathology, and characterized

associations with memory performance in mutation carriers and non-carriers from the Colombian Presenilin-1 (PSEN1) E280A kindred. **Methods:** We used structural MRI, PiB-PET, Flortaucipir (FTP)-PET, and memory testing (CERAD Word List Recall) for the assessment of 12 unimpaired mutation carriers (mean age= 37±3), approximately 7 years before the kindred's median age at mild cognitive impairment (MCI) onset, and 24 age-matched non-carrier family members. Automated brain mapping algorithms were used to compute mean cortical PiB DVRs, entorhinal cortex (EC) and inferior temporal (IT) flortaucipir SUVRs. Cortical thickness was measured in the signature of familial AD (Weston et al., 2016), which included 6 regions: entorhinal cortex, inferior parietal cortex, precuneus, superior parietal cortex, superior frontal cortex, and supra marginal gyrus. Spearman's correlations were used to characterize relationships among these brain imaging and memory measurements. **Results:** Compared to non-carriers, unimpaired *PSEN1* mutation carriers showed cortical thinning in the FAD signature (p=0.001). In the carrier group, cortical thinning in the mean signature summary measure was not associated with amyloid burden, but was associated with EC tau levels (r=-0.75; p-value= 0.02). EC and IT tau were associated with thinning in precuneus, superior frontal cortex, and superior parietal cortex ($p<0.05$). Further, worse memory performance was associated with a lower mean cortical thickness in the familial AD signature (r= 0.73; p-value: 0.005). **Conclusions:** This study provides preliminary information about the limited associations between amyloid burden and cortical thinning in preclinical autosomal dominant AD. Findings suggest that regional tau burden is associated with cortical thinning and memory decline in individuals at virtually certain risk for Alzheimer's disease, more than 5 years prior to symptom onset.

P3-400 A NOVEL METHOD FOR DEFINING INDIVIDUAL METABOLIC NETWORKS DERIVED FROM [18F]FDG PET DATA

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Background: Metabolic brain networks (MBNs), derived from 18F-fluorodeoxyglucose ([18F]FDG) positron emission tomography (PET) inter-subject correlations, can provide information about cerebral energetic architecture in health and disease. In Alzheimer's disease (AD), developing a MBN is usually restrained to group-wise comparisons. In this context, there are no methods available for constructing MBN at the individual level. Here, we developed a novel method to construct individual MBNs (iMBN) and demonstrate their potential to predict abnormalities in cognitively normal (CN) subjects. **Methods:** Regional [18F]FDG-PET data from 22 brain regions were obtained from the ADNI cohort. Groups were composed of Aβ negative CN subjects (Aβ-/CN, n=21), Aβ positive CN subjects (Aβ+/CN, n=20) and AD patients (AD/Aβ+, n=34). Aβ- patients presenting with cognitive decline were removed from our analyses. We adopted Aβ positivity criteria as lower than 1065 pg/ml (Elecsys® β-amyloid (1-42) immunoassay). First we defined a representative MBN (group-wise mean correlation matrix, generated using 100 pseudorandom permutations with 10 random subjects from Aβ-/CN and Aβ+/AD classes). These representative MBNs were then optimized to be more susceptible to wrong-class perturbations by random inclusions. Finally, we estimate the iMBN by adding individual [18F]FDG measures as a perturbation to the group representative MBN. To classify in which representative MBN a determined iMBN belongs we compared Minkowski distances corrected by false discovery rate (FDR). **Results:** Representative MBNs were optimally composed of 10 subjects for Aβ-/CN and 8 subjects Aβ+/AD. By using Minkowski distances, our method differentiated Aβ-/CN and Aβ+/AD iMBNs with 100% accuracy. Applying our model to CN/Aβ+ group we predicted structural and metabolic features significantly altered 6 months later (Figure 1). **Conclusions:** The novel method developed allows the construction of iMBNs, which extends the use of MBNs to the individual level. This method has potential to be used in clinical settings to identify patients at-risk of developing cognitive decline. Also, it is very likely that alterations in metabolic architecture can predict structural and functional abnormalities prior to any cognitive symptom.