The number of CMBs in CMB(+) subjects also correlated significantly with reduced metabolism in the medial temporal lobe ($p<0.05$). Subjects with CMBs were significantly more likely to have deficits on the Clinical Dementia Rating scale (χ 2 p-value = 0.0015). Neither the presence nor number of CMBs was found to be significantly associated with [11 C]PiB SUVR or hippocampal volume. **Conclusions:** In this cohort of very elderly NCs, CMBs are associated with reduced cerebral blood flow, reduced cerebral metabolism, and mild deficits on the CDR scale. Our findings suggest that the small vessel disease associated with CMBs can independently contribute to impaired cognition and functional status, a process likely mediated by chronic hypoperfusion and hypometabolism.

IC-02-06 LONGITUDINAL CHANGES IN BRAIN MRI AND NEUROPSYCHOLOGICAL MEASURES IN ASYMPTOMATIC AND SYMPTOMATIC FAMILIAL FRONTOTEMPORAL LOBAR DEGENERATION WITH MUTATIONS IN MAPT

David Thomas Jones[1], Stephen Weigand[1], Scott Przybelski[1], Jonathan Graff-Radford[1], Senjem Mathew[2], Jeffrey Gunter[3], Jennifer Louise Whitwell[1], David S. Knopman[1], Neill R. Graff-Radford[4], Kieth Josephs[2], Zbigniew Wszolek[4], Prashanthi Vemuri[5], Julie A. Fields[6], Mary M. Machulda[1], Tanis J. Ferman[7], John Lucas[2], Val J. Lowe[3], Ralitza Gavrilova[2], Karen Kuntz[1], Mariely DeJesus Hernandez[2], Matthew Baker[8], Rosa Rademakers[8], Ronald Carl Petersen[3], Kejal Kantarci[1], Clifford Jack, Jr,[1], Bradley F. Boeve[1], *[1]Mayo Clinic, Rochester, Minnesota, United States; [2]Mayo Clinic, Rochester, Minnesota, United States; [3]Mayo Clinic Rochester, Rochester, Minnesota, United States; [4]Mayo Clinic, Jacksonville, Jacksonville, Florida, United States; [5]Mayo Clinic, Rochester, Minnesota, United States; [6]Mayo Clinic College of Medicine, Rochester, Minnesota, United States; [7]Mayo Clinic, Jacksonville, Florida, United States; [8]Mayo Clinic, Jacksonville, Florida, United States. Contact e-mail: Jones.David@mayo.edu*

Background: As disease modifying therapies for familial frontotemporal lobar degenerations (f-FTLD) move into both the symptomatic and asymptomatic patient populations, it will be necessary to develop robust biomarkers that are sensitive to disease progression in both of these populations. In this study we investigated the longitudinal change in brain MRI and neuropsychological measures in asymptomatic and symptomatic carriers of microtubule associated protein tau (MAPT) mutations. **Methods:** All available neuroimaging and neuropsychological data on MAPT mutation carriers (symptomatic = +m CDR≥0.5 and asymptomatic = +m CDR=0) evaluated at Mayo Clinic were analyzed; non-mutation carrier family members (-m CDR=0) were used as controls (Table 1). Longitudinal structural brain MRI scans for each subject were processed using the Symmetric Diffeomorphic Image Normalization method for normalization of serial scans to obtain Tensor Based Morphometry (TBM-SyN) maps. We also compared baseline and longitudinal data on the Controlled Oral Word Association Test (COWAT), Trailmaking Test B (TMT B), Boston Naming Test (BNT) and Category Fluency (Cat Fl). We used linear mixed models with random slopes and intercepts to analyze longitudinal clinical and imaging data with years from baseline as the time scale. **Results:** The +m CDR≥0.5 subjects had non-zero rates of decline in annual % change in all regions analyzed with TBM-SyN. These rates were significantly different from both +m CDR=0 and -m CDR=0 family members (Figure 1a). The +m CDR=0 subjects had a non-zero rate of decline in the temporal ROI ($p = 0.009$) and trends in the composite frontotemporal region ($p = 0.08$) and the ventricular volume ($p = 0.08$). There was no significant difference when comparing the rates between +m CDR=0 and -m CDR=0. A similar pattern was also observed for all neuropsychological measures without any evidence for non-zero rates of change in +m CDR=0 (Figure 1b). **Conclusions:** Regional brain MRI volumes and neuropsychological measures longitudinally decline in +m CDR≥0.5 subjects and may be useful as biomarkers in this phase of the disease. TBM-SyN analysis of +m CDR=0 subjects identified a non-zero rate of temporal lobe change in this relatively young group, which may indicate that brain MRI is a suitable biomarker in the asymptomatic phase of the disease.

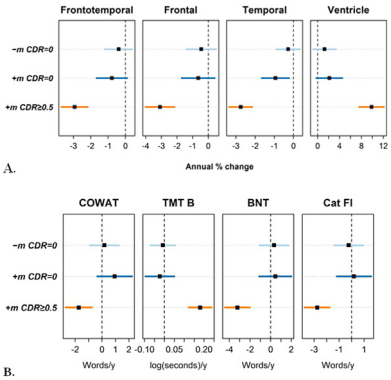

Figure 1. Mean and 95% confidence intervals of annual change in a) frontotemporal regions of interest and ventricular volume and b) neuropsychological measures per group.

Table 1Demographics table of asymptomatic and symptomatic familial FTLD subjects with mutations of MAPT.

	Non-carrier MAPT family members n = 11	Asymptomatic MAPT mutation carriers n = 9	Symptomatic MAPT carriers n = 21
No. of males (%)	4 (36%)	2 (22%)	12 (57%)
Age (y)	39 (9)	35.0 (6.9)	50 (12)
Education (y)	15 (2)	15 (2)	14 (2)
No. of ε4 carriers (%)	3 (27%)	4 (44%)	4 (19%)
Scan interval (y)	4.2 (1.7)	5.2 (2.1)	5.3 (4.0)

Mean (SD) for continuous variables
Count (%) for categorical variable

SATURDAY, JULY 12, 2014
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC-03
NEW DEVELOPMENTS

IC-03-01 IMAGING OF TAU PATHOLOGY IN PATIENTS WITH NON-ALZHEIMER'S DISEASE TAUOPATHIES BY [11C]PBB3-PET

Hitoshi Shinotoh[1], Hitoshi Shimada[2], Shigeki Hirano[3], Shogo Furukawa[3], Yoko Eguchi[4], Keisuke Takahata[4], Yasuyuki Kimura[2], Harumasa Takano[5], Makiko Yamada[4], Satoshi Kuwabara[6], Hiroshi Ito[4], Tetsuya Suhara[4], Makoto Higuchi[4], *[1]National Institute of Radiological Sciences, Chiba, Japan; [2]National Institute of Radiological Sciences, Chiba-shi, Japan; [3]Chiba University School of Medicine, Chiba, Japan; [4]National Institute of Radiological Sciences, Chiba, Japan; [5]National Institute of Radiological Sciences, Chiba, Japan; [6]Chiba University, Chiba, Japan. Contact e-mail: hitoshi.shinoto@nifty.com*

Background: [11 C]PBB3 has been recently developed as a tau imaging PET ligand.The preclinical studies showed high affinity and selectivity of this ligand for tau deposits. Our initial PET study with [11 C]PBB3 demonstrated high [11 C]PBB3 binding in the cerebral cortex including medial temporal lobes in patients with Alzheimer's disease (AD) compared with age-matched controls. The aim of this study is to test the hypothesis that [11 C]PBB3 PET is a sensitive in vivo imaging method for detecting tau lesions in non-AD tauopathies such as progressive supranuclar palsy (PSP) and corticobasal degeneration (CBD). **Methods:** Ten patients with PSP, five patients with corticobasal syndrome (CBS), and 18 age-matched healthy controls (HCs) participated in this study. Sequential PET scans were performed for 70 min following intravenous injection of [11 C]PBB3. PET images were anatomically normalized to the Montreal Neurological Institute space using T1 weighted MRI, and standardized uptake value ratio (SUVR) was calculated using the cerebellar cortex as reference region. One-way ANOVA test was performed among PSP, CBS patients, and HCs using statistical parametric mapping software (SPM 8). Statistical threshold was set to 0.01 with extent threshold of 50 voxels without correction for multiple comparisons. Cerebral beta-amyloid depositions were also estimated using