and whole grey matter volumes were correlated with tau but not Aβ deposits, and frontal dysfunctions were associated with frontal tau accumulation. Additionally, hypometabolic areas detected by [^{18}F] FDG-PET spread in transition from oHC to AD in a pattern following expansion of tau pathologies. **Conclusions:** The present study indicated that Aβ deposition promotes tau propagation, and also supports Aβ-independent and -dependent pathways of tau pathogenesis that can be pursued by PET, in close relation to cognitions of healthy and diseased elderly individuals.

IC-01-03 CLASSIFYING TAU PET POSITIVITY WITH [18F]-AV-1451 IN PRECLINICAL ALZHEIMER'S DISEASE

Shruti Mishra[1], Brian Andrew Gordon[2,3], Karl A. Friedrichsen[1], Yi Su[2,3,4], Jon Christensen[2], Patricia Aldea[5], Nigel J. Cairns[1,3], John C. Morris[3,4], Beau Ances[1,3,4], Tammie LS. Benzinger[3,4], *[1]Washington University School of Medicine, St. Louis, MO, USA; [2]Washington University in St. Louis School of Medicine, St. Louis, MO, USA; [3]Knight Alzheimer's Disease Research Center, St. Louis, MO, USA; [4]Washington University in St. Louis, St. Louis, MO, USA; [5]Washington University in St. Louis, St. Louis, MO, USA. Contact e-mail: shruti.mishra@wustl.edu*

Background: [18F]-AV-1451 is a PET tracer used to evaluation of neurofibrillary tau pathology *in vivo*. It is still unknown what spatial pattern best characterizes an Alzheimer's signature of tau PET uptake in the brain. The objective of this study was to utilize a data-driven method to derive a summary measure of PET tau deposition as measured by [18F]-AV-1451 for staging preclinical AD and to derive a cut-off for tau positivity. **Methods:** Participants were drawn from ongoing studies at Washington University in St. Louis. 51 cognitively normal (CN) subjects (with Clinical Dementia Rating (CDR) =0) and 12 cognitively impaired (CDR > 0, 8 CDR 0.5, 3 CDR=1, and 1 CDR=2) participants underwent PET imaging with AV-1451. Standardized uptake value ratios (SUVRs) normalized to the whole cerebellum and partial volumes corrected were calculated for 36 regions of interest (ROIs) generated using FreeSurfer. A bootstrapped sparse k-means analysis was done on ROI SUVRs from CN participants to cluster them into two groups (k=2). Unlike a normal k-means, sparse k-means cluster utilizes regional weights to determine the ROIs that maximally influenced this clustering. 45 CN and 10 CDR > 0 underwent a comprehensive neuropsychological battery and 50 CN and 12 CDR >0 underwent beta-amyloid PET imaging and were categorized as beta-amyloid positive or negative. **Results:** The highest-weighted ROIs (Figure 1) were: entorhinal cortex, amygdala, lateral occipital cortex, and inferior temporal cortex. The unweighted mean SUVR across these four ROIs correlates with episodic memory, attentional control, and visuospatial memory in both CNs and CDR>0 participants (Figure 2). Amyloid PET positive individuals have significantly higher mean SUVRs across these ROIs (Figure 3). The midpoint between tau negative and positive group means was 1.23. Using this cut-off, tau positive CN participants had significantly higher amyloid PET burden (Figure 4). **Conclusions:** The unweighted mean SUVR of the entorhinal cortex, amygdala, lateral occipital cortex, and inferior temporal cortex ROIs provides a summary measure for

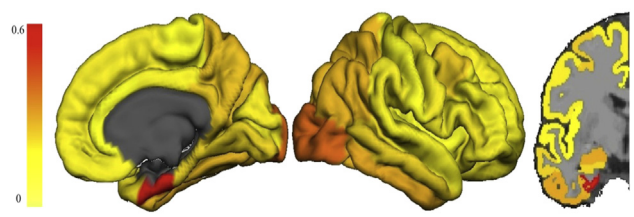

Figure 1. Mean weight for ROIs across 500 simulations of sparse k-means algorithm when clustering CN participants into k=2 groups

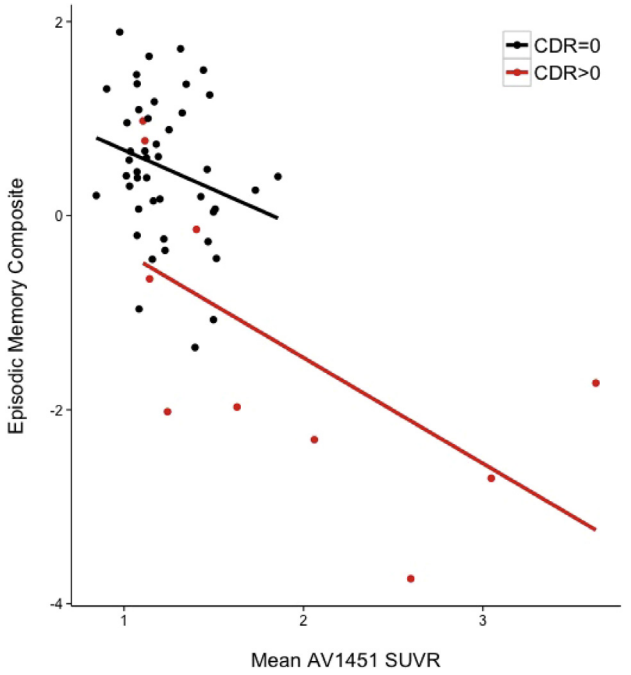

Figure 2a. Relationship between mean AV-1451 SUVR and episodic memory

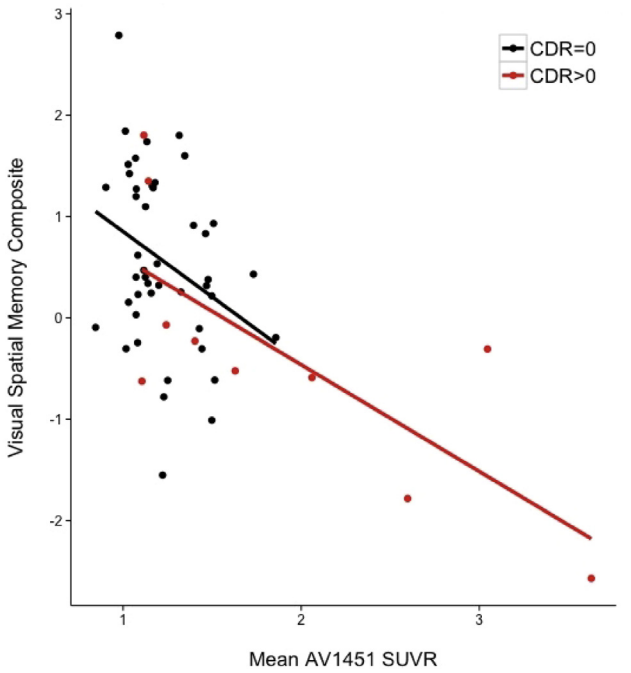

Figure 2b. Relationship between mean AV-1451 SUVR and visual spatial memory

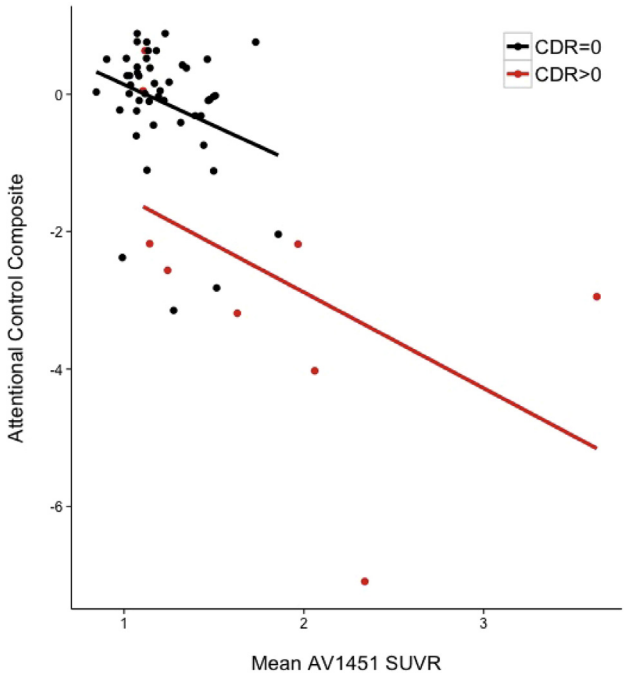

Figure 2c. Relationship between mean AV-1451 SUVR and attentional control

PET Tau deposition that is sensitive to early amyloid PET deposition and early cognitive change. In these regions a cut-off SUVR of 1.23 marks the transition between PET tau positive and negative in CNs.

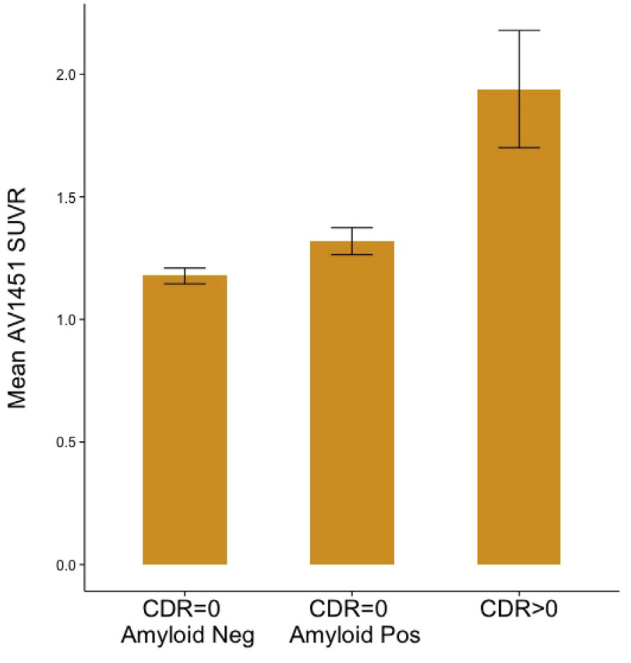

Figure 3. Mean AV1451 SUVR in PET Amyloid Positive vs. Negative Participants

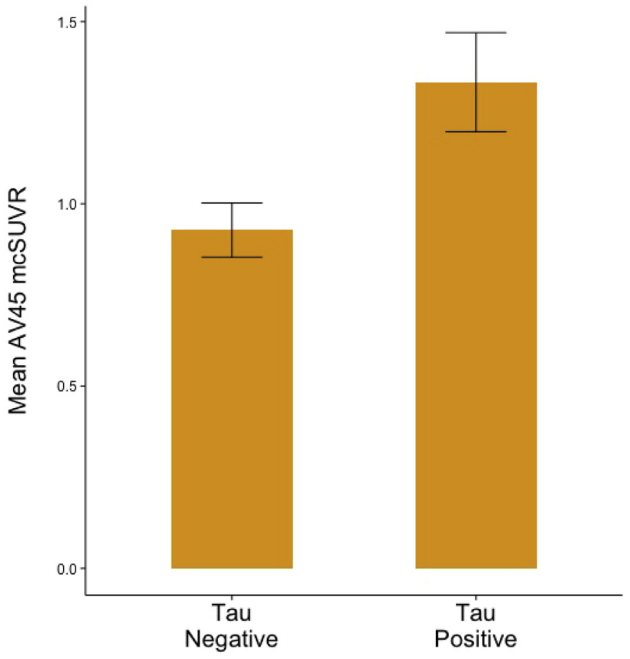

Figure 4. Difference in AV45 mcSUVR in Tau Positive vs. Tau Negative CN Participants

IC-01-04

^{18}F-AV1451 PET DETECTS TAU PATHOLOGY IN *MAPT* MUTATION CARRIERS AND CORRELATES STRONGLY WITH IMMUNOHISTOCHEMISTRY OF TAU AGGREGATES

Ruben Smith[1], Andreas Puschmann[2], Tomas Olsson[2], Elisabet Englund[2], Oskar Hansson[3], *[1]Skåne University Hospital, Department of Neurology, Lund, Sweden; [2]Skåne University Hospital, Lund, Sweden; [3]Clinical Memory Research Unit, Lund University, Lund, Sweden.*
Contact e-mail: ruben.smith@med.lu.se

Background: The Tau PET ligand ^{18}F-AV1451 has been shown to reliably detect paired helical filaments of tau in Alzheimer's disease, but it is not yet known whether it binds to the tau aggregates present in patients with mutations in the gene (*MAPT*) coding for the tau protein. Further, no study has yet compared the cerebral retention of ^{18}F -AV1451 with the tau aggregates revealed using neuropathology. **Methods:** Three patients from a Swedish family carrying the R406W mutation of *MAPT* were assessed with cognitive tests and subjects underwent ^{18}F-AV1451 and ^{18}F-Flutemetamol PET scans. Further one of younger subjects also underwent an ^{18}F-FDG PET scan. The oldest subject died two weeks after the scan and the brain was processed for neuropathology. Tau immunohistochemistry was performed on brain sections from affected and unaffected brain regions. **Results:** Two mutation carriers, aged 56 and 60 years, had disease durations of 5-10 years and still only exhibited mild-moderate episodic memory impairment and no clear behavioural deficits. The MRI revealed only slight cortical atrophy and ^{18}F-AV1451 PET imaging showed uptake in the hippocampus and the temporal lobes, especially in the inferior and anterior parts (Fig 1A, B). The uptake of ^{18}F -AV1451 correlated well with hypometabolism revealed with FGD PET in one of the subjects. The third case, 76 years, had a disease duration of >20 years and exhibited clear cognitive impairment, behavioural disturbances, mutism and dysphagia. The CT