ELSEVIER

Alzheimer's & Dementia 12 (Suppl 7S) (2016)

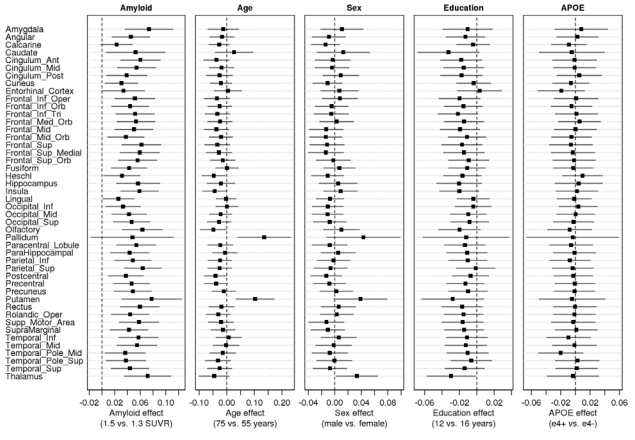
Alzheimer's & Dementia

SATURDAY, JULY 23, 2016
ALZHEIMER'S IMAGING CONSORTIUM (AIC)
IC-01
TAU IMAGING

IC-01-01 PREDICTORS OF REGIONAL TAU-PET UPTAKE: MAYO CLINIC STUDY OF AGING

Prashanthi Vemuri, Val J. Lowe, Heather J. Wiste, Stephen D. Weigand, Matthew L. Senjem, David S. Knopman, Ronald C. Petersen, Clifford R. Jack Jr, *Mayo Clinic, Rochester, MN, USA.*
Contact e-mail: Vemuri.Prashanthi@mayo.edu

Background: To investigate the effects of age, sex, APOE4, education, and amyloid deposition (via ^{11}C PIB-PET) on the degree of regional tau deposition (via AV1451) in cognitively normal elderly. **Methods:** We identified 168 cognitively normal participants aged 52-94 years in the population-based Mayo Clinic Study of Aging who had undergone APOE4 genotyping, with Tau-PET, and PIB-PET scans available. The subjects identified had a median age of 69, 54% male, 29% APOE4 positive, median education of 16, and median PIB SUVR of 1.34. Regional uptake of Tau-PET was assessed in 46 atlas regions by summarizing the median uptake in each region scaled to the median uptake in the cerebellar crus (SUVR). For each region, we fit a linear regression model with Tau-PET SUVR as the response variable and the following potential predictor variables: global amyloid PET, age, sex, education, and APOE4 genotype. In a preliminary regional correlation analyses of PIB with Tau-PET SUVRs, we found that correlations were driven mainly by global amyloid levels. Therefore, we used global and not regional PIB SUVRs in the models presented here. **Results:** The results are shown in Figure 1 in which each row represents an independent regional model fit and summarizes the estimated mean (95% confidence interval) difference in tau deposition for each covariate: amyloid PET, age, sex, education, and APOE4. Although effect sizes varied across regions, we found strong evidence that higher levels of amyloid were associated with increased levels of tau after accounting for age, sex, education, and APOE ($p<0.01$). Except in the pallidum and putamen ($p<0.01$), age was not independently associated with increased levels of tau. We did not see independent effects of sex, education, or APOE4 ($p>0.01$) in any of the regions. **Conclusions:** Global amyloid burden is predictive of tau deposition in a large number of brain regions after accounting for age, sex, education, and APOE4. Independent effects of age were localized to the pallidum and the putamen where non-specific Tau-PET binding has been observed.



IC-01-02 THE ASSOCIATION BETWEEN AB AND TAU ACCUMULATIONS AND ITS INFLUENCE ON CLINICAL FEATURES IN AGING AND ALZHEIMER'S DISEASE SPECTRUM BRAINS: [^{11}C]PBB3 PET STUDY

Hitoshi Shimada[1], Tetsuya Suhara[1], Hitoshi Shinotoh[1,2], Hironobu Endo[1,3], Fumitoshi Niwa[1,4], Soichiro Kitamura[1], Shigeki Hirano[1,5], Yasuyuki Kimura[1], Makiko Yamada[1], Naruhiko Sahara[1], Ming-Rong Zhang[1], Satoshi Kuwabara[5], Makoto Higuchi[1], *[1]National Institute of Radiological Sciences, Chiba, Japan; [2]Neurology Chiba Clinic, Chiba, Japan; [3]Kobe University Graduate School of Medicine, Kobe, Japan; [4]Kyoto Prefectural University of Medicine, Kyoto, Japan; [5]Chiba University, Chiba, Japan. Contact e-mail: shimada@nirs.go.jp*

Background: Senile plaques and fibrillary tau inclusions are neuropathological hallmarks of Alzheimer's disease (AD). Recent neuroimaging and neuropathological studies have revealed that proteinopathies represented by amyloid-β (Aβ) and tau accumulations may occur independently and concurrently as exemplified by primary age-related tauopathy and AD, respectively. To elucidate interactions between Aβ and tau accumulations and its influence on clinical features, we performed a cross-sectional positron emission tomography (PET) study in cognitively healthy and impaired individuals. **Methods:** Participants were 20 patients with AD, 17 patients with mild cognitive impairment (MCI), 24 age-matched healthy controls (oHCs) and 10 young HCs. Parametric [^{11}C] PBB3-, [^{11}C]PiB- and [^{18}F]FDG-PET images were genrated for estimating regional Aβ, tau and brain glucose metabolism, respectively, by voxel-based calculation of standardized uptake value ratio (SUVR) to the cerebellum at 30-50 minutes, 50-70 minutes and 30-60 minutes after radiotracer injections, respectively. We also performed three-dimensional T1-weighted MRI and estimated whole grey matter volume for each subject. **Results:** All AD patients, 10 of 17 MCI patients, and 3 of 24 oHCs were classified as PiB(+), and others were classified as PiB(-) by visual assessment of [^{11}C]PiB SUVR images. PBB3(+) tau deposits were observed in medial temporal regions including the hippocampus of a subset of PiB(-) oHCs, and this was associated with subclinical memory declines. Self-expansion of tau deposition to restricted areas without Aβ was also demonstrated in these and PiB(-) MCI subjects. PBB3(+) tau spread to Aβ-rich areas in PiB(+) oHCs and MCI subjects, and was further expanded to widespread neocortical regions in AD patients. In PiB(+) MCI and AD groups, dementia scales

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

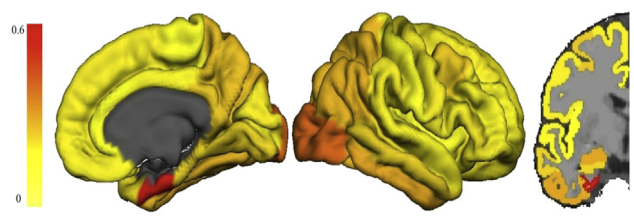


Figure 1. Mean weight for ROIs across 500 simulations of sparse k-means algorithm when clustering CN participants into k=2 groups

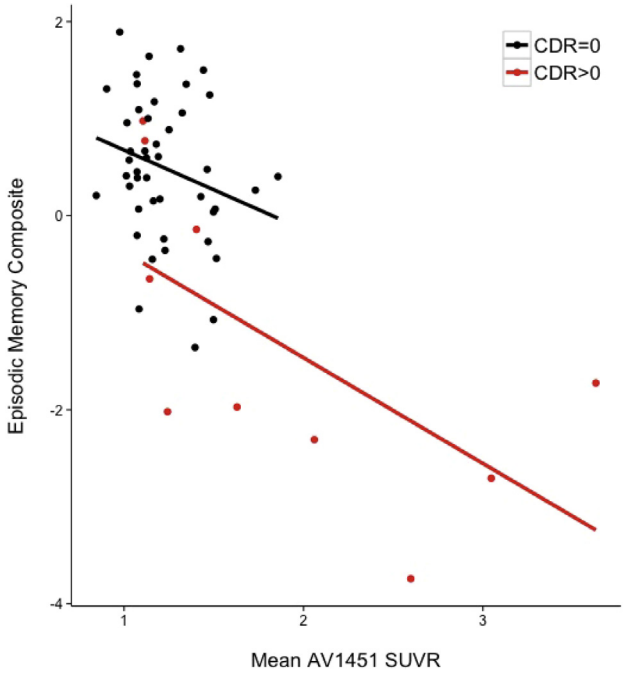


Figure 2a. Relationship between mean AV-1451 SUVR and episodic memory

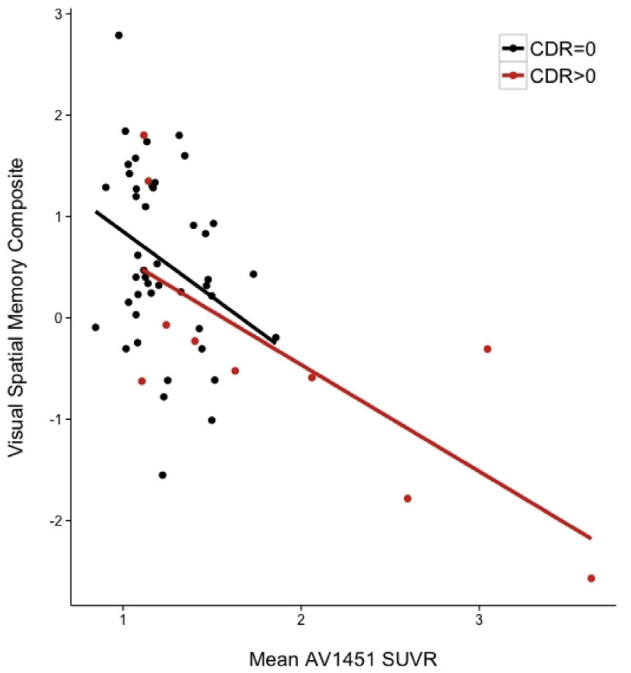


Figure 2b. Relationship between mean AV-1451 SUVR and visual spatial memory