performance. Amyloid load in the AT network correlated with worse BNT (r=-0.13, p=0.001) performance, but even more so with worse DR (r=-0.22, p<0.001). Moreover, after controlling for global cortical amyloid burden, none of the regional associations remained significant. By contrast, globally controlled glucose hypometabolism correlated with cognitive dysfunction in a network-specific manner, correlating with DR in the PM (p<0.001) and with BNT in the AT (p<0.001), but not vice versa (both p>0.05). **Conclusions:** In contrast to FDG-PET measured hypometabolism, network-specific amyloid load does not specifically associate with dysfunction in the respective cognitive domain, corroborating recent evidence of negligible local neurotoxicity of accumulated amyloid-β protein.

P2-371 CEREBRAL MICROBLEEDS ARE ASSOCIATED WITH TEMPORAL LOBE HYPOMETABOLISM IN ALZHEIMER'S DISEASE

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Background: Although cerebral microbleeds (CMBs) are significantly more prevalent in Alzheimer's disease (AD), their ultimate role in AD pathogenesis remains unclear. In this study, we aimed to investigate the relationship between lobar burden of CMBs and both Ab deposition and hypometabolism in AD. We hypothesized that the burden of CMB in each anatomical region is related to neurodegeneration rather than local Ab deposition. **Methods:** Cases with clinical diagnoses of early AD (n=11), Mild Cognitive Impairment (MCI) (n=10), and healthy control (HC)(n=8) underwent ^{11}C- Pittsburg compound B- (PiB) and ^{18}F-fluorodeoxyglucose (FDG)-PET followed by high resolution 3T Susceptibility Weighted Imaging (SWI). Dynamic 90 minute PiB- and 30 minute FDG-PET were performed and images were assessed quantitatively using Standard Uptake Value ratio (SUVR) using cerebellum as reference. The SWI images were assessed by expert neuroradiologists using Microbleed Anatomical Rating Scale (MARS). **Results:** CMBs were present in 80% of AD, 33% of MCI, and 12.5% of HC. There was no significant difference in the age and vascular risk factors of participants in the three groups. Total cortical PiB uptake was significantly higher in cases with CMB (p-value<0.0001) but there was no association between the lobar PiB uptake and presence of CMB. However, while total cortical FDG SUVRs were not different between cases with or without CMB, lobar FDG uptake was significantly lower in temporal lobes that had CMB (p-value:0.009). Parietal lobe uptake was also trending toward significance (p-value:0.09). **Conclusions:** In concordance with previous studies, our data confirmed that presence of CMB is associated with higher total but not lobar PiB uptake. The novel finding of our study is the observed relationship between CMB and hypometabolism in temporal lobes. This suggests that presence of CMB might be associated with neurodegeneration. Further studies are needed to elucidate the causal relationship between hypometabolism and formation of CMBs.

P2-372 UTILITY OF PERFUSION PET MODELS AS MEASURES OF NEURODEGENERATION IN AN AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE POPULATION: REPORT FROM THE DIAN STUDY

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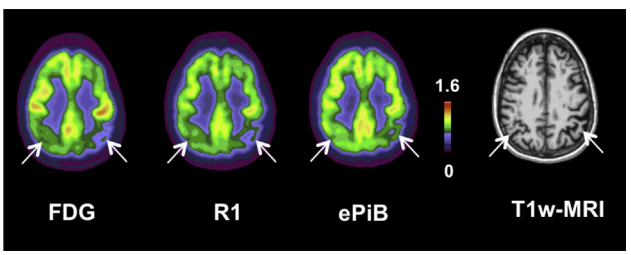
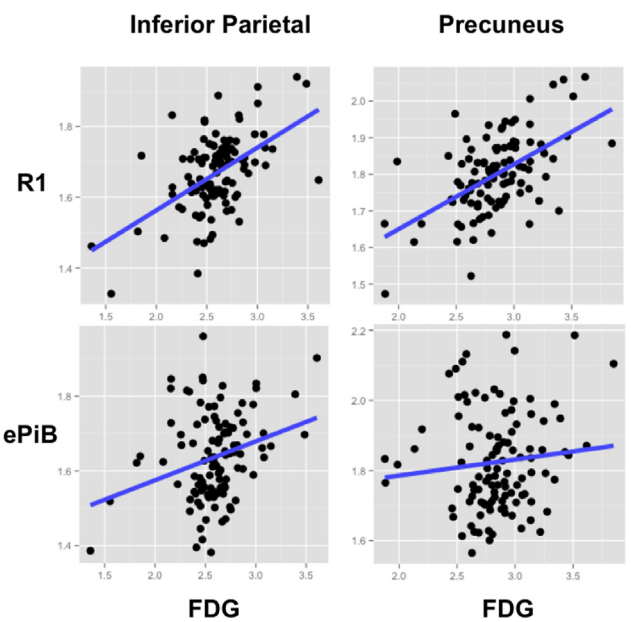
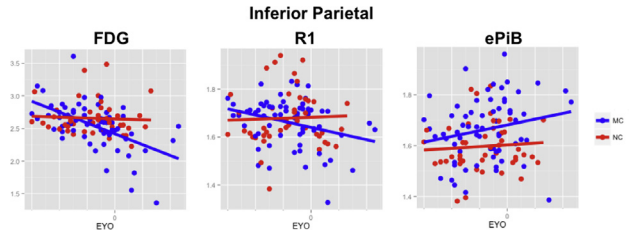
Background: 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is commonly used to estimate neurodegeneration in Alzheimer's disease (AD). Here, we evaluate the utility of surrogate perfusion measurements obtained from models of perfusion using 11C-Pittsburgh compound B (PiB) to estimate neurodegeneration and to potentially decrease participant burden. **Methods:** FDG and full dynamic PiB imaging were obtained from 110 participants from the Dominantly Inherited Alzheimer Network (DIAN), including 45 non-carriers (NC, 38.2±10.1 years) and 65 mutation-carriers (MC, 39.8±12.0 years). Two surrogate perfusion measurements were obtained from the PiB scan. The first measurement







was SUVRs of early frames of PiB (ePiB, 1 to 9min) normalized to the brainstem. The second measurement was the relative tracer influx rate (R1) obtained from kinetic modeling of PiB data, using brainstem as the reference region. Partial volume correction was applied to take into account the atrophic process. Regional cross-sectional analyses were performed to evaluate the correlation between images and estimate the relationship of the imaging biomarkers with estimated time to disease progression based on family history. Nine regions were evaluated, including the precuneus and the inferior parietal cortex, known to be greatly affected by hypometabolism. **Results:** Metabolism and perfusion images were spatially highly correlated, showing decreased signal in similar regions (Figure 1). Across all participants, the R1 values were better correlated to FDG than ePiB was (e.g. r=0.52, p<0.0001 and r=0.54, p<0.0001 for R1 vs. FDG in the inferior parietal and the precuneus, respectively, and r=0.28, p<0.005 and r=0.10, n.s. for ePiB vs. FDG in the inferior parietal and the precuneus, respectively, Figure 2). Regional R1 values and FDG significantly decreased in the MC vs. NC with estimated-year-to-onset (p<0.05 for the inferior parietal) while ePiB did not decrease but increased instead (p<0.05 for the inferior parietal) (Figure 3). Within the MC, R1 values and FDG significantly decreased with dementia severity (p<0.05 for the inferior parietal) while ePiB had no relationship with dementia for any regions. **Conclusions:** Neurodegeneration estimated by R1 may provide a new measure of brain function without added radioactivity. EPiB does not provide good neurodegeneration estimates as it may be contaminated with β-Amyloid deposition.

P2-373 AV1451-PET CORTICAL UPTAKE AND REGIONAL DISTRIBUTION PREDICT LONGITUDINAL ATROPHY IN ALZHEIMER'S DISEASE

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Background: We aimed to assess whether β-amyloid (PIB) and tau (AV1451) PET predict longitudinal atrophy in patients with AD. **Methods:** A group of 10 patients fulfilling NIA-AA criteria for AD dementia likely due to AD were included (age = 63 ± 9, MMSE = 24 ± 4 at baseline). All patients underwent i) a baseline visit with structural MRI and PET imaging with both AV1451 and PIB, ii) a follow-up structural MRI (time between MRIs = 1.06 ± 0.15 years). Structural images were preprocessed using SPM12's longitudinal registration pipeline to obtain voxelwise maps of atrophy showing areas of local contractions and expansions (i.e. Jacobians, see figure 1A). Relationships between baseline PET data (Standardized Uptake Value Ratio (SUVR) images normalized to cerebellar gray matter) and subsequent atrophy were assessed in two complementary ways. First, a global cortical value was extracted for each patient and each modality (figure 1B) and correlations were computed at the group level. Second, we computed voxelwise correlations at the individual patient level to evaluate the similarity between baseline maps of PET uptake and the subsequent atrophy map (figure 1C). **Results:** Using global cortical measures (figure 2A), a significant association was observed between steeper cortical atrophy (lower Jacobians) and higher baseline AV1451 cortical SUVR (rho = -0.76, p = 0.02) but not PIB-SUVR (rho = 0.13, p = 0.73), see Fig 2a. Similarly, voxelwise correlation analyses revealed that maps of atrophy resembled baseline AV1451-PET images (median rho = -0.57), i.e. voxels of higher baseline AV1451-uptake showed a steeper rate of atrophy. Correlation between PIB and atrophy maps were minimal (median rho = -0.14) and significantly different from the correlations with AV1451 (Wilcoxon signed-rank test: p=0.004, Figure 2B). **Conclusions:** These results support the hypothesis that neurodegeneration is more closely related to tau than to β-amyloid pathology, and further suggests that tau pathology precedes and drives neurodegeneration locally. Our results further suggest a potential prognostic role for AV1451 in predicting individual patient longitudinal trajectories. From a clinical perspective, our results suggest that AV1451-PET could have a major clinical utility to predict short-term outcomes in patients.

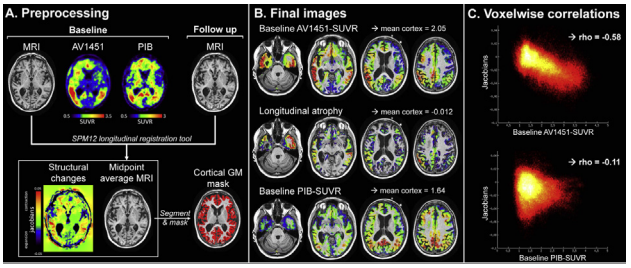

Fig 1. Study design, image preprocessing, and analyses (All images & values are from a representative patient with close to median values)

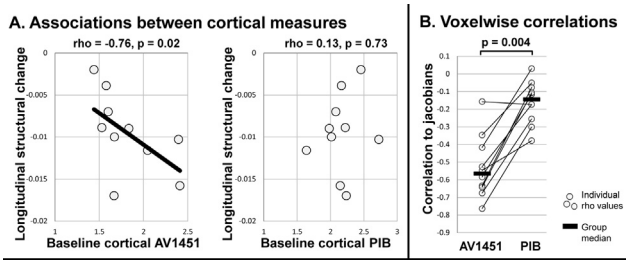

Fig 2. Results of the correlation analyses

P2-374 TAU DISTRIBUTION IN PRECLINICAL ALZHEIMER'S DISEASE: FINDINGS FROM THE KNIGHT ALZHEIMER'S DISEASE RESEARCH CENTER

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