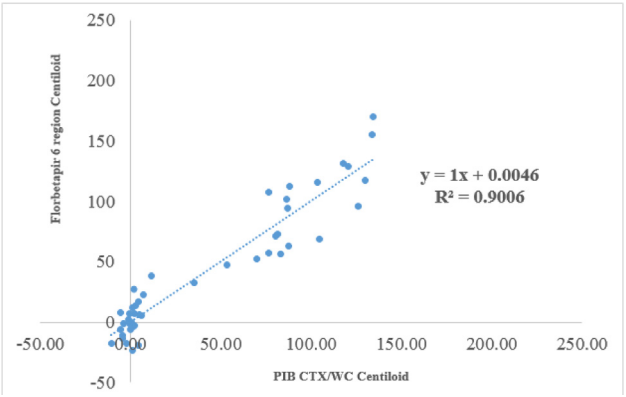

Figure 1b. Centiloids for 46 subjects obtained by linear regression through Figure 1a.

pipeline and determine average PiB SUVr anchor points for stereotypical YCN (n=34) and AD (n=45) subjects using data from the Global Alzheimer's Association Interactive Network (GAAIN). The second step was to employ linear regression to convert florbetapir and PiB SUVr to the Centiloid scale. **Results:** Replicate analysis of GAAIN PiB data resulted in mean SUVr for YCN (n=34) of 1.004±0.048 and AD (n=45) of 2.067±0.204 (R^2 0.997, slope 0.996, intercept -0.002). Our independent study showed that SUVr values (n=46) for florbetapir and PiB were correlated (R^2 = 0.900). The regression equating florbetapir SUVr by the Joshi et al method to PiB SUVr by the Klunk et al method was y = 0.514x + 0.451 and appeared to support a linear relationship between the two tracers (Figure 1). The average YCN SUVr for florbetapir (0.98±0.07) and PiB (1.01±0.03), were converted to 1.51±12.06 and 0.32±2.61 Centiloids, respectively. 74 YCN florbetapir scans from a previous study (Clark et al, 2011), with average SUVr of 0.96±0.04 were converted to Centiloids using the same regression equations yielding an average of -1.60±7.59 Centiloids. Applied to the same study, a threshold of approximately 22 Centiloids, 3 SD above the young controls, was optimal for distinguishing cases with neuropathologically verified no/sparse vs moderate to frequent plaques. **Conclusions:** These findings provide for conversion of florbetapir SUVr to Centiloids, potentially allowing improved tracer independent amyloid quantitation.

IC-P-023 DIFFERENTIAL ASSOCIATION OF BLOOD INSULIN AND HBA1C WITH CEREBRAL AMYLOID DEPOSITION AND REGIONAL GLUCOSE METABOLISM IN MIDDLE- AND OLD-AGED ADULTS

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Background: Preclinical studies indicated that insulin may activate beta-amyloid protein (Aβ) clearance through multiple pathways. Recently, a couple of studies have evaluated whether blood insulin or insulin resistance affect brain Aβ deposition in living human, the results were controversial. We aimed to investigate the associations of blood insulin and hemoglobin A1c (HbA1c) with cerebral amyloid burden and regional cerebral glucose metabolism (rCMglu) in cognitively normal middle- and old-aged adults. **Methods:** One hundred and seventy-four cognitively normal middle- and old-aged adults (mean age = 68.9). Higher levels of blood insulin and HOMA-IR related to lower global PiB retention even after controlling age, gender, APOE4 status, and body mass index (BMI). **Results:** The relationships was much stronger in old-aged participants (age above 65 years) than in mid-aged ones. In addition, both blood insulin level and HOMA-IR were positively associated with rCMglu in the angular gyrus, hippocampus, and parahippocampal gyrus. In contrast, HbA1c and fasting blood glucose had no association with global PiB retention, but both were negatively associated with rCMglu in all the ROIs after controlling age, gender, APOE4 status, and BMI. **Conclusions:** Our results indicate that blood insulin itself may contribute to lowering cerebral Aβ deposition and maintaining brain function in cognitively normal middle- and old-aged adults, old-aged in particular, while higher blood glucose level may have negative influence on brain function through non-amyloid mechanism.

IC-P-024 PIB PET CENTILOID QUANTIFICATION USING CAPAIBL

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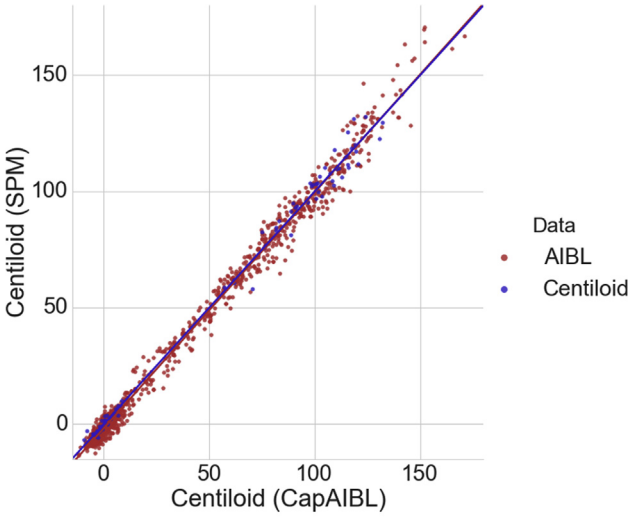
Background: The wide range of Amyloid PET tracers and analysis techniques used in clinical studies can lead to large variability in cut-off values and quantitative assessment of Amyloid load. The Centiloid scale was developed to normalise neocortical retention measured using different tracers and analysis methods. In this study, we evaluate using the Centiloid scale with the PET-only quantification method CapAIBL (capaibl-milxcloud.csiro.au). **Methods:** The 34 YC and 45 AD PiB PET calibration scans from the Centiloid level-1 study were quantified using CapAIBL, using the Centiloid template and reference regions. Additionally, 991 PiB PET scans (639 HC, 161 MCI, 166 AD and 25 others) from the AIBL study were processed using CapAIBL, and compared to the Centiloid values computed using the recommended SPM pipeline. **Results:** Using the calibration scans, the mean whole cerebellum (WC) SUVR values obtained using CapAIBL were within 2% of the published values, (AD:-0.88%, YC:-1.76%). The regression slope (0.99), intercept (0.27) and R2 (0.99) of the Centiloid transformed WC SUVR values were within the accepted range. Using CapAIBL on the AIBL images, the regression slope (0.98) and R2 (0.99) of the Centiloid transformed WC SUVR values (computed using the Centiloid calibration coefficients) were within the accepted range compared to the SPM derived Centiloid values. The intercept (2.03) was however marginally outside the accepted range (<2). Using the AD+ (SUVR>1.5) and HC- (SUVR<1.3) in AIBL, the mean whole cerebellum (WC) SUVR values were within the accepted range (<2%) for the AD+ (-1.13%), but marginally outside for the HC- (-2.70%). This resulted in a mean error in Centiloid values of -0.46% in the AD+



Centiloid values obtained using SPM and CapAIBL using AIBL and Centiloid calibration PiB PET images.

and -7.24% in the HC-. Using the slope and intercept to perform the Centiloid transformation resulted in a reduced mean error of -0.52% in the AD+ and 1.12% in the HC-. **Conclusions:** Reliable Centiloid measures can be obtained for PiB images using the PET-only method CapAIBL using the recommended calibration method. Using the estimated slope and intercept to further correct the estimation of the Centiloid values might however be desirable to reduce the quantification errors.

IC-P-025 [^{18}F]FLORBETAPIR ROC CURVE AT EVERY VOXEL REVELS A WIDE RANGE OF CORTICAL SUVR CUT-OFFS

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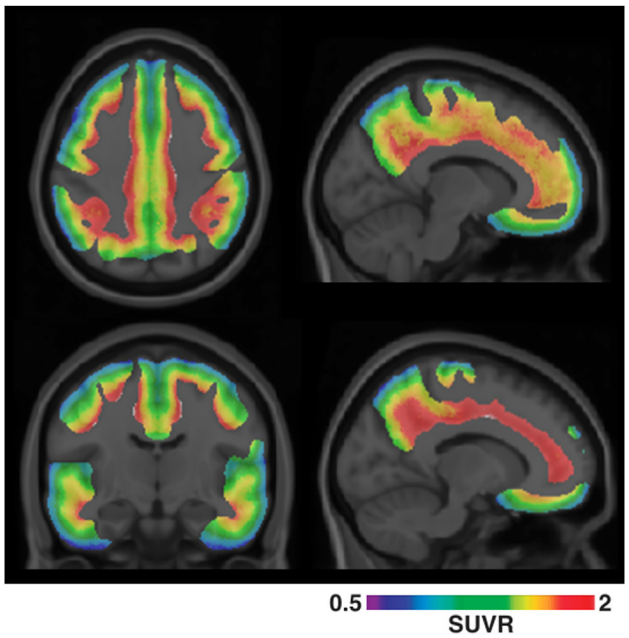
Background: During the last decades researchers have been using global measurements of amyloid−PET ligands to dichotomize subjects into amyloid-β (Aβ) positive or negative groups. The Aβ dichotomization is desirable to enrich clinical trials population and to assess the influences of Aβ abnormalities on Alzheimer's disease (AD) progression. However, dichotomizations using global measurements do not provide information regarding the regional pattern of Aβ abnormalities, which may be important to identifying nondemented individuals fated to AD clinical progression. Here, we tested the framework that cut-off analysis performed at every voxel may provide additional information as compared to global estimates. **Methods:** We assessed cognitively normal (n=209), mild cognitive impairment (MCI; n=311) and AD (n=81) individuals from ADNI cohort who underwent [^{18}F]Florbetapir PET at baseline (Table 1). The standardized uptake value ratio (SUVR) maps were then generated using the cerebellum grey matter and the global white matter as reference regions. First, a receiver operating characteristic (ROC) curve was performed at every voxel contrasting controls and AD participants. Second, the optimal cut-off value at every voxel was calculated using the least distance from (0,1) point to the ROC curve (best operating point) (Figure 1). Third, parametric maps of diagnostic sensitivity and specificity were generated (Figure 2). Finally, probabilistic maps for baseline Aβ positivity at every voxel were generated for MCI converters (n= 55) and non-converters (n= 256) over 2 years (Figure 3). **Results:** The highest SUVR cut-off values were found in the precuneus, anterior and posterior cingulate cortices, whereas the lowest were found in clusters in the temporal lobe (Figure 1). Diagnostic sensitivity and specificity were the highest in clusters in the precuneus, posterior cingulate, temporal, and frontal cortices (Figure 2). Probabilistic maps showed that MCI non-converters did not present a specific pattern of amyloid deposition at baseline, whereas MCI converters reached 100% of positivity in voxels in the posterior cingulate, precuneus, frontal and temporal cortices (Figure 3). **Conclusions:** Our results re-



Figrue 1. [^{18}F]Florbetapir SUVR cut-off values at every voxel.

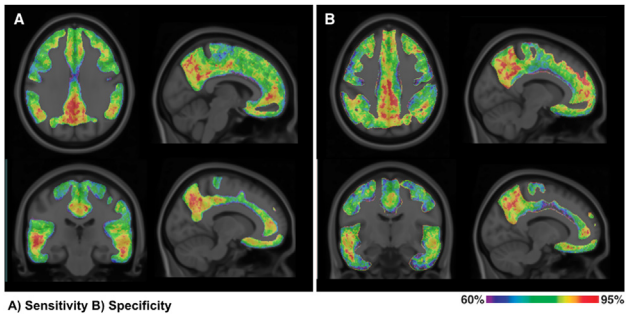


Figure 2. [^{18}F]Florbetapir SUVR cut-off values sensitivity and specificity for a diagnostic of probable Alzheimer's disease at every voxel.