cortex and hippocampus was calculated using imageJ. **Results:** BCAS-operated mice showed no significant changes in the levels of APP, sAPPα and sAPPβ at 5 weeks after the operation, and a significant increase of amyloid plaques in both cerebral cortex and hippocampus was detected 30 weeks after the operation. These data suggested that CCH with BCAS increases Aβ deposits without altering Aβ production. To assess the Aβ clearance, we collected the brain interstitial fluid (ISF) with microdialysis to measure soluble Aβ level in the brain ISF. Basal Aβ40 and Aβ42 levels of the brain ISF in the BCAS-operated mice were significantly decreased, whereas the Aβ42 clearance rate was increased. These data suggested that CCH with BCAS inhibited the dynamics of ISF Aβ, leading to the decreased level and increased clearance of ISF Aβ, thereby facilitating the Aβ aggregation. **Conclusions:** We showed that CCH accelerates Aβ deposition in the brains of APP/PS1 mice by decreasing the level of Aβ40 and Aβ42, and increasing the Aβ42 clearance. Our data suggested that CCH promotes soluble Aβ aggregation resulting in enhanced Aβ deposition.

P2-071 COMPARING CEREBRAL WHITE MATTER, CEREBELLAR, AND PONTINE REFERENCE REGIONS TO CHARACTERIZE FLORBETAPIR PET MEASUREMENTS OF AMYLOID-β BURDEN IN PSEN1 E280A MUTATION CARRIERS AND NONCARRIERS FROM THE COLOMBIAN AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE KINDRED

Valentina Ghisays[1,2], Hillary Protas[1,2], Yinghua Chen[1,2], Eric L. DeMarco[1,2], Pierre N. Tariot[1,2,3], Jessica B. Langbaum[1,2], Yakeel T. Quiroz[4,5], Francisco Lopera[5], Eric M. Reiman[1,2,3,6,7], Kewei Chen[1,2,3,6], *[1]Arizona Alzheimer's Consortium, Phoenix, AZ, USA; [2]Banner Alzheimer's Institute, Phoenix, AZ, USA; [3]University of Arizona, Tucson, AZ, USA; [4]Harvard Medical School and Massachusetts General Hospital, Boston, MA, USA; [5]Grupo de Neurociencias, Universidad de Antioquia, Medellin, Colombia; [6]Arizona State University, Tempe, AZ, USA; [7]Translational Genomics Research Institute, Phoenix, AZ, USA. Contact e-mail: Valentina.Ghisays@bannerhealth.com*

Background: We previously demonstrated that a cerebral white matter reference region could improve the ability of longitudinal florbetapir standard uptake value (SUV) ratios (SUVR) to track changes in amyloid-β (Aβ) levels (Chen et al., 2015). Here we sought to compare white matter to two candidate reference regions to test their the ability to detect Aβ elevations and associations with age and memory decline with cross-sectional florbetapir SUVRs in Presenilin *(PSEN1)* E280A mutation carriers from the Colombian Autosomal Dominant Alzheimer's Disease (ADAD) kindred. **Methods:** Cerebral white matter (corpus callosum[CC], centrum semi-ovale[CSO], and combined[WM]), cerebellar, and pontine reference regions were used to compute cerebral-to-reference region SUVRs using florbetapir PET scans acquired as reported (Fleisher et al., 2012). Nineteen cognitively unimpaired mutation carriers (mean age=32), 11 impaired mutation carriers (mean age=47), and 20 age-matched non-carriers of the PSEN1 mutation were included in the analyses. We compared the ability of different reference regions to detect elevated SUVRs and characterize associations with age and memory performance in the carrier group. Finally, since deceased mutation carriers with cognitive impairment are known to have neuropathological evidence of Aβ burden in the cerebellum, we compared reference region SUVs between our three groups. **Results:** There were significant between-group SUVR differences (impaired carriers>unimpaired carriers>non-carriers) using each of the five reference regions. All reference regions similarly detected elevated levels of Aβ, and showed significant associations of SUVRs with age and worse memory performance in mutation carriers. However, associations with memory performance were stronger when using CC (p=0.02), CSO (p=.002), and WM reference regions (p=.06) compared to pontine. In comparison with impaired mutation carriers and non-carriers, SUVs were significantly greater in impaired mutation carriers in the cerebellar region, but not in white matter or pontine regions. **Conclusions:** Use of a white matter reference region may increase the ability to characterize cross-sectional florbetapir PET measurements of Aβ burden in ADAD mutation carriers, aid in identifying individuals at preclinical stages, and better inform future clinical trials. While our previously employed pontine reference region may be an acceptable alternative, a cerebellar reference region may be confounded by Aβ burden in the clinical stages of ADAD.

P2-072 A STATISTICAL METHOD FOR DETERMINING BIOMARKER THRESHOLD FOR ALZHEIMER'S DISEASE

Yan Li[1], Guoqiao Wang[1], Chengjie Xiong[1], Eric McDade[1], Anne M. Fagan[2], Brian A. Gordon[1], Tammie L. S. Benzinger[1], Andrew J. Aschenbrenner[1], Jason Hassenstab[1], Randall J. Bateman[1], *[1]Washington University in St. Louis School of Medicine, St. Louis, MO, USA; [2]Washington University School of Medicine, Saint Louis, MO, USA. Contact e-mail: yanallicia23@gmail.com*

Background: Neuroimaging and biofluid biomarkers play an important role for early diagnosis, classification and estimating progression of Alzheimer's disease (AD). Even though their values are naturally continuous, there is need to define biomarker cut points to dichotomize them as normal/abnormal to facilitate screening eligible patients for clinical trials and stratify patients at different risk. Various methods have been proposed to determine the biomarker cut points. However, those methods either depend on the results of the cognitive test or the cut point of amyloid positron emission tomography (PET) which themselves are subject to variability, or are based on percentiles which can be arbitrary. To overcome these limitations, we developed a statistical method that can be used to estimate the baseline level where the rate of change first becomes significantly different from 0 (or between groups). **Methods:** Based on a linear mixed effect model, we first derive the distribution of the rate of change of the biomarker conditional on the value at baseline. Then, given any baseline value, we estimate the rate of change and test its significance. Assuming a higher biomarker level is associated with a more severe stage of AD, the smallest baseline biomarker value that results in a significant rate of change is estimated. Bootstrapping is applied to estimate the standard deviation (SD) and confidence interval (CI) of the cutoff point. Simulation studies are conducted to evaluate the performance of the statistical method under different scenarios. **Results:** Applying this new statistical method to the biomarker data from mutation carriers in the Dominantly Inherited Alzheimer Network