Improved associations of AD related glucose hypometabolism with florbetapir PET Aβ SUVR with the alternative cerebral WM reference region

Chen K, Chen Y, Kuang X, Luo J, Bauer R, Koeppe R, Jagust WJ, Weiner MW, Reiman EM, and the Alzheimer's Disease Neuroimaging Initiative
Banner Alzheimer's Institute,
Arizona State University, Translational Genomics Research Institute, University of Arizona, Mayo Clinic Arizona, University of California, Berkeley, University of California, San Francisco, and Arizona Alzheimer's Consortium, Phoenix, AZ, USA

Summary

Using ADNI florbetapir PET data, we previously demonstrated improved power to track longitudinal fibrillar Aβ changes and evaluate Aβ-modifying treatments using a cerebral white matter (Chen et al., 2015) for SUVR calculation ($SUVR_{cwm}$). In addition to our previous data uploads, we now completed $SUVR_{cwm}$ for total 2052 number of visits for total 1086 subjects. In addition, we also completed the computation of the SUVR with the cerebellar reference region ($SUVR_{cereb}$).

Methods

Part 1, $SUVR_{cwm}$ value for each visit of each patent was computed using the WM (eroded corpus callosum/centrum semiovale) reference ROIs. We examined the FDG-PET measured CMRgl association separately with $SUVR_{cwm}$ and with $SUVR_{cereb}$ in patients with AD, mild cognitive impairment (MCI) and in cognitively unimpaired controls (NCs). The summary indices used for CMRgl are the hypometabolic convergence index (Chen et al., 2011) and statistical region of interest (Chen et al., 2010). The sROI and HCI are also part of the data upload. For more details about sROI and HCI, please see our companioning writing 'Trajectories of AD related cerebral glucose hypometabolism in individuals prior to their progression to MCI/dementia'.

Part 2, Image Processing Steps and Names and Versions of Software used
All images downloaded from LONI (http://adni.loni.usc.edu/methods/pet-analysis/pre-processing/) were fully processed by LONI (Co-registered dynamic, Averaged, Standardized Image and Voxel Size, and Uniform Resolution). The images were then spatially normalized to the SPM template using SPM8 (Wellcome Trust Center for Neuroimaging, UCL, UK) in MATLAB R2013a (Mathworks, Natick, MA). The in-house developed procedure was used to calculate the SUVR values with the cerebral white matter reference region and the cerebellar reference region.

Results

For cross-sectional baseline data, our results show that the correlation of either HCI or sROI with $SUVR_{cwm}$ is significantly stronger than that with $SUVR_{cereb}$ for AD patients ($p<0.001$), for MCI patients ($p<0.001$) and for NC patients (overall $p<0.01$). However, such stronger association was only observed in MCI patients for the longitudinal data ($p<0.0001$). Interestingly, more longitudinal $SUVR_{cereb}$ deposits was paradoxically correlated with longitudinal CMRgl increase in AD patients ($p=0.024$) and in NC ($p=0.012$).

Uploaded data:
We uploaded all SUVR value included in our analysis.

Conclusions
As shown in our results, the use of white matter as a reference region for SUVR to quantify beta-amyloid deposits possesses a significantly stronger cross-sectional correlation with HCI or sROI than the use of cerebellar reference region in AD, MCI and NC groups. Such stronger correlation was also observed longitudinally in MCI patients. Additional studies are needed to confirm our findings especially the longitudinal ones. Overall, the use of white matter as a reference region for florbetapir PET can potentially characterize the negative impact of fibrillary beta-amyloid on neuronal activities in addition to serve as a better, more stable biomarker of beta-amyloid load.

Version Information

This is the document submitted from Banner Alzheimer Institute regarding the SUVR calculation using the newly developed cerebral white matter reference region for florbetapir PET image analysis.

Dataset Information
This methods document applies to the following dataset(s) available from the ADNI repository:

Dataset Name	Date Submitted
Reiman/Chen Lab – mcSUVRwm3 Analysis Version 20.0	9 Sep 2016
Reiman/Chen Lab – mcSUVRcere Analysis Version 20.0	9 Sep 2016

About the Authors

This document was prepared by **Kewei Chen and Eric Reiman, Banner Alzheimer's Institute, Imaging Analysis**. For more information please contact Kewei Chen at **(602) 839-4851** or by email at **Kewei.Chen@bannerhealth.com**.

Notice: This document is presented by the author(s) as a service to ADNI data users. However, users should be aware that no formal review process has vetted this document and that ADNI cannot guarantee the accuracy or utility of this document.

Reference List

Chen, K., Ayutyanont, N., Langbaum, J. B., Fleisher, A. S., Reschke, C., Lee, W. et al. (2011). Characterizing Alzheimer's disease using a hypometabolic convergence index. Neuroimage., 56, 52-60.

Chen, K., Langbaum, J. B., Fleisher, A. S., Ayutyanont, N., Reschke, C., Lee, W. et al. (2010). Twelve-month metabolic declines in probable Alzheimer's disease and amnestic mild cognitive impairment assessed using an empirically pre-defined statistical region-of-

interest: findings from the Alzheimer's Disease Neuroimaging Initiative. Neuroimage., 51, 654-664.

Chen, K., Roontiva, A., Thiyyagura, P., Lee, W., Liu, X., Ayutyanont, N. et al. (2015). Improved power for characterizing longitudinal amyloid-beta PET changes and evaluating amyloid-modifying treatments with a cerebral white matter reference region. J Nucl.Med., 56, 560-566.