ADNI Alzheimer's Disease Neuroimaging Initiative

Using Hypometabolic Convergence Index to Detect Longitudinal Metabolic Decline and its Association with Aβ Positivity and Cognitive Degeneration

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Summary

We previously introduced the hypometabolic convergence index (HCI) to characterize the extent to which a person's spatial hypometabolic pattern measured by fluorodeoxyglucose (FDG) positron emission tomography (PET) matches with that seen in patients with probable Alzheimer's disease (AD). In our original cross-sectional study, HCI was found to adequately distinguish AD patients, mild cognitively impaired (MCI) patients, and cognitively normal controls (NL) and to predict conversion from MCI to AD [1]. We worked with our collaborators to compare HCI to other measures of AD-related hypometabolism using ADNI and other data sets, and we reported its ability to distinguish cognitively normal late-middle-aged persons at three levels of genetic risk for AD in the Arizona APOE4 gene dose cohort.

Methods

Part 1, In this funding cycle, we have total of 3340 FDG PET scans from 1407 subjects, 343 cognitively normal subjects, 106 SMC, 307 eMCI, 411 MCI and 240 patients with AD. We further optimized our HCI method using normative data from subjects who remained cognitively normal over 2 years after baseline visits and an improved reference ROI. We then re-calculated the HCI. Using these available HCI values, we attempted to examine the relationship between longitudinal metabolic decline and baseline amyloid-beta (Aβ) load positivity, based on either CSF amyloid-beta$_{1\text{-}42}$ (A$\beta_{1\text{-}42}$) levels or florbetapir PET measurements of mean cortical standardized uptake value ratios (SUVR). Especially, we investigated the capacity of HCI to longitudinally track AD-related metabolic decline in NL, MCI, and AD, as well as its relationship with Aβ positivity and cognitive degeneration.

Part 2, For our own initial analysis, we only considered subjects who had baseline CSF Aβ1-42 measurements, and who also had baseline and 12.0±0.9-month follow-up FDG PET data for 82 NL, 144 MCI and 73 AD subjects, and for 168 NL, 87 MCI and 40 AD subjects, who had baseline and 23.9±1.4-month follow-up FDG PET data as well as a baseline florbetapir PET scan. HCI rate for each subject was calculated as the difference in HCI scores between his/her baseline and follow-up visits divided by the time interval between the two visits. The subjects were divided into amyloid negative (Aβ-) and amyloid positive (Aβ+) subgroups based on either their baseline CSF A$\beta_{1\text{-}42}$ levels or their baseline cerebellum-to-cerebellum SUVR, using a CSF A$\beta_{1\text{-}42}$ threshold value of 192 pg/mL [2] and a SUVR threshold value of 1.18 [3]. HCI rate was compared between Aβ+/- subgroups in NL, MCI, and AD. Finally, HCI rate was correlated with rate of change in cognitive measures for subjects with 12-month follow-up scans in NL, MCI, and AD.

Part 3, 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 R2009b (Mathworks, Natwick, MA). The in-house developed procedure was used to calculate the HCI for each of the new scans.

Results

HCI increase rate was in the order of NC<MCI<AD (linear trend, p=3.91e-10). Overall group pairwise difference in HCI rate between Aβ+/- subjects was significant (p=5.58e-15). The Aβ+/- pair-wise difference in MCI group was also significant (p=6.30e-5). The overall association between HCI rate and rate of change in each of the cognitive measures was significant. We uploaded the HCI values for all the FDG-PET scans that are available to us.

Conclusions

With additional studies to confirm, it is feasible to use HCI as a potential biomarker to longitudinally track AD-related hypometabolic changes in both clinical and preclinical stages.

Version Information

This is the second document submitted from Banner Alzheimer Institute regarding Hypometabolic Convergence Index (HCI) of FDG PET image analysis for all available subjects in ADNI (1/GO/2, as of May 2014).

Dataset Information

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

Dataset Name	Date Submitted
Reiman/Chen Lab – HCI_2014 Analysis Version 18.0	29 August 2014

References

[1] K. Chen, et al. "Characterizing Alzheimer's Disease using a Hypometabolic Convergence Index." *NeuroImage* 56.1 (2011): 52-60.

[2] L. Shaw, et al. "Cerebrospinal Fluid Biomarker Signature in Alzheimer's Disease Neuroimaging Initiative Subjects." *Ann Neurol.* 65.4 (2009): 403-413.

[3] A. Fleisher, et al. "Using Positron Emission Tomography and Florbetapir F 18 to Image Cortical Amyloid in Patients With Mild Cognitive Impairment or Dementia Due to Alzheimer Disease." *Arch. Neurol* 68.11 (2011): 1404-1411.

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