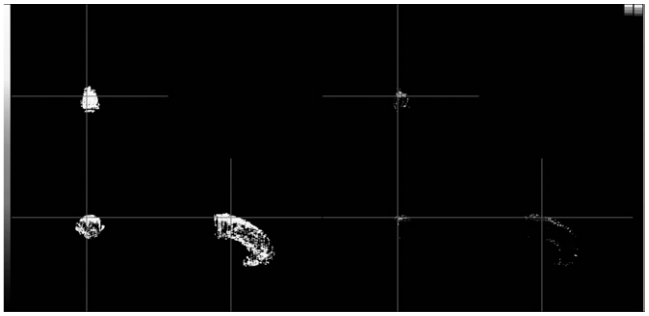

IC-P2-114 META-ANALYSIS ROIs AND MINIMAL DEFORMATION TEMPLATES IMPROVE PET-FDG AS A CANDIDATE BIOMARKER IN ALZHEIMER'S DISEASE

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Background: Research consistently finds hypometabolism of [18F]Fluorodeoxyglucose (FDG-PET) in patients diagnosed with Alzheimer's Disease (AD). Identifying abnormalities in metabolism requires precise delineation of affected areas in order to maximize differences between groups, detect change over time and minimize variance. We generated meta-analysis ROIs (MetaROIs) from frequently cited coordinates in existing studies, and compared these regions with standard anatomical ROIs across three image preprocessing streams in order to identify potential bio-marker regions using data from the Alzheimer's Disease Neuroimaging Initiative (AD = 13), (Normal=12). **Methods:** Six terms relating to FDG-PET, AD, and Mild Cognitive Impairment (MCI) were used to search PubMed, resulting in 18 cross-sectional studies. Study coordinates were used to generate MetaROIs. A minimal deformation template (MDT) was generated for each group (AD, MCI, Normal), using high-resolution MR images, based on the method by Kochonuv et al. (2001). Preprocessing was done with three methods: (1) individual FDG-PET images were spatially normalized to the MNI FDG template, (2) individual MR images were spatially normalized to a group-specific template, then this transformation was applied to individual coregistered FDG-PET images, (3) same as (2) but additionally the FDG-PET image was masked with an individual gray-matter mask. Effect size and percent annual change delineated the most effective processing stream. **Results:** MetaROIs included frequently cited regions in bilateral posterior cingulate, bilateral angular gyri, and primarily left-sided frontal and temporal regions. MetaROIs exhibited larger mean group difference between AD and Normals compared to corresponding AAL MNI regions (effect size in posterior cingulate increased from 0.48 to 1.82). Normalization to MDT template further improved effect size by 7-15%. MetaROIs also increased twelve month percent change in AD patients (posterior cingulate increased from 8% to 11%). The same region in normals showed little change (MNI ROI= 0.4% vs MetaROI= 0.3%). **Conclusions:** The use of research-defined MetaROIs, along with a processing stream that reduced deformation and used individual gray matter masks, greatly improved the viability of FDG-PET as a candidate biomarker in AD.

IC-P2-115 REGIONAL METABOLISM IN MCI PREDICTS CLINICAL DECLINE AND STRUCTURAL VOLUME LOSS: INITIAL RESULTS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

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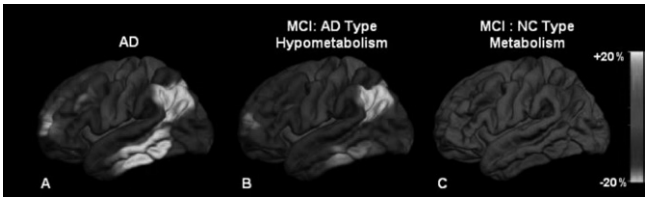
Background: Mild cognitive impairment (MCI) is a heterogeneous risk factor for Alzheimer's Disease (AD), with some individuals progressing rapidly, others remaining stable for years, and some reverting to normal cognitive status. **Objective:** To determine whether a pattern of regional hypometabolism characteristic of AD can be identified and used to predict clinical decline and structural volume loss in MCI. **Methods:** Data from a subset of subjects from the AD Neuroimaging Initiative, including 51 normal controls (NC, mean age 75.9 ± 5.4 years, 28 M), 69 MCI (74.3 ± 7.5y; 55 M), and 38 probable AD (76.2 ± 6.6y; 23 M) were analyzed. A semi-automated procedure developed within the Morphometry Biomedical Informatics Research Network was used to quantify PET activity within individually-specific anatomical regions-of-interest (ROIs) defined on each subject's MRI. A linear discriminant function was trained on NC and AD data to identify a pattern of regional hypometabolism characteristic of AD then applied to MCI data. **Results:** A pattern of hypometabolism in isthmus cingulate, mesial temporal, inferior parietal, and frontal ROIs best discriminated AD from NC. Figure 1 shows the percent difference in metabolism relative to NC for the AD group (Fig 1A) and the two MCI subgroups defined by application of the discriminant function to MCI data. The degree to which MCI individuals expressed the AD hypometabolic pattern was predictive of 1-year decline on the Mini Mental State Exam ($r = 0.43$; $p < .001$) and 1-year structural volume loss, as measured with quantitative MRI, in middle ($r = 0.49$ $p = .002$) and inferior ($r = 0.48$ $p = .003$) lateral temporal cortices. MCI subjects with phenotypic AD hypometabolism (Fig 1B) showed a significantly higher conversion rate to probable AD (9/30) than did those showing the NC metabolic phenotype (Fig 1C; 1/39) ($p = .002$). **Conclusions:** Patterns of regional hypometabolism at baseline are predictive of 1-year clinical decline and structural volume loss in individuals with MCI. These results suggest that PET measures may be of value for individual patient prognosis and for increasing the efficiency of large-scale clinical trials. Supported by: Morphometry BIRN U24-RR021382; ADNI U01-AG024904



IC-P2-116 LONGITUDINAL ATROPHY RATE AS A BIOMARKER OF DISEASE PROGRESSION IN FRONTOTEMPORAL LOBAR DEGENERATION

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Background: Cerebral atrophy rate measured using serial brain MR volumetry is a promising biomarker for disease progression in neurodegenerative disorders. Its utility has been established in clinical trials of disease-modifying therapies in Alzheimer's disease. However, the value of atrophy rate measures as biomarkers has yet to be established in frontotemporal lobar degeneration (FTLD), the second most common cause of young-onset dementia. **Methods:** Thirty-three FTLD patients (12 behavioural variant (bvFTLD), 11 semantic dementia (SD) and 10 progressive non-fluent aphasia (PNFA)) and 14 age-matched healthy controls underwent two serial volumetric MRI scans (mean interval=383 days). Rates of annual whole-brain atrophy and ventricular enlargement were obtained from volume differences between manually segmented regions on baseline and repeat scans. The scan pairs then underwent 12 degrees of freedom (dof) registration, followed by application of the boundary shift integral (BSI) technique, allowing direct automated calculation of brain atrophy rates (BBSI) and ventricular enlargement (VBSI). The automated and manual techniques were compared. These measures of volume change