we conclude that specialists must be concerned even when PIB scan is negative since patients could have dementia due to other causes.

IC-P-010 COMBINATORIAL BIOMARKER ENRICHMENT STRATEGIES FOR MCI CLINICAL TRIAL DESIGN

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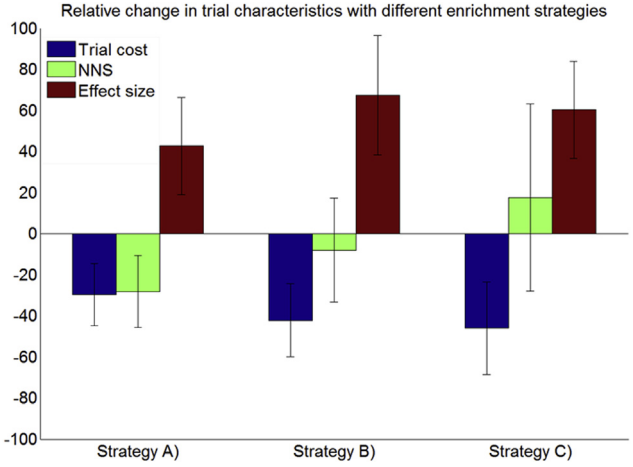
Background: Brain amyloid is part of the definition of Alzheimer's disease (AD) and increasingly used in clinical trial screening. ApoE genotype is associated with presence of brain Amyloid. Biomarkers of neurodegeneration reflect disease progression and can yield theoretical power advantages in mild cognitive impairment (MCI) trials. Whether and how these different markers can be combined, and the implications for trial design, remain open questions. **Methods:** We propose different strategies for patient selection in trial design: A): Screen out amyloid negative (AM-) subjects. B): Screen out subjects with no neurodegeneration. Then further screen out AM- subjects. C): Screen out subjects with no ApoE risk factor. Then further screen out subjects with no neurodegeneration. Strategy A) is the implementation of the Amyloid hypothesis into trial design. Strategy B) follows the hypothesis that amyloid positive (AM+) MCI subjects with neurodegeneration are closer to clinical onset of AD and can have operational advantages over A). Strategy C) hypothesizes that MCI subjects at genetic risk and with neurodegeneration are closer to clinical onset of AD. We hypothesize that Strategy C) is similar with Strategy A) with lower costs. All strategies were assessed on 152 ADNI I and 112 ADNI II subjects with an amyloid marker and clinical follow-up over 24 months. AM+ was defined using established criteria. Neurodegeneration was defined as hippocampal volume below the 15th percentile of healthy subjects. All subjects carrying at least one ε4 allele were defined as being at genetic risk of AD. Trial cost, the number of subjects needed to screen (NNS) and effect size were calculated for both studies and three clinical endpoints, MMSE, CDR-SB and ADAS-Cog 13. **Results:** All three enrichment strategies increased effect size and reduced trial cost in both ADNI studies (Figure 1). Strategy C) resulted in a trial population with 96% AM+ subjects. **Conclusions:** Additional or alternative biomarkers can have operational advantages over using amyloid markers alone for patient selection: Strategy B) helps further reduces costs and screens out slowly progressing AM+ subjects; Strategy C) screens out most AM- subjects without actually measuring amyloid marker.



IC-P-011 COMPARISON OF GLOBAL AND VOXEL-BASED DIAGNOSTIC CLASSIFICATION USING [^{18}F]FLORBETAPIR ROC ESTIMATES

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Background: Accurate diagnosis of Alzheimer's disease and its prodromal state is of paramount importance for effective intervention. Recent studies have shown that imaging biomarkers provides excellent knowledge for classification but failed to account to a compelling classifier due to usage of consolidated information (global SUVR measurements). We hypothesize that using voxel-based information we would be able to better classify Alzheimer's individuals from cognitively normal individuals. **Methods:** [^{18}F]Florbetapir PET images were acquired from 83 subjects (65 Cognitively Normal [CN], 18 Alzheimer's Disease [AD]) from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. The respective standardized uptake value ratio (SUVR) maps were subsequently generated using cerebellar grey-matter as reference region. Corresponding cortical uptake values (vertex based) were extracted using an average mid-surface structure generated using the study subjects and vertex based Receiver Operating Characteristic (ROC) analysis was carried out to identify the brain regions that best discriminates patients from cognitively normal individuals. ROC analysis based on the consolidated measurements was also carried out as a comparison study. **Results:** Based on the Area Under the Curve (AUC) values, brain regions including precuneus, posterior cingulate cortex, medial orbitofrontal cortex and temporal lobe showed the best separation between patients and normal individuals with an AUC value of over 0.8. The same regions show sensitivity values of over 0.7 and specificity values of over 0.8 (Figure 1). In the study done using consolidated measures, the best separation resulted in AUC of 0.6872 with a specificity of 0.8 and sensitivity of 0.722. **Conclusions:** ROC estimate of regional concentrations of brain [^{18}F]Florbetapir may contribute to the identification of pathological patterns of amyloidosis in predementia population and will enable accurate and effective classification in to the disease stages. The preliminary data reported here support the hypothesis that regional amyloidosis might contribute to a better discrimination between AD patients and cognitively normal individuals when compared with a global measurement, and the regions that allows best separation need to be used to generate a better consolidated measurement.