AD/PD™ 2023
ADVANCES IN SCIENCE & THERAPY
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Alzheimer's and Parkinson's Diseases
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P1098 / #176

POSTERS: J04. IMAGING, BIOMARKERS, DIAGNOSTICS

VISUAL ASSESSMENT OF [18F]MK-6240 PET SCANS IN EARLY ALZHEIMER'S DISEASE

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Aims: Assessment of tau deposition plays an important role in the selection of subjects for clinical trials. [^{18}F]MK-6240 tau PET scans were included in a substudy of the Phase 2 study of tilavonemab in early Alzheimer's disease (AD) (NCT0288095) at baseline, week 44, and week 96. Here we report the application of a visual read algorithm which provides both a categorical outcome and regional characterization of abnormal tau deposition.
Methods: [^{18}F]MK-6240 scans were assessed by evaluating for abnormal tau deposition and the extent of tracer retention (readers mark 'none', '<25%', '25%-75%', or '>75%' of a region) in 16 brain regions from the temporal and extra-temporal lobes, relative to cerebellar gray matter. Subjects were binned into four categories according to the decision tree in **Figure 1**. Each scan was read by up to 3 readers to reach a consensus. Scans were processed and prepared for SUVR analyses in Braak regions I-VI and whole brain, normalized to inferior cerebellar gray matter.

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OD108 / #713

ON-DEMAND SYMPOSIUM: FLUID BIOMARKERS AND IMAGING IN AD, PD AND LBD
30-03-2023 07:00 - 08:30

COMPLEX INTERACTION OF 20 CLINICAL VARIABLES CAN PROVIDE PROGNOSTIC BIOMARKER FOR PD SUBTYPES IN PPMI COHORT

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Aims: Parkinson's disease (PD) is a complex, age-related condition with heterogeneous patterns of clinical progression. We propose a machine learning-based prognostic biomarker for multi-modality subtyping of PD. Of the diverse modalities that we integrate, serum neurofilament light (Nfl) is the strongest indicator of fast disease progression.
Methods: We assembled longitudinal clinical data from the Parkinson's Progression Markers Initiative (PPMI) with subjects having five-year longitudinal data. Only participants from the Control (n=154) or PD (n=254) diagnostic groups are included in this study. Overall, 122 clinical features across six visits went through data imputation, vectorization, and min-max normalization. Curated data were exposed to non-negative matrix factorization and Gaussian mixture models to delineate coherent PD subtypes. Baseline data were used in a machine learning framework to classify patients into subtypes accurately.
Results: We identified three data-driven clusters, the fastest progressing group showed significantly higher rates of cognitive and motor decline than the other, more moderate groups (Fig. 1). Using five-fold cross-validation, our proposed machine learning model shows 0.91 ± 0.02 (95% CI) area under the receiver operating characteristic curve (with 20 out of 122 baseline measures) in segregating the PD subtypes. Model interpretation identifies Hoehn and Yahr stage, Global Spontaneity of movement and Facial expression as top predictors. Nfl values show significantly different regression slopes across time after adjusting for age at baseline and sex. (Non-PD: 0.37±0.2, PDvec1: 1.09±0.4, PDvec2: 1.17±0.4, PDvec3:
2.35±0.83)

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OD335 / #2359

ON-DEMAND SYMPOSIUM: PET 03
01-04-2023 07:00 - 08:30

VALIDATION OF [18F]FLORBETABEN PET QUANTITATION BASED ON THE ANALYSIS OF 15 SOFTWARE PIPELINES

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Aims: Amyloid positron emission tomography (PET) with [18F]florbetaben is an established tool for detecting Aβ deposition in the brain *in vivo* based on visual assessment of PET scans. Quantitative measures are, however, commonly used in the research context and allow continuous measurement of amyloid burden. The aim of this study was to demonstrate the robustness and added value of florbetaben PET quantification, focusing on Centiloid-based analysis.
Methods: This is a retrospective analysis of florbetaben PET images, consisting of 589 subjects. Florbetaben PET scans were quantified with 15 analytical pipelines using nine software packages (MIMneuro, Hermes BRASS, Neurocloud, Neurology Toolkit, statistical parametric mapping (SPM8), PMOD Neuro, CapAIBL, non-negative matrix factorization (NMF), Amyloid^{IQ}) that used several metrics to estimate Aβ load (SUVR, Centiloid, amyloid load and amyloid index). Six analytical pipelines reported Centiloid (MIMneuro, standard Centiloid pipeline, Neurology Toolkit, SPM8 (PET-only), CapAIBL, NMF). All results were quality controlled.
Results: The mean sensitivity, specificity and accuracy was 96.1±1.6%, 96.9±1.0% and 96.4±1.1%, respectively, for all quantitative methods tested and 96.1±1.6%, 97.4±1.2% and 96.7±1.2% for Centiloid-based approaches. The mean percentage of agreement between binary quantitative assessment across all 15 pipelines and visual majority assessment was 92.4±1.5% and 93.2±0.4% for the Centiloid-based sub-analysis.
Conclusions: Software quantification methods, such as Centiloid analysis, can complement visual assessment of florbetaben PET images. Based on this study, quantification of [18F]florbetaben PET as an adjunct to visual assessment was recently approved by the European Medicines Agency (EMA) in the EU for Neuraceq®.