widespread reduction in CVR, with the exception of occipital CVR. Results support the notion that older adults with cognitive impairment may experience an altered cerebrovascular state in which compensatory dilation relates to CBF in areas at elevated risk and further relates to diminished CVR in anterior regions. These results provide novel insight into intracranial structural-functional relations that cannot be explained by shared systemic vascular risk factors or advancing age.

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OLIGOMERIC AMYLOID-BETA TARGETED MRI CONTRAST AGENT
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Background: One of the peptides showing an aberrant distribution in Alzheimer’s disease (AD) patients is amyloid-beta (Aβ). The objective of this study was to develop a novel MRI contrast agent to target the oligomer Aβ, allowing for the in vivo determination of the early forms of the AD pathology by monitoring the signal changes after intravenous injection of the contrast agent. Methods: The new contrast agent was developed by combining the commercially available gadolinium (Gd)-Dota with an oligomeric Aβ-specific DNA aptamer (called as oAB). The aim of conjugating to aptamer was not only to increase the targeting ability vs. the oligomeric forms of beta amyloid but also to increase the conjugates’ BBB penetrability. This new agent was called as Gd-oAB. We confirmed the protein size with Aβ polymerization in aspect of molecular masses when polymers were formed. We performed the several experiments in the cell level and AD-model mice. Results: First, confocal microscopy imaging with oAB showed that Rod-shaped QD-oAB particles were homogenously dispersed in an aqueous solution, and the hydrodynamic particle size measured using transmission electron microscopy (TEM) was about 24.5nm. Second, Gd-oAB-cy5 probe-treated bEND3 highly expressed caveolin1 and transferrin receptor but HT22 cells highly expressed almost gate-mediated endocytosis. Finally, in a non-Tg mouse, signals in the brain after injection of the new contrast agent were almost similar to those of before injection of the contrast agent. However, in the young (4 month-old) and old (11 month-old) APP/PS1apoE KD mice, signals in the brain were increased after injection of the new contrast agent. Conclusions: We report a discrete T1 molecular MRI contrast agent specifically designed to be specific for oligomeric Aβ as well as amyloid plaques. The complex, comprising an Aβ-specific aptamer conjugated to a MRI contrast agent is selective and exhibits a high affinity to oligomeric Aβ both on cells and brain tissues.

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PRE-CLINICAL CHARACTERIZATION OF THE NOVEL TAU PET LIGAND [18F]-JNJ’067
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Background: PET imaging of tau pathology promises to be a biomarker for early diagnosis, staging and monitoring disease progression in AD, as well as monitoring target engagement in tau directed therapies. Methods: We have developed JNJ’067, a potent and selective tau PET ligand with an excellent PK profile and no obvious off-target binding. Results: In a competitive binding assay JNJ’067 bound to neurofibrillary tangles (NFTs) from AD brain samples with a Kd of 2.4 nM with high selectivity versus aggregated β-amyloid (Kd of 3212 nM). High selectivity and very low non-specific binding was also confirmed by autoradiography combined with immunohistochemistry on human AD brain sections. In vitro profiling (CEREP, DiscoverX, monoamine oxidases A and B) showed no significant off-target activity, which was confirmed by μPET studies in rats and a rhesus monkey, where no retention was observed in any brain region. μPET studies in rats and a rhesus monkey revealed desirable properties for a PET ligand, such as rapid and abundant uptake of JNJ’067 in the brain, combined with fast clearance, in accordance with its high intrinsic clearance in rat and monkey microsomes and hepatocytes. The similarly high intrinsic clearance in human microsomes and hepatocytes suggests a fast clearance in man. Metabolite ID studies in rat, monkey and human liver microsomes predicted significant defluorination in rat, but not in monkey and human. Indeed bone uptake was observed in the rat μPET study, indicative of some defluorination, yet no bone uptake was observed in the rhesus monkey μPET study. Conclusions: JNJ’067 is a promising candidate tau PET tracer with potential for diagnosis, monitoring of disease progression and drug target engagement in AD.

P3-317

DHA BRAIN UPTAKE AND APOE4 STATUS: A PET STUDY WITH [1-13C]-DHA
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Background: The APOE ε4 (APOE4) allele is the strongest genetic risk factor identified for developing Alzheimer’s disease (AD). Among brain lipids, alteration in the omega-3 (ω-3) polyunsaturated fatty acid docosahexaenoic acid (DHA) homeostasis is implicated in AD pathogenesis. APOE4 may influence both brain DHA metabolism and cognitive outcomes. Methods: Using positron emission tomography (PET), regional coefficients (K*) rates (Jin) of DHA incorporation from plasma into the brain using [1-13C] DHA, and regional cerebral blood flow (rCBF) using [15O]water were measured in 22 younger healthy adults (mean age 35). Data
were partial volume error corrected for brain atrophy. APOE4 phenotype was determined by protein expression and unesterified DHA concentrations were quantified in plasma. An exploratory post-hoc analysis of the effect of APOE4on DHA brain kinetics was performed. **Results:** In this group, (APOE4 non-carriers, n=13, carriers, n=9), the mean global gray matter DHA incorporation coefficient, K*, was significantly higher (16%) among APOE4 carriers (n=13) compared to non-carriers (n=9, p=0.046). A significantly higher global DHA incorporation coefficient was observed in several brain regions, particularly in the entorhinal subregion, an area higher global DHA incorporation coefficient was observed in several brain regions, particularly in the entorhinal subregion, an area affected early in AD pathogenesis. Cerebral blood flow, unesterified plasma DHA, and whole brain DHA incorporation rate (J\textsubscript{o}) did not differ significantly comparing the APOE4 groups. **Conclusions:** Significantly greater values of K* for DHA in APOE4 carriers suggests an alteration in brain DHA homeostasis. These findings may contribute to understanding how APOE4 genotypes affect AD risk.

**P3-318 BIOMECHANICAL CHARACTERIZATION OF BRAIN ATROPHY IN COGNITIVELY NORMAL AND MCI GROUPS**

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**Background:** The pathophysiological processes leading to Alzheimer’s disease (AD) begin well before the onset of clinically detectable symptoms. Imaging methods for early detection are paramount to facilitate interventions that may decrease progression and morbidity associated with this devastating disease. The purpose of this study was to explore new longitudinal imaging biomarkers of mild cognitive impairment (MCI) using a novel technique to quantify voxel-wise directional deformation of brain structure. **Methods:** “ADNI1 Standardized 3T List” was used to characterize brain atrophy patterns between the baseline and 1 year in MCI (n=56) compared to cognitively normal (CN) (n=39). Within-subject registration was performed across the data acquisition time points using Advanced Normalization Tools’ (ANTs) SyN nonlinear registration algorithm. Using longitudinal changes in deformation field between paired images, the voxel-wise volume change ratio (Jacobian Determinant, JD) and associated directional stretches/shrinks were estimated using an in-house morphometry analysis algorithm based on finite strain theory in X (anterior-posterior), Y (medial-lateral), and Z (superior-inferior) directions. We focused on gray matter (GM) region to avoid confounding effects of white matter (WM) and cerebrospinal fluid during image registration. **Results:** Within-group analysis results (Fig.1) demonstrate statistically significant gray matter volumetric decreases in both CN (top) and MCI (bottom) groups. Atrophy in the NL group was observed primarily at the interfaces of GM and WM, whereas the pattern of atrophy in the MCI group was more diffuse. Regional evaluation demonstrated statistically significant between group differences in rates of atrophy in bilateral hippocampal, caudate, putamen, thalamus and amygdala, where hippocampal and amygdala atrophy was characterized primarily by X-directional shrinkage (Fig. 2). Directional strains provided additional information that was not detectable with conventional volumetric analysis based on JD, with significant difference in X-directional contraction in insular cortex and right inferior temporal gyrus and Z-directional difference in bilateral middle cingulate gyri. **Conclusions:** Directional strains derived from longitudinal MRI may underlie anisotropic volumetric changes and identify additional changes in brain regions that were not detected with conventional volumetric analysis based on JD. This approach may be useful in subsequent studies that aim to identify early structural brain changes predicting future conversion from MCI to AD using a larger cohort study and longer-term follow-up.

**P3-319 MILD COGNITIVE IMPAIRMENT CLASSIFICATION USING DEEP LEARNING**

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**Background:** Recently, it is known that brain degeneration is associated with accumulated tau protein in Alzheimer’s diseases. And tau-PET imaging could serve to classify mild cognitive impairment in early stage. Deep learning methods have been widely used for neuroimaging classification. In the present study, we develop a deep learning-based method for classifying tau-pet imaging patterns. **Methods:** Tau-pet imaging offers representative information that could be used as a bio-marker of Alzheimer’s disease in an early stage. The proposed method first performs a preprocessing step, co-registration of tau-PET image to T1-weighted MR image. Then, the registered tau-PET image acquires volume-level correspondence between all subject’s PET images. Second, the Louvain method (gamma=0.7) discriminated MCI subjects (n=54) to three groups. We finally use principle component analysis for dimension reduction and apply a neural network-based deep learning method for classification of those clusters. We validated the proposed method using a leave-one-out cross validation method. **Results:** In binary classification, our method discriminated subgroups 1 and 2 with high accuracy (accuracy 90.91%, sensitivity 100.0% and specificity 81.82%). For sub-groups 2 and 3, we have accuracy of 80.49% (sensitivity 85.29% and specificity 57.14%). Tau-pet