intensive period of treatment from 3.03 [3.03-3.2] % at baseline up to 11.37% [11.37%-14.45%] (median-IQR, p<0.05) before the last PE; while untreated group did not show any change. This effect was associated with the treatment intensity and, interestingly, correlated with Aβ mobilization observed in plasma after TPE in the same Phase II study (r=0.6022; p<0.0001). Conclusions: Albumin from AD patients is impaired, at least in its antioxidant capacity, in comparison with healthy subjects. TPE with albumin replacement in AD patients seems to have an effect on albumin oxidation status that correlates with plasma Aβ mobilization. Further investigation is warranted to better understand the mechanisms underlying AD therapy based on TPE followed by albumin replacement.

P2-068 RATIONAL DESIGN OF APOE4 MUTANTS AS A TOOL FOR CELLULAR STUDIES IN ALZHEIMER’S DISEASE
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Background: The incidence rate of Alzheimer’s disease (AD) is rising, thus, there is an urgent need for new therapeutic avenues. In this regard, the ApoE4 genotype is considered the most important genetic risk factor for AD. One leading hypothesis is that the ApoE4 protein accesses an intermediate conformational state, which may cause mitochondrial stress, beta-amyloid aggregation, and tau protein post-translational modifications, ultimately leading to AD. However, ApoE4 amphipathic properties constitute a major hurdle for comprehensive protein folding, and structural studies, as well as for structure-based drug design campaigns. Currently, an NMR-derived structure of a monomeric ApoE mutant, and a computational model of an ApoE4 intermediate state have been reported in literature. These two structural models may provide insight into the ApoE4 pathological mechanisms implicated in AD. The goal of this study is to rationally design mutations that alter the structural stability of the native and intermediate conformations of ApoE4 with the aim to clarify the role of these specific states in AD onset. Methods: Models for the native and intermediate conformations of wild type (WT) ApoE4 have been derived using NMR spectroscopy data and discrete molecular dynamics simulations, respectively. Mutations altering the structural stability of the two ApoE4 conformations have been modeled using Eris, an in-house developed software that evaluates the relative thermodynamic stability (ΔΔG) of potential mutations in a given protein structure. Results: Several mutations, computationally introduced throughout the WT-ApoE4 structure, exhibited ΔΔG values that specifically alter the conformational stability of the ApoE4 intermediate state. In particular, the hydrophobic mutations R213Y, K242I and E231I, are directly responsible for the further stabilization of N- and C-terminal domain interactions, which characterize the ApoE4 intermediate conformation. Additionally, destabilizing mutations such as W210P and R90F are found within regions of intradomain protein interactions or in ApoE4 distal helices. Conclusions: The set of predicted mutations suggests the possibility to control the stability of different conformational states of ApoE4. This data can provide useful information on the role of an ApoE4 intermediate state in AD pathogenesis, and provide a tool for the future development of conformation-driven in-cell studies.

P2-069 RESTING-STATE ABNORMALITIES IN AMNESTIC MILD COGNITIVE IMPAIRMENT: A META-ANALYSIS
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Background: Amnestic mild cognitive impairment (aMCI) is a prodromal stage of Alzheimer’s disease (AD). Once diagnosed, AD is irreversible and there is currently no effective drug that can cure this disease. Therefore, early diagnosis and intervention for aMCI are urgently needed. The standard diagnostic procedure of aMCI primarily relies on subjective neuropsychological examinations that required the judgment of experienced clinicians. It is necessary for the development of other objective and reliable aMCI markers, such as neural markers. Previous neuroimaging studies revealed abnormalities in regional resting-state activity in MCI patients, however, the findings are being inconsistent. The current study provided an updated activation likelihood estimation (ALE) meta-analysis of resting-state functional magnetic resonance (fMRI) data on aMCI. Methods: The authors searched on the MEDLINE/PubMed databases for whole-brain resting-state fMRI studies on aMCI published until March 2015. Twenty-one wholebrain resting-state fMRI studies that reported a total of 156 distinct foci in either Montreal Neurological Institute (MNI) or Talairach coordinates were included. Studies were excluded if (1) only non-amnestic MCI or only subtypes of aMCI were included and without a control group; (2) subjects had a history of neurological, psychiatric, or any systemic disease that could influence cognitive functions (e.g., stroke, depression, alcoholism, drug abuse); (3) a priori region of interest (ROI) analysis or a seed-based functional connectivity analysis was conducted; or (4) the effects of medication were tested without reporting fMRI data at baseline. Results: Significant regional resting-state differences were consistently found in the posterior cingulate cortex (PCC), right angular gyrus, right parahippocampal gyrus, left fusiform gyrus, left supramarginal gyrus and bilateral middle temporal gyri in patients with aMCI relative to controls. Conclusions: Our findings support that abnormalities in resting-state of these regions may serve as neuroimaging markers for aMCI.

P2-070 SEEAB: A NOVEL METHOD FOR VOLUMETRIC ANALYSIS OF AMYLOID PLAQUES
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Background: One of the main neuropathological hallmarks of Alzheimer’s disease (AD) is the presence of plaques which consist of aggregated extracellular amyloid beta (Aβ) protein. Patients with early onset or familial AD (FAD) often harbor genetic mutations that bias processing towards this amyloidogenic outcome, accelerating disease onset and worsening disease severity. Elevated levels of Aβ peptides are thought to be a key component of the disease state; thus, characterizing the spatial and temporal profile of amyloid plaque deposition may yield important insights into the mechanisms that cause and...