proceeded with a stratification based on cardiovascular risk, calculated by categorizing each CRF (expressed as 0 - normative level, 1 - moderate increase, 2 - considerable increase), summing, and dichotomizing all scores (0-2 for low risk, 3 and higher for high risk). **Results:** The best-obtained model, with area under ROC curve of 80.1, contained the following variables: hypertension, triglycerides, cholesterol, glucose, right hippocampus, right inferior lateral ventricle, right middle temporal, and parahippocampal left-right difference. Stratification by cardiovascular risk provided two models: (a) low cardiovascular risk and right middle temporal and parahippocampal left-right difference resulted in ROC 72.6%, accuracy 65.8%, sensibility 57.5% and specificity 70.1%, positive likelihood ratio 1:,9 and negative likelihood 0:,6 at the probability level of 0.6; (b) high cardiovascular risk and right hippocampus and right inferior lateral ventricle resulted in ROC 81.5%, accuracy 71.4%, sensibility 86.0% specificity 44.4%, and positive/negative likelihood ratios of 1.55 and 0.32 respectively at the probability level of 0.5. **Conclusions:** The results from our models to predict progression in those aMCI with low global cognition using CRF and volumetric data have comparable positive/negative likelihood ratios than those described for MRI alone in the general aMCI population (LR+: 2.6; LR-: 0.46-0.5). Thus, in this dataset, the impact of cardiovascular factors on aMCI progression to AD is considerable, and stratification by cardiovascular status could have clinical sense.

P4-114 PROGNOSTIC UTILITY OF MRI ATROPHY MEASURES IN AMNESTIC MILD COGNITIVE IMPAIRMENT PATIENTS WITH MINIMAL COGNITIVE DECLINE

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Background: The utility of MRI atrophy measures for predicting progression of amnestic MCI (aMCI) to Alzheimer's disease (AD) is limited, as evidenced by proven prognostic likelihood ratios (LR; positive LR = 2,9; negative LR = 0,49-0,56)(Frisoni et al., Neurology 2013) that are outside the ranges usually required for clinical implementation (LR+ >= 5,0 and LR- <= 0,2). We tested the hypothesis that stratification of patients by global cognitive function could improve the prognostic value of MRI. **Methods:** We selected 147 aMCI subjects from the ADNI-1 database with MMSE = [28-30] at baseline and 195 with MMSE = [24-27] for which we had complete MRI volumetric results (FreeSurfer) and general primary-level information. We created a prognostic model for progression to AD within 36 months based on these measures. **Results:** The model that included left hippocampal volume and left mid-temporal cortical thickness, when adjusted for intracranial volume, age and sex, had a 87.4% area under ROC curve (AUC), 80.3% classification accuracy, 53.8% sensitivity, 88.2% specificity, LR+ = 4,81 and LR- = 0.49 (with classification cut-point of disease probability = 0.4). After excluding statistical outliers (three subjects; impact chi-square (dl 6)=12.59), the same model had AUC of 91.1%, 81.9% classification accuracy, 71.4% sensitivity, 85.3% specificity, LR+=4.9 and LR-=0.3 (with classification cut-point of 0.3). Applying the same model to the ADNI aMCI subjects with baseline MMSE in the [24-27] range gave a AUC of 64.5 %. In fact, simply adding a dichotomous variable in the MRI model for cognitive status (i.e. baseline MMSE in range [24-27] or [28-30]) gives a AUC of 73.3% for all aMCI in the ADNI-1 population. **Conclusions:** A clinically relevant prognostic significance for left hippocampal volume and left mid-temporal cortical thickness, when adjusted for intracranial volume, age and sex, has been observed in ADNI-1 aMCI subjects with baseline MMSE in the [28-30] range. The prognostic LR+ and LR- observed in these strata is higher than previously described for a more general population and reaches clinical applicability.

P4-115 ALTERED FUNCTIONAL CONNECTIVITY AND GLOBAL NETWORK PROPERTIES IN AMNESTIC MILD COGNITIVE IMPAIRMENT

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Background: Amnestic mild cognitive impairment (aMCI) patients demonstrate lower global network interactions. However, graph theory (GT) analysis has not been used to examine networks compromised by strong amyloid (A β) deposition, such as the default mode network (DMN). In addition, no study directly compared GT and functional connectivity (FC) analysis between healthy controls (HCS) and aMCI with respect to Aβ and APOE genotype. Based on the known structural and functional impairments in MCI, we hypothesize that FC and global network interactions are reduced in MCI and in subjects with Aβ load and ε4 allele presence. **Methods:** We compared 24 HCS to 15 matched aMCI by resting-state fMRI. FC (within the DMN) and GT (whole-brain) analyses were performed with the toolbox CONN at $p<0.05$ (corrected). Three group comparisons were examined: HCS versus aMCI, PiB- versus PiB+ (i.e., significant global PiB load), and APOE+ (ε4 carrier) versus APOE-. The DMN regions were: superior prefrontal cortex (sPFC), medial PFC (mPFC), ventral PFC (vPFC), anterior (aPFC), posterior cingulate cortex (PCC), lateral posterior parietal cortex (PPC), retrosplenial cortex (RSC), parahippocampal gyrus (PHG), cerebellar tonsils (CT), and inferior temporal cortex (ITC). For GT we looked at global- and local efficiency (LE), clustering coefficient (CC), and cost. **Results:** HCS demonstrated stronger FC between sPFC - RSC, left PPC - right sPFC, and mPFC - left sPFC. PiB+ subjects showed lower FC for: mPFC - CT, vPFC - aPFC, vPFC - left sPFC, aPFC - left sPFC, and left PPC - dACC. PiB+ showed stronger FC between left and right PHG, left PPC - RSC, and left PHG - aPFC. APOE- demonstrated higher FC between left PPC - dACC, vPFC - aPFC, left sPFC - left PPC, mPFC - right ITC, vPFC - RSC, and aPFC - ITC. HCS showed higher cost in the sPFC and PCC, and LE in the dorsolateral PFC. PiB- yield stronger LE and cost in temporal, visual, and frontal regions. APOE- exhibits higher LE and CC in temporal and visual areas. **Conclusions:** The spatial extent of FC reductions (especially in prefrontal-related connections) depends on the presence of Aβ and APOE. GT results suggest lower local network interactions and cost in MCI, as well as higher efficiency in PiB- and APOE-individuals.

P4-116 DIRECT *IN VIVO* ASSESSMENT OF SEX-RELATED METABOLIC DIFFERENCES IN A MOUSE MODEL OF ALZHEIMER'S DISEASE BY MRI

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Background: Emerging evidence suggests that Alzheimer's disease (AD) disproportionately affect women in both occurrence and severity. However, little is known about the biological mechanisms underlying these sex differences. There are evidences that changes in metabolism may be present earlier than structural brain changes during AD development. In this study, we present a systematic longitudinal *in vivo* MRI study in combination with in vivo spectroscopy to investigate the sex-related structural and metabolic differences in various brain regions of AD mouse. **Methods:** *In vivo* metabolic profile and anatomical differences were monitored longitudinally in same male and female AβPPswe, PSEN1dE9 and AβPPswe transgenic (tg) mice and wt littermates using MRI and novel localized two dimensional MR spectroscopy at 9.4T. At each time point histological analysis were performed in separate male and female mice of same age group. To investigate significant age, sex and tg related differences, a mixed model analysis was performed. **Results:** Our results show difference in metabolic profile in male and female AD mice including apparent decline in glucose, excitatory neurotransmitter glutamate as well as decrease in neuronal marker N-acetylaspartate (NAA) in cortex and hippocampus. Histological comparisons show that some of these metabolic changes appear earlier than the pathological differences and may have mechanistic role in sex-specific differences in AD development. **Conclusions:** Our results provide evidence that metabolic changes during AD development are clearly influenced by sex. These results are in line with the known higher risk of AD in women.