is defined by neuritic plaques and neurofibrillary tangles accumulation that lead to the loss of synapse in the neurons. Degeneration is associated with an increase of cholesterol levels in the plasmatic membrane of the neurons. The cholesterol excess can be eliminated of the cell by several routes: cholesterol can be esterified and stored within the cell as cholesterol esters or it can be oxidized and turned into oxyesterols. The oxyesterols are more soluble than cholesterol and are excreted of the cell associated with lipoproteins particles. Several authors have reported an increased risk of Alzheimer's disease and intronic variants in CYP46A1. In Mexico, molecular studies do not exist that allow to identify the risk factors related to Azheimer's disease. Objective of this work is determine if the presence of two intronic polymorphism (rs754203 and rs4900442) in CYP46A1 is related to Alzheimer disease in Mexican patients and their association with ApoE4 genetic variant. **Methods:** Genotyping of SNPs was performed by using qPCR, in cinically diagnosed patients with AD and controls, in a Mexican population and its association with ApoE4. The diagnosis included medical history, neurological and psychiatric examinations, screening laboratory tests and electroencephalography. **Results:** Genotype distributions in case and control groups for the rs754203 or rs4900442 markers shows an association with Alzheimer's disease patients, but does not exist with relation to ApoE4. **Conclusions:** We propose that the CYP46 intron 2 polymorphism could confer increased susceptibility for AD in our patient. Nevertheless it is important to identify the ApoE4 distribution and then to define the role of this marker as risk factor in Alzheimer's disease in Mexican population.

P-023 ARTERIAL SPIN-LABELING MR IMAGING IN MIDDLE-AGED ADULTS AT RISK FOR ALZHEIMER'S DISEASE: ASSOCIATION OF CLINICAL MEASURES OF GLOBAL VASCULAR RISK WITH QUANTITATIVE CEREBRAL PERFUSION

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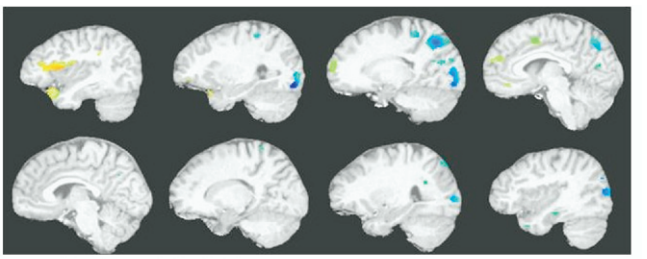
Background: Cerebrovascular dysregulation is one of the earliest pathologic changes in the development of Alzheimer's disease (AD). While studies strongly support an association between vascular risk factors and the development of AD, little is known about the relationship between global vascular risk and quantitative cerebral blood flow (qCBF) in asymptomatic middle-aged adults at risk for AD. **Objective:** To describe the relationship between an established measure of global vascular risk (Framingham 10-Year Cardiovascular Disease [CVD] Risk %) and qCBF using arterial spin-labeling MRI (ASL-MRI) in asymptomatic middle-aged adult children of persons with AD. **Methods:** In a cross-sectional preliminary analysis, 11 participants had ASL-MRI performed using a background suppressed pseudo-continuous arterial spin labeling sequence on a 3T GE Signa scanner using an 8 channel head coil. Vascular risk factors were measured and Framingham risk % was calculated, which factors in measures of age, total and HDL cholesterol, smoking status, and systolic blood pressure. Images were spatially normalized to a template brain space, smoothed, and voxel-wise statistical analyses were performed using a voxel-level threshold $P<0.005$ and corrected voxel number and cluster size, equivalent to group level $P<0.05$. Regions of interest were isolated and mean qCBF for each region was measured. **Results:** Participant characteristics are shown in the Table. Mean Framingham risk score was 12 ± 3 points, corresponding to a 10-year CVD risk of 4%. On ASL-MRI, qCBF was inversely correlated with 10-year CVD risk % on voxel-based analyses (Figure). When regions of interest were isolated, 10-year CVD risk % was consistently inversely related to qCBF in the superior frontal gyrus ($r=-0.817$, $p=0.002$), middle temporal gyrus ($r=-0.787$, $p=0.004$), parietal lobe ($r=-0.773$, $p=0.005$), posterior cingulate ($r=-0.744$, $p=0.009$), parahippocampus ($r=-0.691$, $p=0.019$), and hippocampus ($r=-0.594$, $p=0.054$). **Conclusions:** In a preclinical population of middle-aged adults at risk for AD, increased global vascular risk burden may already be negatively affecting CBF in areas of the brain involved with memory and learning. Future clinical trials are needed to clarify the impact of reduced cerebral perfusion on the risk of developing AD in asymptomatic adults.

Table
Participant Characteristics (n=11)

Characteristic	Value (mean ± SD)
Age, y	54.6 ± 7.9
Women, n (%)	9 (82)
APOE4 carriers, n (%)	4 (36)
Systolic blood pressure (mm Hg)	130.3 ± 19.4
Current tobacco use, n (%)	2 (18)
Total cholesterol, mg/dL (mmol/L)	212.3 ± 34.5 (5.5 ± 0.9)
HDL cholesterol, mg/dL (mmol/L)	68.9 ± 19.6 (1.8 ± 0.5)
Body mass index (BMI), kg/m^2	27.9 ± 4.7
Diabetes mellitus, n (%)	0 (0)



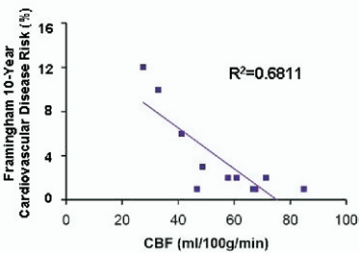


Figure. Correlation of ASL qCBF with a global measure of vascular disease risk (Framingham 10-year % risk for coronary heart disease) in 11 middle-aged adults at risk for AD (using a voxel-level threshold P<0.005 & corrected voxel number & cluster size; equivalent to group level P<0.05). Areas showing significant associations include left precuneus, left inferior frontal gyrus, left medial frontal gyrus, & right middle occipital gyrus.

P-024 THE PATTERN AND SEVERITY OF FDG PET ABNORMALITIES IN ALZHEIMER'S DISEASE AND AMNESTIC MILD COGNITIVE IMPAIRMENT: PRELIMINARY FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

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Background: Patients with Alzheimer's disease (AD) [18]F-fluorodeoxyglucose (FDG) positron emission tomography (PET) measurements of the cerebral metabolic rate for glucose (CMRgl) in posterior cingulate, precuneus, and parietotemporal regions, which are correlated with dementia severity. Patients with amnestic mild cognitive impairment (MCI) who

subsequently convert AD also have abnormally reduced CMRgl in some of these same brain regions. In this study, we used PET images from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (www.loni.ucla.edu\ADNI) to directly compare the FDG PET images of patients with AD, patients with MCI and elderly normal controls (NC). **Objective(s):** To compare the pattern and magnitude of regional-to-whole brain CMRgl reductions in ADNI patients with AD and MCI. **Methods:** FDG PET images from 16 AD patients, 27 MCI patients and 27 NC were analyzed using SPM5. An ANOVA with pair-wise comparisons contrasted regional CMRgl in the three subject groups. A conjunction analysis characterized brain regions with significantly reduced CMRgl in both patient groups. A simple linear regression characterized the relationship between the magnitude of regional CMRgl reductions and clinical severity after assigning the NC, MCI and AD groups to clinical severity values of 0, 1 and 2, respectively. **Results:** In comparison with the NC, the AD and MCI groups each had lower CMRgl in posterior cingulate, precuneus, and parietotemporal regions ($P<0.05$ after correction for multiple comparisons), search regions implicated in a previous PET study of AD; they also had lower CMRgl in occipital cortex, the hippocampus, parahippocampal gyrus and fusiform gyrus ($P<0.005$, uncorrected for multiple comparisons). Based on the conjunction analysis, the AD and MCI groups each had lower CMRgl than the NC in the same posterior cingulate-precuneus and parietotemporal regions. CMRgl reductions in the posterior cingulate, precuneus and parietotemporal regions were correlated with group-related increases in clinical severity ($P<0.05$ after correction for multiple comparisons in the whole brain using FWE). **Conclusions:** This direct comparison of three subject groups confirms the similar distribution of FDG PET abnormalities in patients with AD and MCI, and its correlation with clinical severity. It also supports the comparability of measurements from different sites and scanners in the ADNI.

P-025 MRI ATROPHY IN MCI IS SPECIFIC, NOT SENSITIVE, FOR PROGRESSION TO ALZHEIMER DISEASE

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Objective: To develop simple and useful predictors of progression to dementia for patients with Mild Cognitive Impairment (MCI) encountered in a North American Memory Clinic using bedside testing and MRI volumetrics. **Background:** Over half of MCI individuals will progress to dementia within 3 to 5 years, and if there is amnestic MCI this is usually AD. We have found that simple clinical stratification of risk is possible in many cases. Atrophy on MRI is another known risk for progression. **Methods:** Forty elderly subjects referred to a teaching hospital Memory Clinic and meeting criteria for Amnestic MCI (with or without added cognitive deficits), were followed longitudinally up to 10 years since symptom onset. A large battery of neuropsychological tests, cognitive reaction time markers, along with MRI volumetric measurements of hippocampal volume and ventricular atrophy were carried out. **Results:** At end of a mean seven year follow-up period (10 years since symptom onset) 26 subjects had deteriorated to dementia, and 14 had not. It was found that a clinical algorithm with four cut-off scores (for Age, MMSE, orientation, and clock drawing) would have accurately stratified risk of progression for 22/40 into subgroups showing a very low risk or a very high risk of progression. The other 18 subjects were termed borderline or uncertain in terms of risk. Complementary use of cut-off scores from MRI imaging (an atrophy ratio measure) would have added another 4/40 subjects to the very high or very low risk subgroups. All of those 15 subjects showing atrophy beyond normal range progressed to dementia, while 12 of the 23 lacking atrophy also progressed. **Conclusions.** MRI added prognostic precision above simple clinical stratification in 4/40 cases. The presence of MRI atrophy in MCI is a specific, but not a sensitive marker for risk of progression.

P-026 VALIDITY OF THE CDR-SOB AND MMSE AS A MEASURE TO MONITOR THE PROGRESSION OF ALZHEIMER'S DISEASE

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Background: The Mini-Mental State Examination (MMSE) has been popularly used to monitor AD progression. However, as an AD progression measure, the MMSE has some limitations including its poor ability for measuring executive function and visuoconstructional ability, and floor effect in severely demented cases. The sum of boxes of clinical dementia rating (CDR-SOB) is based on detailed clinical interview and expected to overcome the limitations of the MMSE in monitoring AD progression. **Objective(s):** This study aimed to compare the validity of the CDR-SOB and MMSE as a measure of AD progression by elucidating the functional neuroanatomical correlates related to each measure. **Methods:** 128 AD patients were included after a standardized clinical assessment and neuropsychological testing. All candidates were examined by neuropsychiatrists according to the protocol of the Korean Version of the Consortium to Establish a Registry for Alzheimer's disease Assessment Packet (CERAD-K). All AD subjects underwent [18F] fluoro-deoxyglucose positron emission tomography (18F-FDG PET) scan. Correlation between regional cerebral glucose metabolic rate (rCMRglu) and the CDR-SOB or MMSE was analyzed on voxel-by-voxel basis using SPM99. A height threshold p-value of <0.001(uncorrected for multiple comparisons) was applied to test the significance of correlations. The MNI coordinates of the local maximum of each voxel cluster were converted into Talairach coordinates. **Results:** Significant negative correlations between CDR-SOB scores and rCMRglu were found in right inferior parietal lobules ($\times$, y, z = 50, -56, 43, $Z=3.40$, Brodmann area (BA) 40), right posterior cingulate cortex (4, -38, 26, $Z=3.37$, BA 31), and left inferior parietal lobule (-50, -54, 45, $Z=3.29$, BA 40) in 128 AD patients. Positive correlations between MMSE scores and rCMRglu were found in the left inferior parietal lobule (-48, -60, 44, $Z=4.36$, BA 40), left superior temporal gyrus (-38, -53, 25, $Z=3.92$, BA 39), and left precuneus (-4, -73, 52, $Z=3.25$, BA 7) in the same AD patients. **Conclusions:** Whereas the MMSE was related only to left side brain function, the CDR-SOB was correlated with bilateral brain function. This finding indicates that the CDR-SOB is a more valid measure to monitor AD progression than the MMSE.

P-027 CSF TRANSTHYRETIN LEVELS ARE ASSOCIATED WITH APOE GENOTYPE AND CSF Aβ42 IN AD

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Background: Transthyretin (TTR) is a carrier protein that binds retinol, thyroxine, and β-amyloid (Aβ). TTR facilitates the transport of Aβ from the brain, prevents amyloid formation, and may thereby reduce Aβ deposition. Transthyretin expression may be reduced in AD brain, and proteomic studies have documented differential post-translational oxi-