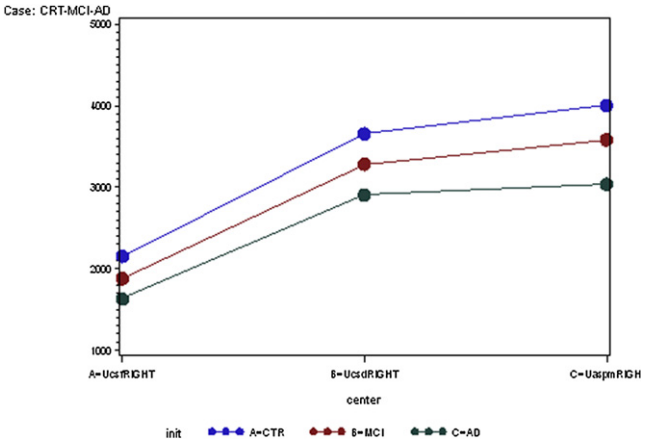
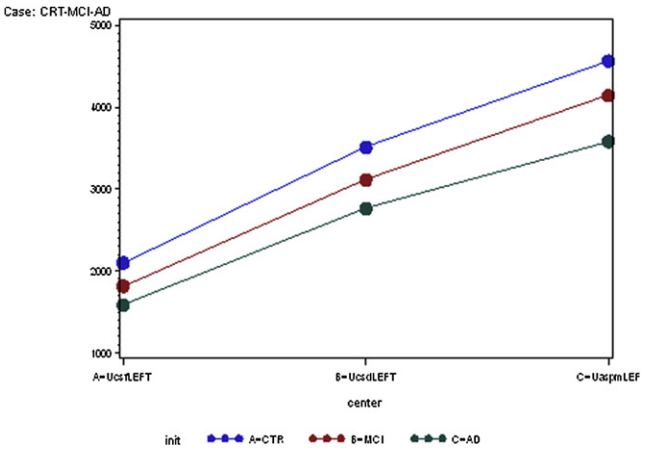
(e.g. manual segmentation), it is impossible at this point to determine which, if any, of the technique is more desirable. However, results point to the necessity of a harmonized HC segmentation protocol that would serve to reduce measurement variability.





Automatically generated HC volumes for three centers

Group (N)	Left HC (mean (SD) in mm3)	Right HC (mean (SD) in mm3)
CTRL (149)	UCSF - 2101 (284)	UCSF - 2154 (306)
	UCSD - 3511 (386)	UCSD - 3660 (462)
	UASPM - 4568 (751)	UASPM - 4004 (910)
MCI (266)	UCSF - 1818 (364)	UCSF - 1882 (375)
	UCSD - 3115 (529)	UCSD - 3285 (565)
	UASPM - 4145 (854)	UASPM - 3585 (992)
AD (116)	UCSF - 1584 (319)	UCSF - 1629 (3610
	UCSD - 2762 (474)	UCSD - 2907 (525)
	UASPM - 3584 (743)	UASPM - 3039 (854)

P4-123 ROBUST IDENTIFICATION OF AMNESTIC MCI PROGRESSORS TO PROBABLE AD VIA BASELINE MRI ANALYSIS

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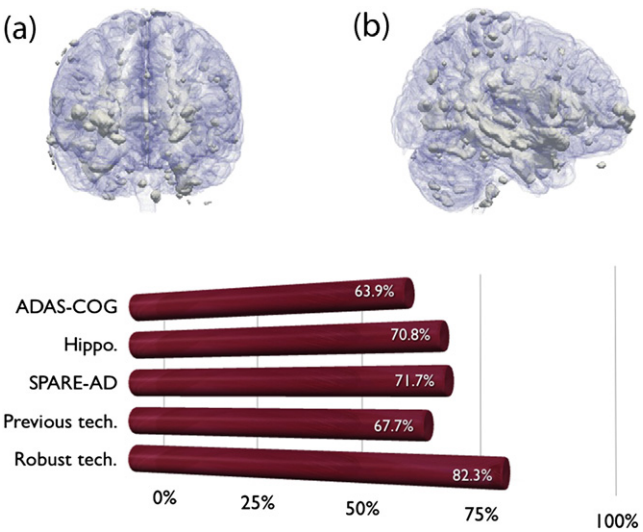
Background: MR images taken from different centers appear dissimilar due to a variety of scanner-dependent effects. This situation is particularly acute in large, multi-centric settings such as ADNI. Our goal was to assess the accuracy of prediction to progression to AD for ADNI MCI subjects for an automated classification technique (Duchesne et al, Neurobiol. Aging 2008). **Methods:** A total of 481 subjects were available for final analysis. The Volume of Interest (VOI) Group consisted in 75 probable AD and 75 age-matched controls from the LENITEM dataset. The Study Group consisted in 331 MCI subjects from ADNI (129 progressors (1.50 years (SD: 0.69 years)) and 202 stable). MRI data for the VOI Group were acquired in Italy on a 1.0T scanner; ADNI data were acquired on 56 different 1.5T scanners. To increase technique robustness, we added noise removal and intensity standardization to the previous image pipeline. Model features were local volume change and standardized intensity sampled in a pathology-specific VOI, defined as areas of grey matter differences between AD/controls in the VOI group (Figure 1). We randomly split the Study Group in a Model Group of 166 and a Test Group of 165 subjects. We generated a linear model of 134 normally distributed image features explaining 95% of data variance from the Model Group. We projected Test Group data in the model space, and assessed classification accuracy with forward, stepwise linear discriminant analysis (p-to-enter = 0.15) in a k-fold fashion (k=10), averaged over 5 trials. **Results:** We obtained 82.3% accuracy, 77.5% specificity, and 85.9% sensitivity with a median number of 37 variables in the discrimination function. We performed comparison studies using other publicly available data (ADAS-COG; hippocampal volumes; SPARE-AD) (these were not available for all subjects). Of note, classification based on SPARE-AD reached 71.7% accuracy on a subset of 61 MCI (Figure 2). **Conclusions:** With a predictive accuracy of 82.3%, on average 1.5 years before progression to clinically observed AD, the technique has the potential to alter patient management in a timely fashion, by tailoring follow-up and therapy choices.



P4-124 DEVELOPMENT AND VALIDATION OF A BRIEF COGNITIVE SCREENING INSTRUMENT: THE SWEET 16

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Background: Cognitive impairment contributes to loss of independence, decreased quality of life, and increased health care costs among older adults, but is often unrecognized. Current screening instruments are underutilized, may lack sensitivity in particular groups, and may be restricted by copyright

laws. **Objective:** To develop and validate the Sweet 16, a new open-access screening instrument for cognitive impairment. **Methods:** The Sweet 16 was developed in a cohort of 918 participants from the Yale Delirium Prevention Trial. Performance of the Sweet 16 was compared against the Mini-Mental State Examination (MMSE) and modified Blessed Dementia Rating Scale (mBDRS). Equipercentile equating was used to identify cutpoints correlating with clinically acceptable cutpoints of the MMSE. Performance characteristics of the Sweet 16 were also validated in a separate cohort of 709 participants from the Aging, Demographics, and Memory Study by comparison against the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) as an independent reference standard for cognitive impairment. **Results:** The instrument can be administered in 3 minutes or less with minimal training. In the development cohort, the Sweet 16 was highly correlated with the MMSE (Spearman's rho=0.80, P<.001) and the mBDRS (Spearman's rho=-0.38, P<.001). When validated against the IQCODE, the area under the curve (AUC) was 0.84 for the Sweet 16, and 0.81 for the MMSE (P=0.06). A Sweet 16 score <14 (approximately equivalent to MMSE <24) with a sensitivity of 81% and specificity of 76%, performed better than the MMSE, which had a sensitivity of 64% and specificity of 86%. Analysis by education demonstrated that for higher education (≥12 years) the AUC for the Sweet 16 was 0.89 and for the MMSE 0.84 (p = 0.03). The sensitivity of the Sweet 16 score <14 was superior to the MMSE across every quartile of education. **Conclusions:** We have developed and validated a brief cognitive screening instrument that is quick, easy to administer, and will be open-access. We have identified cutpoints on the Sweet 16 that are consistent with those widely used for the MMSE, and the performance characteristics of the Sweet 16 are superior to the MMSE across all levels of education.

P4-125 APP ANTISENSE REVERSES LEARNING AND MEMORY DEFICITS IN TWO MOUSE STRAINS OF ALZHEIMER'S

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder of the central nervous system (CNS). Learning and memory deficits are the hallmark of Alzheimer's disease. Studies have revealed that beta amyloid (Aß) plays a key role in these deficits. Elevated brain levels of Aß lead to oxidative damage in the brain resulting in learning and memory deficits. The SAMP8 mouse has a natural mutation that produces an age-related impairment in learning and memory that is driven by an age-related increase in brain levels of Aß. All of these AD-like characteristics are reversed by administration into the brain of antibody to Aß and antisense oligonucleotide, termed mOL-1 that is directed at amino acids 17-30 of Aß1-42, a region homologous between human and mouse. **Methods:** Here, we tested mOL-1 in SAMP8 mice and Tg2576 mice two models of Alzheimer's disease using both peripheral and central injections. SAMP8 mice were tested in object recognition with a 24 hour delay after tail vein injection. We also tested our mOL-1 in the Tg2576, that overexpresses the human APP gene and have an age-related impairment in learning and memory, elevated brain levels of Aβ, and increased oxidative damage in the hippocampus. We administered mOL-1, intracerebroventricularly (ICV) to 13 month old Tg2576 mice. We tested the mice in T-maze foot shock avoidance. **Results:** The SAMP8 mice that received a random control antisense spent 39.67% of the time investigating the novel object whereas the mice which received OL-1 spent 59.9% of the time exploring the novel object. The Tg2576 mice treated with mOL-1 took 9.00 ± 0.72 trials to make an avoidance whereas the Tg2576 mice treated with random antisense took 14.50 ± 1.73. The age-matched wild type controls took 10.09 ± 0.66. On the one week retention test the mOL-1 treated Tg2576 mice took 8.73 ± 0.63 to reach criterion 5 avoidances in 6 consecutive trials, the Tg2576 mice that received random antisense took 16.20 ± 2.58 and the wild type controls took 9.00 ± 0.58 trials to reach criterion. **Conclusions:** The current findings indicate that antisense oligonucleotide can reverse learning and memory impairment produced by Aβ in both strains of mice.

P4-126 COGNITIVE PERFORMANCE CORRELATES WITH RESTING STATE CONNECTIVITY AND IS EFFECTED BY APOE STATUS

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Background: Deactivation of the default mode network (DMN) has been identified during performance of multiple cognitive tasks. The mechanism coordinating DMN deactivations during cognitive tasks is unknown, but the fronto-insular cortex (FIC) has been theorized to play an important role. It has been established that the DMN's ability to deactivate is impaired in Alzheimer's disease (AD) suggesting differences in DMN in populations at risk for AD i.e. APOE ϵ4 allele carriers. In this study, we investigated differences in the correlation of neuropsychometric performance in multiple cognitive domains with DMN resting state connectivity in cognitively normal (CN) elderly with and without ϵ4 alleles. **Methods:** We studied 47 (mean age = 79.9) CN ϵ4 non-carriers and 46 age, gender, and education matched CN ϵ4 carriers. Subjects underwent EPI-BOLD resting state functional MRI (fcMRI) scanning sessions. Seed based voxel-wise connectivity maps were created for each subject using a 6mm seed in the posterior cingulate cortex (PCC). The r-z transformed results were then correlated with performance on summary indices in the major cognitive domains (memory, attention, language, and visual-spatial) in a multiple regression model utilizing regressors created from the domain scores from formal neuropsychometric testing. **Results:** Figure below shows the within-group multiple regression result for non-carriers (left) and carriers (right). In CN non-carriers, decreases in all cognitive domain scores correlated with an increase in PCC connectivity to the left FIC (FDR $p < 0.006$) and decreases in the PCC connectivity to the right FIC and bilateral precuneus (uncorrected $p < 0.001$). In CN carriers, decrease in all cognitive domain scores correlated with an increase in PCC connectivity to the right temporoparietal junction (FDR $p < 0.003$) and a decrease in the PCC connectivity to the left lateral orbitofrontal cortex and cerebellar vermis (FDR $p < 0.05$). **Conclusions:** Within CN non-carrier and carrier groups, cognitive performance was associated with resting state connectivity of the PCC. However, the qualitative nature of correlations between PCC connectivity and cognitive performance differed between carriers and non-carriers. We conclude that the FIC appears to be integral to maintaining healthy network dynamics, and connectivity in this region may serve as a biomarker for cognitive function.

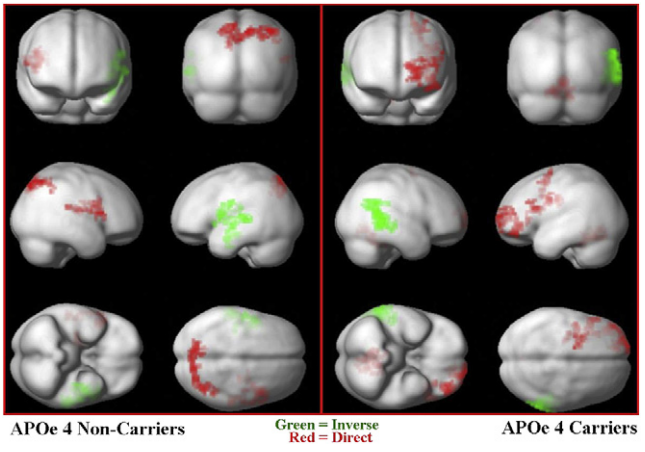

Fig 1. Within-group VW-PCC connectivity multiple regression with all cognitive domains.