without a positive score on the Disinhibition item or the Aberrant Motor Behavior item. In a follow-up analysis, we examined correlations between Agitation factor score and metabolism in the three cortical volumes identified in the SPM analysis. Agitation factor score was inversely correlated with metabolic activity in each (rs = 0.35 - 0.36; p < .001), indicating that symptom severity is associated with the extent of hypometabolism.

**Conclusions:** Dysfunction in right temporal/midfrontal and bilateral cingulate cortex contributes to angry, irritable, and hostile behavior in AD, but impulsive, disinhibited, and repetitive motor behaviors may not localize to discrete cortical circuits in AD. Distinct biomarkers for specific “agitated” behaviors can reveal intermediate phenotypes that can improve understanding of behavioral phenomenology and promote optimal interventions in AD.

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**IC-P-176 COGNITIVE RESERVE AND ALZHEIMER’S DISEASE BIOMARKERS ARE INDEPENDENT DETERMINANTS OF COGNITION**

Prashanthi Vemuri, Stephen Weigand, Scott Przybelski, David Knopman, Glenn E. Smith, John Trojanowski, Leslie Shaw, Charlie DeCarli, Owen Carmichael, Matt Bernstein, Paul Aisen, Michael Weiner, Ronald Petersen, Clifford Jack, Rochester, Minnesota, United States; University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, United States; University of California at Davis, Davis, California, United States; UC San Diego, La Jolla, California, United States; VA Medical Center, San Francisco, California, United States.

**Background:** To investigate how a measure of educational and occupational attainment, a component of cognitive reserve, modifies the relationship between biomarkers of pathology and cognition in AD. The biomarkers evaluated were neurodegeneration via MRI atrophy, neuronal injury via CSF t-tau, brain Aβ amyloid load via CSF Aβ42 and vascular disease via white-matter hyperintensities (WMH) on T2/PD MRI.

**Methods:** We included 109 cognitively normal (CN), 192 amnestic-MCI and 98 AD subjects from the ADNI-study who had baseline lumbar-puncture and MRI. We combined MCI and AD subjects in a group labeled “cognitively-impaired” subjects. STAnD-scores, which reflect the degree of AD-like anatomic features on MRI were computed for each subject. We assessed ADAS-Cog and MMSE as measures of general cognition and AVLT delayed recall, Boston naming and Trails B as measures of

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**Figure 1.** Scatter plots of Mini Mental State Exam (MMSE) versus imaging and CSF-based neuropathology markers. Superimposed line represents estimated mean MMSE as a function of the neuropathology marker for varying levels of AMNART. The red line represents the 15th percentile of 4 errors on AMNART indicating a “good” score, the blue line represents the median of 12 errors indicating an “average” score, and the green line represents the 85th percentile of 24 errors indicating a “bad” score. The shaded region about the blue line indicates a 95% bootstrap confidence interval. These estimates come from penalized ordinal logistic regression models as described in the methods.

**Figure 2.** Model illustrating the independent effect of cognitive reserve on the relationship between biomarkers of pathology and cognition in subjects with (A) Low (B) Average and (C) High cognitive Reserve. Clinical disease stage is indicated on the horizontal axis and the magnitude of biomarker abnormalities (from normal to maximally abnormal) on the vertical axis. The biomarker curve labels are indicated in panel A. In panels A and C, the levels of Aβ are indicated by a square and the levels of atrophy are indicated by a circle at the point where CN progress to MCI. This illustrates that an equivalent clinical diagnostic threshold, subjects with high CR have greater biomarker abnormalities than low CR subjects.
specific domains in both groups of subjects. The number of errors on American National Adult Reading Test (AMNART) was used as a measure of environmental enrichment provided by educational and occupational attainment, a component of cognitive reserve. **Results:** Among CN, none of the biomarkers correlated with the measures of cognition whereas AMNART was significantly correlated with Boston naming and MMSE. Incognitively-impaired subjects, AMNART and all biomarkers of neuronal pathology and amyloid load were independently correlated with all cognitive measures. Exceptions to this general conclusion were absence of correlation between CSF Aβ42 and Boston naming and Trails B. In contrast, WMH were only correlated with Boston naming and Trails B in the cognitively-impaired. When all subjects were included in a flexible ordinal regression model that allowed for nonlinear effects and interactions, we found that AMNART had an independent additive association such that better AMNART performance was associated with better cognitive performance across the biomarker distribution (Fig. 1). **Conclusions:** 1) In CN, the variability in cognitive performance is explained partly by AMNART and not by biomarkers of AD. 2) In cognitively-impaired subjects, AMNART, biomarkers of neuronal pathology and amyloid load all independently explain variability in cognition. 3) Finally, the association between cognition and AMNART was found to be additive rather than to interact with biomarkers of AD (illustrated in Fig. 2).

**IC-P-177**  
THE IMAP* PROJECT: THE PARADOX OF THE POSTERIOR CINGULATE CORTEX IN ALZHEIMER’S DISEASE: ATROPHIC, HYPOMETABOLIC, BUT STILL ABLE TO SHOW PRESERVED FMRI ACTIVITY DURING A SELF-RELATED TASK

Nicolas Villain1, Béatrice Desgranges1, Nathastja Morel1, Florence Mézinge1, Renaud La Joie1, Marine Fouquet1, Katell Mevel1, Audrey Perrotin1, Brigitte Landeau1, Vincent de La Sayette1,2, Fausto Viader1,2, Francis Eustache1, Gicél Chételat1,2,3,4,5,6,7,  
1Inserm-EPHE-Université de Caen/Basse-Normandie, Unité U923, GHP Cycleron, CHU Côte de Nacre, Caen, France; 2Département de Neurologie, CHU Côte de Nacre, Caen, France.

**Background:** Functional MRI (fMRI) studies have reported paradoxical posterior cingulate cortex (PCC) preservation in Mild Cognitive Impairment (MCI) patients when performing a self-reference task. It is still unknown whether this preserved PCC activity is an early phenomenon that remains stable despite severe metabolic and structural PCC alterations occurring in the course of Alzheimer’s disease (AD). The aim of the present study was to address this question by measuring PCC activity during a self-referential task together with PCC volume and metabolism in the same demented AD patients. **Methods:** Six AD patients and 12 healthy controls (HC) matched for age, sex and education, all from the IMAP project, were included in these preliminary analyses. All participants underwent a self-referential fMRI session1,2, a T1-MRI acquisition and a FDG-PET scan. Data were transformed in comparable parametric maps after correction for geometrical distortions3 and partial volume effects. Self-Referential BOLD response was then assessed using voxelwise statistics. PCC values were finally extracted from the three neuroimaging datasets and values of each patient were z-score transformed using the corresponding values of the controls4,5. All PCC statistics were performed using non-parametric tests. **Results:** Both HC and AD showed significant voxelwise self-referential BOLD activations in a large network including the PCC with no significant difference between the two groups. As compared to controls, AD patients showed a significant PCC FDG-PET hypometabolism and a trend for PCC atrophy (p = 0.097), while there was no difference in PCC Self-Referential BOLD response magnitude. The repeated-measures ANOVA performed on the three neuroimaging modality z-scores was significant (Figure 1). Paired t-tests revealed that FDG-PET PCC Z-scores were significantly more negative than both the PCC volume and Self-Referential BOLD response z-scores, as well as a trend for more negative z-scores for PCC volume than PCC Self-Referential BOLD response (p = 0.093) (Figure 1). **Conclusions:** This preliminary work is the first to highlight a functional preservation of the PCC in AD. Besides, it showed that this preservation occurs despite simultaneous glucose hypometabolism and atrophy. It thus reveals the complexity of neuronal alterations of the PCC in AD, by pointing a paradox between the altered glucose metabolism and the preserved self-referential BOLD response.

**IC-P-178**  
1H MAGNETIC RESONANCE SPECTROSCOPY FINDINGS OF NORMAL INDIVIDUAL AND ALZHEIMER’S DISEASE PATIENTS

Kin-Wah Liu, Prince of Wales Hospital, Hong Kong, Hong Kong.

**Background:** Proton magnetic resonance spectroscopy (1H-MRS) offers a non-invasive way in vivo metabolic study. It is a useful tool for the diagnosis of different forms of dementia. Screening for the dementia in symptomatic elderly patients is necessary for the initiation of the medications to slow the progression of AD and allows patients and their family members to plan for future. MRS studies in AD reveal a decrease of N-acetylaspartate (NAA) and an increase of Myo-inositol (mI) compared with the healthy subjects. However, local normal reference of the neurometabolites is lacking. The present study is to describe the findings of the proton magnetic resonance spectroscopy (1H-MRS) in the normal subjects recruiting from community. **Methods:** Normal consecutive subjects and Alzheimer Disease (AD) patients are assessed by geriatricians, neuropsychiatric test, Magnetic Resonance Imaging, Arteriography and Spectroscopy. A single voxel sequences (TE 30ms, TR 2000 ms) was carries out via 1.5T-MRS was performed at Posterior Cingulate Gyrus of each individual to study metabolites including N-acetylaspartate (NAA), Creatine (Cr), Choline (Cho) and Myo-inositol (Mi). The diagnosis were relied on assessment of the Mini-Mental State Exam (MMSE), Cognition Dementia Rating (CDR), Geriatricians and the results correlated with the 1HMRs results. **Results:** Thirty-Two normal subjects (mean age 61.6 S.D. 8.90, range 50-79) were recruited. On the other hand, ninety-six AD subjects (mean age 71.8 SD 9.55 range 50-89) were recruited. Their mean NAA of normal and AD subjects are 1.242 +/- 0.141 and 1.19 +/-0.180. The mean of Mi of normal and AD subjects are 0.731 + / - 0.144 and 0.973 +/-0.178 respectively. There

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