



**Title: Regional Cerebral Glucose Metabolism at Baseline Predicts Symptom Onset in Normal ADNI Subjects and Correlates to Disease Progression**

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Regional glucose metabolism (rCMglc) in 32 regions of interest was measured in the baseline FDG-PET scans of 250 ADNI subjects (78 female, 172 male; age 59 – 88, average 76 years; 79 NL, 111 MCI, 60 AD at initial diagnosis). Regions included left and right hippocampi (HIP), amygdala, posterior cingulate cortex, inferior parietal lobes, medial, lateral, and superior temporal lobes, normalized to the cerebellum and age-corrected. An automated method was employed that has been demonstrated to achieve accurate, rapid sampling, and to optimize sensitivity and specificity without compromise from spatial normalization, smoothing, adjacent region spillover, and atrophy (Mosconi, 2005). Subjects were stratified into 7 subgroups across normal (NL), MCI, and AD categories, based upon initial diagnosis and progressive CDR, GDS scale, and MMSE scores. We observed a significant correlation between rCMglc in several regions and clinical progression from stable NL (NL-nonDecl, n=14) to NL with subsequent clinical decline (NL-Decl of decline, n=74, subdivided by extent of decline), to subcategories of MCI (MCI-nonDecl, n=77 and MCI-Decl and mild-AD, n=37) and AD. Among all regions examined, HIP rCMglc was the most sensitive predictor of decline and discriminator between disease stages. As compared to stable NL, HIP CMRglc was reduced by 5% in NL-Decl 5%, 11% in stable MCI, 15% in MCI-Decl ( $P < 0.048$ ), and 24% in AD ( $P \leq 0.001$ ). These results provide multi-regional insight to disease progression, demonstrate the importance of HIP rCMglc in disease prediction and differentiation in a broadened population, and provide a basis for correlation to structural change, amyloid accumulation, and other biomarkers.