

peting known effect of e4) and the +DEB group showed reductions in visual cortices known to be preferentially affected in DLB and left ventral striatum/basal forebrain. These exploratory findings suggest that DEB/RBD may correlate with early dopaminergic denervation of ventral striatum/basal forebrain regions, and early involvement of visual cortices that are affected by DLB. Further study is needed to confirm these findings in polysomnographically confirmed RBD patients, and to determine the relative contribution of APOE e4 to these findings, their future progression, and the possibility that they are predictive of future DLB.

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P-122 REGIONAL CEREBRAL METABOLISM IN PSAPP DOUBLE-TRANSGENIC MICE CHANGES WITH AGE AND GENOTYPE

Jon Valla^{1,2}, Lonnie Schneider^{1,2}, Eric M. Reiman^{3,2}; ¹Barrow Neurological Institute, Phoenix, AZ, USA; ²Arizona Alzheimer's Research Consortium, Phoenix, AZ, USA; ³PET Center, Banner Good Samaritan Medical Center, Phoenix, AZ, USA

Background: While transgenic mice hold great promise in the study of AD, uncertainties remain about the extent to which they model the disorder and how best to characterize its progression. Using fluorodeoxyglucose (FDG) autoradiography, we found very old homozygous PDAPP transgenic mice have preferentially and progressively reduced activity in posterior cingulate/retrosplenial cortex, similar to PET results in persons affected by AD or at genetic risk. However, the PDAPP mice have a significant white matter abnormality (i.e., a truncated corpus callosum), which may confound normal brain structure/function and preclude their use in *in vivo* metabolic imaging studies. If another model of AD demonstrates significant declines in regional metabolic activity, absent morphological abnormalities, it may be possible to track progression of such and screen candidate treatments more efficiently. **Objective(s):** To assess cerebral metabolic measures in double-transgenic PS1 x TG2576APP (PSAPP) mice, which do not have pronounced white matter alterations. **Methods:** Cytochrome oxidase (CytOx) histochemistry was used to compare regional/whole brain activity in PSAPP mice and controls at 4 and 16 months of age. As each age was analyzed separately, within-age t-tests were first performed, followed by a genotype x age omnibus ANOVA. **Conclusions:** Learning/memory circuits including the interconnected hippocampal subiculum, posterior cingulate, and anteroventral thalamic nucleus were decreased significantly in the older mice while only the anteroventral thalamus showed a decline in the younger animals. Young PSAPP transgenic mice showed significant alterations in CytOx activity, primarily increases, in several primary and secondary sensory and striatal areas; older mice showed changes in similar circuits, with some overlap of specific ROIs, possibly correlating with behavioral hyperarousal displayed by these mice at both ages. In the omnibus ANOVA, across ages, many of these changes remained prominent. No significant differences between whole brain metabolism or white matter readings indicated that changes were localized to specific ROIs. These results are currently being extended with FDG autoradiography. Four-month-old PSAPP mice demonstrate a relatively light amyloid load compared to 16-month-old mice; progression of select regional cerebral metabolic changes may occur in kind, potentially increasing the usefulness of this model of AD in clarifying disease mechanisms and screening candidate treatments.

P-123 QUANTITATIVE MRI R2 RELAXOMETRY IN ELDERLY PARTICIPANTS REPORTING MEMORY LOSS: A USEFUL TOOL FOR THE POTENTIAL EARLY DIAGNOSIS OF AD?

Jonathan K. Foster¹, Michael J. House², Timothy G. St Pierre², Ralph N. Martins¹, Roger Clarnette³, Jodie Ricci⁴; ¹Ageing & Alzheimer's, School of Exercise, Biomedical & Health Sciences, Edith Cowan University, Joondalup, Australia; ²School of Physics, University of Western Australia, Crawley, Australia; ³School of Medicine and Pharmacology, University of Western Australia - Fremantle Hospital, Fremantle, Australia; ⁴SKG Radiology, St John of God Hospital, Subiaco, Australia

Background: Memory loss is a hallmark of early Alzheimer's disease (AD) and is associated with significant brain biomarkers of AD. Elevated brain iron concentrations in grey matter in AD suggest a disruption in iron homeostasis, while demyelination processes in white matter increase the water content. The transverse proton relaxation rate, R2, is an MRI parameter affected by changes in both brain iron concentration and water content. **Objective(s):** To assess whether R2 changes can be detected in cortical and sub-cortical grey and white matter in elderly participants with mild to severe levels of cognitive impairment, and to determine the degree to which any changes are associated with changes in cognitive functioning. **Methods:** Twelve elderly participants reporting memory problems, and 11 healthy volunteers, underwent single-spin-echo MRI in a 1.5 T scanner, with subsequent neuropsychological testing outside the magnet. R2 data were collected from 14 brain regions in all participants. The memory complainers were separated into two further subgroups, MC1 (no objective cognitive impairment), and MC2 (mild to severe objective cognitive impairment). **Conclusions:** R2 values in the MC2 subgroup were significantly higher in the temporal cortex and significantly lower in the internal capsule, and in the frontal and temporal white matter, compared to healthy controls. Two grey matter regions from the combined memory complainer group (MC1+MC2), the thalamus and particularly the red nucleus, showed statistically significant negative correlations between immediate, short-delay and long-delay free recall scores from the CVLT and R2 values. R2 measurements from both sides of the red nucleus also showed significant negative correlations with global cognitive status. Taken together, these findings suggest that *vivo* quantitative transverse relaxation rates appear capable of characterising grey and white matter pathology associated with age-related cognitive impairment, and may offer a useful tool for the early diagnosis of AD.

P-124 FRONTAL HYPOPERFUSION CORRELATES WITH EPISODIC MEMORY DEFICITS IN MILD COGNITIVE IMPAIRMENT

Audrey Duarte¹, Satoru Hayasaka¹, Antao Du¹, Joel Kramer², Geon-Ho Jahng¹, Norbert Schuff¹, Bruce Miller², Michael Weiner¹; ¹SF VAMC, San Francisco, CA, USA; ²UCSF, San Francisco, CA, USA

Background: Mild Cognitive Impairment (MCI) is a significant risk factor for the development of dementia, but few studies have been performed to assess the relationship between alterations of cerebral blood flow and cognitive impairments in this group. **Objective:** To determine if reductions of cerebral perfusion (after correcting for partial volume effects) correlate with cognitive deficits in MCI. **Methods:** 35 MCI patients and 28 controls were administered cognitive tests and a resting state Arterial Spin Labeling Perfusion MRI (ASLpMRI) scan. Using the cognitive tests for which MCI patients were impaired, positive correlations between these scores and perfusion in partial volume corrected images were calculated. Correlations were corrected for age and the other cognitive test scores in order to ensure the specificity of the observed effects. Relative to controls, MCI patients were impaired in measures of immediate recall ($p < .0001$), delayed cued recall ($p < .001$), delayed free recall ($p = .015$) and delayed recognition ($p = .018$). For immediate recall, there were significant correlations with perfusion in left middle and inferior frontal gyri ($p < .0001$), left superior

parietal cortex ($p = .001$), left posterior cingulate cortex ($p < .001$), right inferior frontal gyrus ($p = .002$) and bilateral frontopolar regions (p 's $< .001$). For delayed cued recall, correlations were identified in left superior frontal gyrus ($p = .01$), right superior frontal gyrus ($p < .001$) and right superior parietal cortex ($p < .001$). No significant correlations were identified for delayed free recall or delayed recognition. **Conclusion:** These results suggest that in MCI, cognitive impairments are associated with reduced cerebral perfusion. Furthermore, since we corrected for partial volume effects, correlations between perfusion and cognition cannot be explained by brain tissue loss alone. Memory impairments in MCI may be those most influenced by executive functioning, as evidenced by the greatest deficits in immediate and delayed cued recall. Furthermore, the results from the correlations highlight the importance of multiple frontal regions as well as posterior association areas, typically implicated in MCI, in potentially substantiating these cognitive impairments. In conclusion, these results suggest that perfusion MRI can be used to stage cognitive deficits in MCI.

P-125 **INFLUENCE OF AGE, GREY MATTER, AND MEMORY PERFORMANCE ON FMRI ACTIVATION IN OLDER ADULTS**

Meredith N. Braskie, Gary W. Small, Susan Y. Bookheimer; *University of California, Los Angeles, Los Angeles, CA, USA*

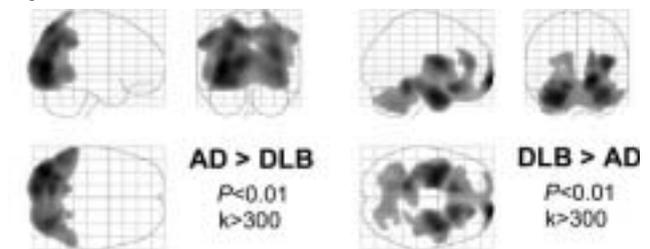
Objective: To evaluate the relationships between functional MRI (fMRI) brain activation during a verbal paired associates memory task, age, task score and grey matter (GM) volume percentage. **Background:** fMRI is a sensitive tool shown to detect brain activation differences in subjects with Alzheimer's disease (AD)1 mild cognitive impairment (MCI)1 and in normal subjects genetically at risk for AD2. In these studies, groups were often matched for factors such as age or memory ability. Identifying what contribution such factors have on brain activation in an aging population may help toward the goal of using fMRI as a tool in the early diagnosis of incipient AD. This study used an unrelated verbal paired associates task, which has been shown to engage medial temporal, parietal and prefrontal regions typically affected by AD2. We examined the association of task activation with age, task score, and GM percentage. **Methods:** Subjects were 20 volunteers (mean age=60) with memory from normal to age-consistent impairment, selected such that age and task score were not significantly correlated. fMRI scans were performed (Siemens 3T MRI) using gradient echo, echo-planar acquisition (3.1x3.1x3mm) while subjects performed the paired associates task. Structural scans were obtained using an MPRAGE sequence (1.3x1.3x1mm). We used FSL to analyze the fMRI data (FEAT)3,4, automatically segment the MPRAGEs (FAST)5, and determine the volume of the brain tissues. **Conclusions:** In non-demented, older adults, age, task score, and GM percentage had different effects on fMRI paired associates activations. Activation in the cingulate, parietal cortex, retrosplenium, and supplementary motor areas was inversely correlated with age. Conversely, activation in the transverse temporal gyrus, superior and medial temporal gyri, hippocampus, and superior frontal lobe was inversely correlated with score on the memory task. No areas were positively correlated with age or score, and there was no significant correlation between activation and GM percentage. These findings suggest that in non-demented subjects, age and task success influenced brain activity more than GM percentage.

P-126 **DIFFERENTIATION OF EARLY STAGE OF ALZHEIMER'S DISEASE AND DEMENTIA WITH LEWY BODIES BY FDG-PET**

Kenji Ishii¹, Keiichi Kawasaki¹, Yoko Saito¹, Keiichi Oda¹, Kiichi Ishiwata¹, Yuko Saito¹, Shigeo Murayama¹, Kazuko Mitani², Kazutomi Kanemaru², Hiroshi Yamanouchi²; ¹Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan; ²Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

Background: The FDG-PET has revealed to be quite useful for the diagnosis of Alzheimer's disease (AD) even in very early stage such as

mild cognitive impairments (MCI). The dementia with Lewy bodies (DLB) is the second frequent cause of senile dementia next to AD, and the FDG-PET image of DLB appeared that it somehow resembles that of AD. However, the diagnostic power of FDG-PET in early DLB is not known. **Objective:** The motivation of this study is to examine the characteristics of FDG-PET image in early AD and DLB whose diagnosis were confirmed retrospectively, and to extract useful functional neuroimaging markers for the differential diagnosis of these disorders in MCI stage. **Methods:** Among 191 consecutive FDG-PET studies in the PET Center of Tokyo Metropolitan Institute of Gerontology for the diagnosis of degenerative neurological disorders, we extracted 70 cases of AD and 27 cases of DLB whose diagnosis were supported by clinical evidences other than PET, such as the clinical course more than one year after the PET study, the biomarkers in cerebrospinal fluid, and the pre- and post-synaptic nigrostriatal dopaminergic function evaluated by PET with ¹¹C-CFT and ¹¹C-raclopride. Then we further selected cases who had only mild cognitive impairments (MMSE score 24 or above) at the moment of FDG-PET study and 18 cases of MCI-AD and 10 cases of MCI-DLB were obtained. The pattern of their regional cerebral glucose metabolism was evaluated with region of interest (ROI) method and statistical parametrical mapping (SPM) in comparison with 51 healthy controls. **Conclusions:** Both MCI-AD and MCI-DLB groups commonly showed the hypometabolism in bilateral posterior cingulate regions and bilateral parieto-temporal cortex. However, the significant differences ($P < 0.01$) were found in the regions of bilateral occipital cortex (MCI-AD $>$ MCI-DLB), bilateral medial temporal regions and bilateral striatum and thalamus (MCI-DLB $>$ MCI-AD). Therefore, the ratio of glucose metabolism in the striatum (or hippocampus) over the occipital lobe will be a good marker to differentiate AD and DLB in MCI stage.



P-127 **CORTICAL RADIOACTIVE BRAIN UPTAKE (CRBU) - A NEW, PRACTICAL METHOD TO SCREEN FOR ALZHEIMER'S DISEASE AND OTHER DEMENTIAS**

Harold T. Pretorius¹, John D. Idoine², Christopher Kircher¹, Kavya Prasad¹, Geraldine Wu¹, Mike F. Harrell¹, Jose Arias¹, Luis Pagani¹; ¹Cincinnati Cognitive Collaborative, Cincinnati, OH, USA; ²Kenyon College, Gambier, OH, USA

Background: Functional neuroimaging detects many causes of cognitive impairment including Alzheimer's disease, other neurodegenerative disorders (eg. Lewy body and fronto-temporal), cerebrovascular and psychiatric diseases. At least two coexisting causes, often Alzheimer's and cerebrovascular disease, are present in the majority of cases. Thus, effective screening should sensitively and accurately distinguish both neurodegenerative and cerebrovascular diseases. **Objective:** A practical method to assess abnormal brain metabolism and perfusion patterns in Alzheimer's disease and other dementias. **Methods:** We used a modified thyroid uptake probe with a lead-shielded 5.08 cm NaI detector placed as close to the scalp as 1 cm to optimize sensitivity. By adjusting aperture size in the shield between the detector and the patient, Cortical Radioactive Brain Uptake (CRBU) is measured in about a 3 ml region of cortical brain, with tissue attenuation and distance limiting counts from deeper brain tissue. We