information linked to routine hospital and mortality data, and to be contacted again by the researchers. A second wave of data collection is ongoing (2014-2017) with additional questions on memory, carers and diet. The cohort is also being replenished and coverage widened to include the entire Yorkshire and Humber region (pop 5.25mn). The new recruitment target for the cohort is 50,000. In the first wave of recruitment 28,000 adults (1,700 aged 75 or over) returned completed Health Questionnaires. The response rate was 17%. As expected, respondents were more likely to be female, over 55 years, and living in areas of low deprivation. However, the population is broadly representative of the reference population. To date 12 health studies have identified and recruited over 1100 participants to their studies (including randomised controlled trials, qualitative interviews, matched case control studies) and local authorities are using the data to inform their Joint Strategic Needs Assessments. With over 3000 participants likely to receive a diagnosis of dementia in the next five years, the Yorkshire Health Study provides an opportunity to test a range of individual and public health level interventions to treat, manage and/or prevent dementia and to understand more about the health related behaviours that affect the onset and trajectory of dementia.

O3-02-06 WHAT IS THE LONG-TERM EMOTIONAL AND BEHAVIORAL IMPACT OF GENETIC RISK ASSESSMENT FOR ALZHEIMER'S DISEASE? FINDINGS FROM THE REVEAL STUDY

J. Scott Roberts[1], Kurt Derek Christensen[2], Leo B. Waterston[3], Jake Duggan[4], Stephen Alerhand[5], L. Adrienne Cupples[6], Peter J. Whitehouse[7], Thomas O. Obisesan[8], Robert C. Green[4] The REVEAL Study[4], *[1]University of Michigan School of Public Health, Ann Arbor, Michigan, United States; [2]Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, United States; [3]Brigham and Women's Hospital, Boston, Massachusetts, United States; [4]Brigham and Women's Hospital, Boston, Massachusetts, United States; [5]Icahn School of Medicine at Mount Sinai, New York, New York, United States; [6]Boston University, Boston, Massachusetts, United States; [7]Case Western Reserve University, Cleveland, Ohio, United States; [8]Howard University Hospital, Washington, District of Columbia, United States. Contact e-mail: kchristensen@genetics.med.harvard.edu*

Project Description: Research has shown that disclosing genetic risk information about Alzheimer's disease (AD) to volunteer populations does not create distress in the year following disclosure, and can motivate changes to advance planning and health behaviors. However, little is known about the long-term impact of disclosure. The potential exists for distress to increase over time and motivation for behavior change to decrease. The REVEAL Study is a series of multisite randomized controlled trials examining the psychological and behavioral impact of using APOE genotyping to determine AD risk. A subset of individuals who participated in the first three trials were asked to complete validated scales assessing general anxiety, general depression, and test-related distress 1.5-10 years after genotype disclosure. Additional yes/no questions asked about behavioral responses. Of 472 individuals invited, 291 (62%) responded (mean age 62.5; 63% female; 13% African American; 90% with AD-affected parent or sibling). Mean scores were 3.9 (95%CI: 3.3-4.5) on the Beck Anxiety Inventory and 7.5 (95%CI: 6.6-8.4) on the Center for Epidemiological Studies Depression Scale, well below cutoffs for clinical concern and with no differences by genetic risk status (p=0.08 and 0.64, respectively). Mean test-related distress, as measured by the Impact of Event Scale, was also well below cutoffs for clinical concern, but was greater among ε4-positive respondents than ε4-negative respondents (4.7 vs 2.8, p=0.022). ε4-positive respondents were also more likely to report adding long-term care insurance (12% vs 4%, p=0.022), modifying living wills (5% vs 1%, p=0.035), and improving health behaviors (64% vs 41%, p<0.0001). Current age was unassociated with any psychological or behavioral outcomes except health behavior changes, where those who were older than 65 were less likely to report modifications than those who were younger than 65, regardless of APOE genotype (OR=0.57, p=0.026). This is the first study to evaluate the long-term impact of disclosing APOE genotyping results. Findings suggest that differences described previously between ε4-positive and ε4-negative individuals on psychological outcomes and health-related behaviors persist for years. Findings also show no evidence of increased psychological risks, even as subjects approach ages of potential AD onset.

TUESDAY, JULY 15, 2014
ORAL SESSIONS
O3-03
NEUROIMAGING: NEUROIMAGING FOR TRACKING DISEASE PROGRESSION AND FOR PROGNOSIS

O3-03-01 DETECTION OF PRODROMAL ALZHEIMER'S DISEASE WITH 18F-FLORBETABEN AB IMAGING: A PROSPECTIVE OUTCOME STUDY

Kevin Ong[1], Victor L. Villemagne[2], Alex Bahar-Fuchs[3], Fiona Lamb[4], Narelle Langdon[2], Ana Catafau[5], Andrew Stephens[6], John Seibyl[7], Ludger Dinkelborg[8], Cornelia Reininger[9], Barbara Putz[10], Beate Rohde[10], Colin Louis Masters[11], Christopher Cleon Rowe[12], *[1]Austin Health, Heidelberg, Australia; [2]Austin Health, Melbourne, Australia; [3]The Australian National University, Canberra, Australia; [4]Austin Health, Melbourne, VIC, Australia; [5]Piramal Imaging GmbH, Berlin, Germany; [6]Piramal Imaging, Berlin, Germany; [7]MNI Imaging, New Haven, Connecticut, United States; [8]Piramal Imaging, Matran, Switzerland; [9]Bayer Healthcare, Berlin, Germany; [10]Bayer Schering Pharma, Berlin, Germany; [11]Florey Institute, Parkville, Australia; [12]Austin Hospital, Melbourne, Australia. Contact e-mail: drkevinong@gmail.com*

Background: Beta-amyloid (Aβ) imaging has been approved for clinical use. We sought to better understand its clinical utility in mild cognitive impairment (MCI). We aimed to evaluate the prognostic accuracy of Aβ imaging with 18 F-florbetaben (FBB) for progression from MCI to AD, compare semi-quantitative assessment with visually assessed scans, explore relationships between Aβ, hippocampal volume and memory over time, and examine whether progressive Aβ accumulation is detectable. **Methods:** Forty-five elderly MCI referred from memory clinics underwent FBB PET, MRI and neuropsychological assessment at baseline and 2 years. Participants and informants were contacted to 4 years. Positive FBB (FBB+), was defined by a cortical-to-cerebellar cortex uptake ratio (SUVR) $\geq$ 1.45, was compared with increased cortical uptake if visible to at least 3 of 5 readers. Hippocampal volume (HV) was measured by NeuroQuant®.Amnestic MCI (aMCI) was defined by a composite episodic memory (EM) Z-score of $<$ -1.5. **Results:** At baseline, 24 (53%) MCI were FBB+. Majority reads strongly agreed with SUVR classification (kappa 0.96). In 2 years, 18 (75%) FBB+ progressed to AD compared to 2 (9.5%) FBB-, giving a predictive accuracy of 82% [95%CI:67-90%] and hazard ratio of 11.1. Four FBB- developed non-AD dementia. Predictive accuracies of HV (58% [95%CI:42-73%]) and aMCI status (73% [95% CI:58-81%]) were lower. Combinations did not improve accuracy. By 4 years, 21 (87.5%) FBB+ had AD whereas 5 (24%) FBB- had non-AD dementia. The two FBB- AD were MCI and FTLD at 4 years. FBB PET predictive accuracy for AD was 93.3% (p<0.0001). A strong baseline linear association between SUVR and EM (r=-0.41, p<0.05) declined over 2 years (r=-0.27) while an association of EM with HV developed (r=0.36, p<0.05 at 2 years). SUVR increased 2.2%/year in FBB+ with no change in FBB-. **Conclusions:** Aβ imaging with 18 F-florbetaben facilitates accurate detection of prodromal AD. As AD neurodegeneration progresses, hippocampal atrophy may overtake Aβ in driving memory impairment. Progressive accumulation of Aβ can be detected with serial FBB PET.

O3-03-02 TWO-YEAR LONGITUDINAL CHANGE IN AMYLOID DEPOSITION, GLUCOSE METABOLISM, AND HIPPOCAMPAL ATROPHY IN ADNI-2 PARTICIPANTS: RELATION TO GENETIC RISK

Shannon Leigh Risacher[1], Sungeun Kim[1], Kwangsik T. Nho[1], John D. West[2], Ronald C. Petersen[3], Paul S. Aisen[4], Clifford R. Jack, Jr,[5], William J. Jagust[6], Robert Koeppe[7], Michael Walter Weiner[8], Andrew J. Saykin[9], *[1]Indiana University School of Medicine, Indianapolis, Indiana, United States; [2]Indiana University School of Medicine,*

Indianapolis, Indiana, United States; [3]Mayo Clinic Rochester, Rochester, Minnesota, United States; [4]UCSD, La Jolla, California, United States; [5]Mayo Clinic, Rochester, Minnesota, United States; [6]University of California, Berkeley, Berkeley, California, United States; [7]University of Michigan, Ann Arbor, Michigan, United States; [8]Center for Imaging of Neurodegenerative Diseases, VA Medical Center and UCSF, San Francisco, California, United States; [9]Indiana University School of Medicine, Indianapolis, Indiana, United States. Contact e-mail: asaykin@iupui.edu

Background: Longitudinal change in amyloid deposition, glucose metabolism, and medial temporal lobe atrophy are important biomarkers for studies of Alzheimer's disease (AD). The goal of this study was a comparative assessment of two-year change in amyloid deposition, glucose metabolism, and hippocampal atrophy in participants from the Alzheimer's Disease Neuroimaging Initiative (ADNI) with special emphasis on prodromal stages. **Methods:** 320 participants, including 106 healthy controls (HC), divided by genetic risk (family history of AD and/or APOE ε4 positive), 130 patients with early (EMCI) and 44 participants with late mild cognitive impairment (LMCI), and 29 patients with AD, were included in this analysis. Florbetapir PET scans and structural MRI scans were downloaded from the ADNI site for the baseline Florbetapir visit and the two-year follow-up visit and processed using previously described techniques [1]. FDG PET scans were also downloaded from these timepoints and processed using standard techniques. Average Florbetapir SUVR, FDG SUVR, and structural grey matter density (GMD) were extracted from target ROIs at both visits, including the global cortex for the PET and bilateral mean hippocampus for MRI. Annualized percent change (APC) was calculated from these regions and compared between groups. **Results:** No group differences were observed for change in amyloid deposition. However, glucose metabolism decline and hippocampal GMD atrophy rate showed significant group differences ($p<0.001$, Fig. 1A&B). AD showed faster glucose decline and hippocampal atrophy than all other groups except LMCI ($p<0.01$). LMCI had a greater hippocampal atrophy rate than HC without risk and EMCI ($p<0.05$). HC at genetic risk showed a non-significant trend toward greater decline in glucose metabolism and hippocampal GMD than HC without risk ($p=0.1$ for GMD). **Conclusions:** Mean amyloid deposition does not appear to significantly change over two years in any stage of cognitive impairment. However, declining glucose metabolism and hippocampal atrophy rates appear to accelerate in later disease stages (LMCI, AD). Cognitively normal older adults at risk for AD due to genetic background may show greater rates of hippocampal atrophy and glucose metabolic decline than those without genetic risk but larger samples and replication are needed to further investigate this issue.[1] Risacher et al. (2013) Front Aging Neurosci

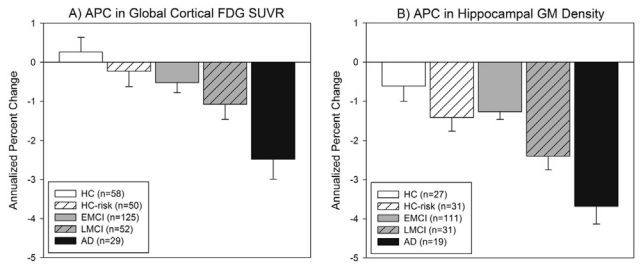

Figure 1. APC in Glucose Metabolism and Hippocampal GM Density

O3-03-03 MAPPING 3-YEAR RATES OF DECLINE IN JOINTLY ASSESSED GRAY MATTER VOLUME AND FDG-PET IN Aβ+ NON-DEMENTED SUBJECTS

Miguel Ángel Araque Caballero[1], Matthias Brendel[2], Andreas Delker[3], Jinyi Ren[4], Axel Rominger[5], Peter Bartenstein[2], Michael Walter Weiner[6], Michael Ewers[7], *[1]Institute for Stroke and Dementia Research (ISD), Martinsried-Planegg, Germany; [2]University of Munich, Munich, Germany; [3]Nuklearmedizin, Klinikum der Universität München, München, Germany; [4]Institute for Stroke and Dementia Research, Klinikum der Universität München, Martinsried-Planegg, Germany; [5]Nuklearmedizin, Klinikum der Universität München, Munich, Germany; [6]Center for Imaging of Neurodegenerative Diseases, VA Medical Center and UCSF, San Francisco, United States; [7]Institute for Stroke and Dementia Research, Ludwig Maximilian University, Munich, Germany. Contact e-mail: miguel.caballero@med.uni-muenchen.de*

Background: Beta-amyloid (A β) deposition occurs years before the onset of Alzheimer's disease (AD) dementia, but its relation to grey matter (GM) changes and FDG-PET metabolism in the pre-dementia stages remains unclear. Here we examined the effect of abnormally high A β on the regional rates of GM and FDG-PET change separately, and assessed the joint spatial variations across both modalities over 3 years. **Methods:** Forty cognitively healthy (HC) and fifty-three mildly impaired (MCI) adults underwent annual MRI and FDG-PET imaging for three years within the Alzheimer's Disease Neuroimaging Initiative (ADNI). Based on CSF A β 1-42 and global brain amyloid-PET (Av-45 and PiB-PET), the HC and MCI subjects were dichotomized into groups with high (A β +) and low (A β -) amyloid burden, according to pre-established criteria. Voxel-wise rates of change in GM, FDG-PET and atrophy-corrected FDG-PET were estimated for each subject. In voxel-wise analyses, the rates of change in each modality were compared between groups, controlling for age, gender, years of education and ApoE genotype. In joint independent component analysis (jICA) the patterns of covariance in the change across modalities were assessed. **Results:** HC A β + subjects showed faster rates of GM atrophy in the medial parietal lobe (MPL) and medial temporal lobe (MTL) when compared to HC A β -. No differences in the FDG-PET rates of change were found. For MCIs, A β + subjects showed faster rates of GM atrophy than A β - in the MTL, MPL, frontal and temporal lobes. Faster decline in FDG-PET metabolism was found throughout the forebrain, but not within the MTL. After correcting for atrophy, MCI A β + showed increasing FDG-PET metabolism within the MTL when compared to MCI A β - (Figure). The jICA analysis assessing covarying changes between modalities showed higher rates of decline in both FDG-PET and GM. However, after atrophy correction, decreasing GM volume was associated with increasing FDG-PET. **Conclusions:** At the pre-symptomatic stages of AD, A β-related changes in GM volume are apparent primarily within medial temporo-parietal regions. At the mild symptomatic stage, atrophy spreads to adjacent regions and is accompanied by FDG-PET decline in cortical areas. The A β -associated increase in FDG-PET after atrophy correction within the MTL suggests the existence of compensatory mechanisms in MCI.