Background: Disclosure of predictive genetic test results has traditionally been provided in-person to optimize understanding, psychosocial support, communication to relatives and adoption of risk reduction behaviors. In the API APOE4 Trial, homozygotes and a random sample of non-homozygotes will be invited to trial sites for screening and disclosure of APOE genotype. Limited availability of genetic counselors with expertise in AD presents a potential barrier to implementation of the trial. Telephone and real-time videoconferencing (RTVC) are two methods for remote communication which can provide access to genetic providers in medical systems without genetic counselors. The relative advantages of RTVC over telephone have not been evaluated in a randomized trial. **Methods:** Ongoing and completed National Cancer Institute (NCI) funded studies evaluating telephone and RTVC as alternative delivery modalities for genetic counseling in *BRCA1/2* testing have informed a randomized evaluation of telephone versus RTVC disclosure of APOE genotype in the API APOE4 Trial Genetic Testing and Counseling Program (GTCP). **Results:** Telephone counseling has been found to be equivalent to in-person counseling for *BRCA1/2* testing in two NCI funded randomized studies (Schwartz et al, Kinney et al) published in 2014. Communication protocols and results from an ongoing NCI funded multi-site randomized study evaluating telephone disclosure of genetic test results for a broader range of cancer susceptibility test results and powered to evaluate differences in outcomes among patients receiving a positive result have informed telephone delivery protocols and outcomes in the API APOE4 GTCP. In a separate NCI funded study, RTVC has been found to be feasible, valued by patients and associated with increased in knowledge and favorable psychosocial outcomes for cancer susceptibility genetic testing. Similarly, RTVC protocols for genetic counseling have been adapted for AD and the RTVC comparison arm in the API APOE4 GTCP. **Conclusions:** The API APOE GTCP randomized evaluation of two remote genetic counseling models will support enrollment into the API APOE4 Trial and provide protocols for clearly and safely communicating sensitive genetic information. Results from the GTCP will provide crucial information regarding the implementation and delivery of APOE genotype results relevant to clinical practice and precision medicine.

F3-03-03 DISCLOSURE OF AMYLOID STATUS IN THE A4 TRIAL

Reisa A. Sperling[1,2,3], Jason Karlawish[4], Joshua D. Grill[5], **Jeffrey M. Burns**[6], David Sultzer[7], Keith A. Johnson[8], Paul S. Aisen[9], *[1]Harvard Medical School, Boston, MA, USA; [2]Brigham and Women's Hospital, Boston, MA, USA; [3]Massachusetts General Hospital and the Athinoula A. Martinos Center for Biomedical Imaging, Boston, MA, USA; [4]University of Pennsylvania, Philadelphia, PA, USA; [5]UCLA, Los Angeles, CA, USA; [6]University of Kansas Alzheimer's Disease Center, Fairway, KS, USA; [7]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [8]Massachusetts General Hospital, Boston, MA, USA; [9]University of California, San Diego, La Jolla, CA, USA. Contact e-mail: jburns2@kumc.edu*

Background: The A4 Study is a secondary prevention trial in preclinical AD that will test the hypothesis that an anti-amyloid treatment can slow cognitive decline in clinically normal older individuals with evidence of elevated amyloid accumulation on screening PET imaging. The Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) Study will follow a similar cohort withoutevidence of elevated amyloid. We developed a process to safely disclose amyloid status during screening for the A4 study and are evaluating the impact of amyloid disclosure on longitudinal measures of cognition, behavior, and concerns about AD. **Methods:** Potential participants undergo education about amyloid pathology, PET amyloid imaging and the current state of knowledge on risk of cognitive decline before and during the A4 consent process. Questionnaires are administered to assess psychological well-being; individuals who score above threshold levels for potential concern about anxiety or depression are evaluated for appropriateness to undergo PET amyloid imaging. The disclosure of PET amyloid results is performed in person by investigators who have undergone training in amyloid disclosure procedures and certification by the ADCS. Participants are permitted to have a study partner accompany them to the disclosure visit if desired. There is an additional phone call within 72 hours to assess the impact of disclosure and ensure that any adverse events are captured and appropriate follow-up is provided. Participants complete questionnaires on their concerns about developing AD, their reasons for undergoing amyloid imaging, and perceptions about their future during screening before and after disclosure, and longitudinally over the 3.3-year study. **Results:** Nearly 1000 individuals have been screened for the A4 Study to date, with only a very small number of individuals considered to be inappropriate to undergo PET scans on the basis of their screening assessment of psychological well-being. Over 300 amyloid disclosure visits have been conducted successfully thus far. Longitudinal assessment of the impact of disclosure is ongoing. **Conclusions:** The amyloid disclosure process in the A4 study is working well thus far and should provide important information on how to translate amyloid disclosure to the broader population should secondary prevention trials prove successful.

F3-03-04 THE ALZHEIMER'S PREVENTION INITIATIVE: GENETIC TESTING, DISCLOSURE, AND COUNSELING STRATEGIES

Jessica B. Langbaum[1], Jason Karlawish[2], J. Scott Roberts[3], Elisabeth McCarty Wood[2], Scott Kim[4], Angela R. Bradbury[2], Linda Patrick-Miller[5], Deborah Blacker[6], Richard J. Caselli[7], Doris Zallen[8], Gary E. Marchant[9], Carolyn Langlois[1], Eric M. Reiman[1], Pierre N. Tariot[1], *[1]Banner Alzheimer's Institute, Phoenix, AZ, USA; [2]University of Pennsylvania, Philadelphia, PA, USA; [3]University of Michigan, Ann Arbor, MI, USA; [4]National Institutes of Health, Bethesda, MD, USA; [5]University of Chicago, Chicago, IL, USA; [6]Harvard University, Charlestown, MA, USA; [7]Mayo Clinic Airzona, Scottsdale, AZ, USA; [8]VirginiaTech, Blacksburg, VA, USA; [9]Arizona State University, Tempe, AZ, USA. Contact e-mail: Jessica.Langbaum@bannerhealth.com*

Background: The Alzheimer's Prevention Initiative (API) was established to evaluate preclinical Alzheimer's disease (AD) treatments in people who, based on age and genetic background, are at imminent risk for developing symptoms of AD. The API Autosomal Dominant AD is enrolling mutation carriers and non-carriers so as to not require disclosure of mutation status. In comparison the API APOE4 Trial (pending health authority approval) will only enroll apolipoprotein E (APOE) *e4*homozygotes. To support this and future trials, the API established an APOE Genetic Testing and Counseling Program (GTCP) involving an interdisciplinary committee. **Methods:** Substantial work informed the creation of the GTCP, including (1) two research studies to assess attitudes towards and responses to APOE genetic testing and disclosure; (2) pilot study of APOE genotyping (without disclosure) using saliva collection tubes sent via US Postal Service; (3) establishment of

the GTCP Committee responsible for the development and implementation of the genetic testing and counseling program, including review of best practices in other diseases, and (4) updating APOE risk curves capitalizing on data from several epidemiological cohort studies. **Results:** APOE genotyping will be conducted through the Alzheimer's Prevention Registry (www.endALZnow.org) using a buccal swab kit sent via mail. APOE4 homozygotes and a random sample of non-homozygotes who appear to meet basic trial eligibility criteria will be invited to trial sites for additional screening and disclosure of APOE genotype. Given limited availability of genetic counselors specializing in AD, we will evaluate outcomes of two remote post-test counseling approaches in a randomized sub-study of telephone versus real-time videoconference counseling, as well as longitudinal outcomes of APOE disclosure including psychological, behavioral and cognitive effects. **Conclusions:** The GTCP is a key element of the API program, facilitating the enrollment into the API APOE4 Trial and establishing processes for clearly and safely communicating genetic information. We anticipate that the program will also identify a large pool of prospective participants for future trials. Results from the counseling program will provide crucial information regarding the implementation and delivery of APOE genotype results relevant to clinical practice and precision medicine, as well as lessons learned for future trials in genetically-enriched populations.

TUESDAY, JULY 21, 2015
PLENARY SESSIONS
PL-03
TUESDAY PLENARY

PL-03-01 MICROINFARCTS: KEY TO PREVENTION OF THE VASCULAR BURDEN IN DEMENTIA?

Geert Jan Biessels, *University Medical Center Utrecht, Utrecht, Netherlands. Contact e-mail: g.j.biessels@umcutrecht.nl*

Background: Cerebrovascular disease is an important cause and contributor to cognitive impairment and dementia, often in combination with other etiologies, such as Alzheimer's disease. Because vascular disease is so common, it is an important target for dementia prevention. Conventional MRI markers of vascular damage - including white matter hyperintensities, lacunes and microbleeds - do not fully capture this vascular burden in dementia. Neuropathological studies have identified microinfarcts as a common vascular pathology related to dementia and cognitive decline. **Methods:** My talk will address recent developments with high field 7T MRI, that now enable detection of microinfarcts in vivo. **Results:** I will first review neuropathological evidence on the links between microinfarcts and dementia. I will then discuss in vivo detection of microinfarcts at 7T MRI, validation of these findings in post-mortem brain material, and translation of microinfarct detection to 3T MRI, allowing widespread dissemination. I will present emerging data on clinical correlates of microinfarcts in memory clinic populations, but also from studies in other cohorts. I will discuss how microinfarcts and other novel MRI markers of cerebral microvascular disease may further our understanding of the etiology of the vascular burden in dementia and how that may support development of treatment. **Conclusions:** Microinfarcts are an emerging MRI marker of the vascular burden in dementia. These lesions can be detected on 7T MRI, but also on 3T MRI. The latter should allow rapid implementation of microinfarct detection in the dementia field, also on already acquired datasets.

PL-03-02 INGE GRUNDKE-IQBAL AWARD FOR ALZHEIMER'S RESEARCH: PROGRANULIN PROTECTS AGAINST AMYLOID B DEPOSITION AND TOXICITY IN ALZHEIMER'S DISEASE MOUSE MODELS

Li Gan, *University of California, San Francisco, San Francisco, CA, USA, Gladstone Institutes, San Francisco, CA, USA. Contact e-mail: lgan@gladstone.ucsf.edu*

Abstract not available.

TUESDAY, JULY 21, 2015
ORAL SESSIONS
O3-01
NEUROIMAGING: IMAGING — EFFECTS OF LIFESTYLE AND MEDICAL INTERVENTIONS

O3-01-01 INTERACTIONS OF DIABETES AND POSTMENOPAUSAL HORMONE THERAPY ON BRAIN VOLUMES: WHIMS

Christina E. Hugenschmidt[1], Susan M. Resnick[2], Roberta Diaz-Brinton[3], JoAnn E. Manson[4], Kristine Yaffe[5], A. Leslie Vaughan[1], Suzanne Craft[6], Beatrice J. Edwards[7], Ramon Casanova[1], Kamal Masaki[8], Mark A. Espeland[1], WHIMS-MRI2 Study Group, *[1]Wake Forest School of Medicine, Winston-Salem, NC, USA; [2]National Institute on Aging, Baltimore, MD, USA; [3]University of Southern California, Los Angeles, CA, USA; [4]Brigham and Women's Hospital / Harvard Medical School, Boston, MA, USA; [5]University of California, San Francisco, San Francisco, CA, USA; [6]Wake Forest University Health Sciences, Winston Salem, NC, USA; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [8]University of Hawaii at Manoa, Honolulu, HI, USA. Contact e-mail: chugensc@wakehealth.edu*

Background: The Three-City Study observed a significant interaction between circulating levels of estradiol and diabetes on risk for all-cause dementia in older women, and the Women's Health Initiative Memory Study (WHIMS) found that diabetes and assignment to hormone therapy (HT) were separately associated with smaller brain volumes and poorer cognition. In addition, randomization to HT vs placebo increased the risk for cognitive impairment in older women. Here, we assessed for an interaction between assignment to HT and diabetes status on brain volumes in the WHIMS cohort. **Methods:** Brain imaging and cognitive data from 1,402 women from the magnetic resonance imaging substudy of the Women's Health Initiative (WHIMS-MRI) were used. All participants were part of the Women's Health Initiative study, a clinical trial where women were randomized to receive HT (0.625 mg/day conjugated equine estrogens with or without 2.5 mg/day medroxyprogesterone acetate) or placebo. For this analysis, diabetes status was determined based on self-report of treatment for diabetes or fasting plasma glucose $\geq$ 126 mg/dL in women where this was measured. Brain volumes were derived from T1-weighted anatomical images. Relationships were assessed using general linear models. Diabetes status, HT assignment, and their interaction were included as fixed effects to assess their relationship with brain volumes and changes in brain volumes. **Results:** Women with diabetes assigned to HT had a mean [95% confidence interval] decrement of -18.6 [-29.6, -7.6] in total brain volume relative to women with diabetes assigned to placebo. For women without diabetes, this mean decrement was -0.4 [-3.8,3.0].The interaction between diabetes status and HT assignment on brain volume was significant for total brain (p=0.002), grey matter (<0.001), and hippocampal (p=0.006) volumes, but not for white matter (p=0.92) or frontal lobe (p=0.24) volumes. Differences between HT treatment and placebo groups were consistently smaller for women without