cortex (BA 38) from cases of Alzheimer's disease, diffuse Lewy-body disease and non-neurologic normal controls. Libraries were prepared from extracted RNA using Illumina's Directional RNA-seq and DSN normalization protocols. Each sample was run on one lane of Illumina's HiSeq2000, generating 40-65 million reads. Using the alignment program TopHat, approximately 80% of the reads aligned to the reference genome. The Cufflinks program assembled transcripts and determined expression values. **Results:** An average of 85,000 unique transcripts were found in each sample with average coverage of 600 reads per transcript. Each sample expressed approximately 16,000 annotated reference sequence (RefSeq) genes. To date, 2,579 novel isoforms of RefSeq genes were discovered with several of them belonging to genes previously associated in AD (e.g. BIN1, PICALM, etc). In total, 76,000 novel transcripts (un-annotated transcripts) were observed, most mapping to intronic regions of genes (41%), the antisense strand of a known gene (46%), or the intergenic regions of annotated genes (6%). Our results also reveal hundreds of anti sense transcripts. Initial results have identified ten novel antisense transcripts that overlap genes or regions that have shown genome wide association to AD. Four of these have been verified, with the analysis of the other six currently underway. **Conclusions:** A significant amount of the AD transcriptome consists of novel transcripts, suggesting considerable uncharacterized regulation. In addition we have detected over 2500 previously uncharacterized alternative splicing events in AD and novel antisense RNA transcripts to known AD candidate genes and/or regions. Studies of these antisense transcripts and novel isoforms may yield valuable insight into the etiology of AD.

O1-01-08 DEVELOPMENT OF A GENETIC EDUCATION AND GENETIC RISK DISCLOSURE PROTOCOL FOR INDIVIDUALS WITH MILD COGNITIVE IMPAIRMENT

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Background: The Risk Evaluation and Education for Alzheimer's Disease (REVEAL) Study is a series of randomized controlled trials evaluating the impact of disclosing genetic risk for Alzheimer's disease (AD). During the fourth REVEAL trial, we developed a risk communication protocol to disclose *APOE* genotype and three-year risk of progressing to AD to individuals with amnestic-Mild Cognitive Impairment (MCI). **Methods:** We generated risk estimates using data obtained from a clinical trial involving 769 amnestic-MCI patients, which provided three-year conversion data stratified by *APOE* genotype (Petersen et al., 2005). We used an evidence-based approach in risk communication to develop graphics and language to communicate *APOE* genotype and a numerical risk estimate. Consensus was reached on specific issues including how to discuss the protective nature of the *APOE*e2 allele in an *APOE*e2/e4 genotype and the presence of two copies (versus one) of *APOE*e4. **Results:** Three-year risks for each age-group were: 8.4% for *APOE*e4 negative and 42.0% for *APOE* e4 positive individuals (ages 55-70), 20.5% for *APOE*e4 negative and 47.4% for *APOE* e4 positive (ages 71-77), and 30.7% for *APOE*e4 negative and 57.1% for *APOE* e4 positive (age 78 or older). Estimates based on MCI diagnosis and age alone (excluding genotype information) were 25.2% (ages 55-70), 34.0% (ages 71-77) and 43.9% (ages 78 or older). Educational materials were created to describe the possible *APOE* genotypes, an individual's *APOE* genotype result and three-year AD conversion risk. For all risk estimates, pictographs and risk curves were created. Pictographs had 100 total boxes with colored-in boxes depicting a numerical risk percentage for AD. Comparison pictographs were created to display general population three-year risk for AD (5%) and three-year AD conversion risk among individuals with MCI of the same age (excluding genotype). Language was incorporated for risk disclosure of the "protective" e2 allele and the presence of two e4 alleles which may decrease or increase risk, respectively, and may not be accurately reflected in our risk estimates. **Conclusions:** We developed a tool for potential use in a clinical setting when individuals with MCI inquire about *APOE* genotype and risk of progressing to dementia.

SUNDAY, JULY 17, 2011
ORAL
O1-02
PREVENTION INTERVENTIONS

O1-02-01 ASSOCIATION OF HDL CHOLESTEROL LEVEL WITH THE SEVERITY OF ALZHEIMER'S DISEASE AND IMPROVEMENT FOLLOWING EXERCISE

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Background: Low plasma HDL cholesterol level has been associated with increased risk of Alzheimer's disease (AD). However, there have been no studies on the association between HDL cholesterol levels and the severity of AD and improvement following exercise. We have therefore investigated the association of HDL cholesterol levels and the severity of AD and looked at the impact of exercise on HDL levels, cognitive and physical functioning in a 4-month randomised controlled trial of patients with AD. **Methods:** 85 consecutive patients with AD were selected from the Memory Disorders Clinic in Launceston, Australia, of whom 40 patients were randomly allocated to either the treatment (exercise) group or the control group. Patients in the treatment group participated in a four month at-home exercise program and controls received their usual treatment only. Patients were assessed at baseline and four months follow-up on measures of cognitive and physical functioning, and fasting plasma lipids were measured using standard assessment tools. **Results:** Fifty women and 35 men participated in the study, mean age of 74.4 years (range 51-90 years) and a mean Mini Mental State Examination (MMSE) score of 18.6 (range 4-28). Using multiple regression analysis, HDL cholesterol level was independently positively correlated with MMSE score (ß coefficient 6.7, $p = 0.007$). Patient with sever AD (MMSE score of 13 or less), compared with mild to moderate disease (MMSE score > 13), had lower HDL level by 0.23 mmol/L or 20%, $p = 0.008$). At 4 months follow-up, patients who exercised, compared with controls, were 2.9 seconds faster on Timed Up and Go ($p = 0.004$), had increased MMSE scores by 2.6 points ($p < 0.001$) and had increased plasma HDL by 0.16 mmol/L ($p = 0.016$). These analyses were adjusted for confounding factors using general linear modelling. **Conclusions:** This study suggests that a low plasma HDL cholesterol level was associated with the severity of AD. Exercise may help to improve cognitive and physical functioning and this may be partly explained by the increase in plasma HDL level.

O1-02-02 PREVENTING COGNITIVE DECLINE IN THE ELDERLY THROUGH PHYSICAL ACTIVITY IN MIDLIFE

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Background: Despite advances in healthcare for those with Alzheimer's disease and other forms of dementia, the absence of an effective long-term treatment means that the prevalence of age-related cognitive decline