P3-213 DECISION QUALITY AND THE USE OF CARDIAC RHYTHM REGULATING DEVICES IN ADULTS WITH COGNITIVE IMPAIRMENT

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Background: Along the course of cognitive impairment, patients and their family face a number of decisions about medical care for both dementia and for co-morbid conditions. It is unknown how many older adults with cognitive impairment are faced with the decision to implant a cardiac device (e.g., a pacemaker or implantable cardiac defibrillator [ICD]) following the development and identification of MCI and dementia. The objective of this study is to estimate the prevalence, incidence, and association of cardiac device implantation in adults with normal cognition, MCI and dementia. **Methods:** The study population was composed of subjects from the National Alzheimer's Coordinating Center Uniform Data Set gathered prospectively from 33 Alzheimer's Disease Centers. Subjects underwent annual clinical exams, which included cognitive and functional testing and assessment of comorbid conditions. This analysis focused on 16,245 subjects who had a baseline visit and at least one follow-up visit between September 1, 2005 and December 31, 2011. Measures included prevalence of pacemaker and ICDs at baseline, percent of new incident devices by year and cognitive status, and associations between incident device and cognitive status. **Results:** The overall prevalence of pacemakers at baseline was 2.6%. By cognitive status, prevalence of pacemakers was 2.1% for those with normal cognition, 2.9% with MCI, and 3.1% for dementia. Prevalence of ICDs at baseline was <1% for all groups. Over a 7 year study period, rates of new pacemaker devices averaged 4.1% for people with normal cognition, 4.8% for MCI, and 5.6% for dementia. After controlling for age, sex, race, geographic region, functional status, and cardiac co-morbidities, subjects with dementia are 1.92 (p<0.01)more likely to get a pacemaker and subjects who have MCI and experience cognitive decline are 1.96 more likely (p<0.01) to get a pacemaker than subjects with normal cognition. **Conclusions:** Patients with cognitive impairment are frequently faced with the decision whether or not to implant cardiac device. In a national sample, incidence rates of new pacemakers were higher for those with MCI and dementia compared to subjects with normal cognition. After controlling for demographics and clinical indications, patients with dementia were more likely get new pacemaker devices than non-demented peers.

P3-214 ASSOCIATION BETWEEN BONE MINERAL DENSITY AND COGNITIVE IMPAIRMENT AMONG COMMUNITY-DWELLING ADULTS WITHOUT DEMENTIA AND STROKE

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Background: Low bone mineral density (BMD) has been associated with an increased risk of dementia and stroke. However, this association is unclear in adults aged 50 years and above without a history of stroke or dementia. **Methods:** BMD and cognitive function using Korean mini mental state examination (MMSE) were assessed in 650 stroke- and dementia-free subjects older than 50 years (mean age, 62.9 ± 8.0 years) who were recruited for an early health check-up program between 2009 and 2010. **Results:** Mean BMD was lower in the low MMSE group (<24 score) compared to the high MMSE group (≥24 score) (p<0.01). In the unadjusted analysis, age, education level, and BMD were significantly associated with cognitive impairment based on MMSE score in both women and men. In women, education level and BMD were also significant (odd ratio, 1.17, 95% confidence interval, 1.15-2.55, P<0.01, odd ratio, 2.17 95% confidence interval, 1.46-3.22, p<0.01, respectively) after adjusting for age, sex, education level, and smoking. **Conclusions:** These findings suggest that BMD is correlated with cognitive impairment among community-dwelling adults aged 50 and above without any medical history of stroke or dementia. Further understanding of this association may be important for prevention of dementia

P3-215 THE NEED FOR A LARGE REGISTRY AND CLINICAL TRIALS IN YOUNG- AND MIDDLE-AGED APOLIPOPROTEIN E ε4 HOMOZYGOTES

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Background: The prevalence of apolipoprotein E4 (ApoE4) homozygotes is about 2-3% in the United States. Individuals that are ApoE44 have at least a 50% risk of developing dementia by the time they are 80 years of age. Risk of dementia associated with ApoE44 is increased 12-fold as compared to ApoE33. Similarly, E44s have probably over a 50% increased risk of developing clinical coronary artery disease (CAD) primarily because of effects on ApoB lipoprotein metabolism. **Methods:** Practically all individuals who are ApoE4 heterozygotes, even "cognitively normal" at an older age, have substantial amyloid deposition in the brain and very high risk of dementia. Reasons why ApoE4 is associated with increased amyloid include lipoprotein metabolism, amyloid beta (Abeta) production in the brain, inflammation and clearance of amyloid out of the brain, direct effect on neuronal viability. **Results:** Younger ApoE44 individuals in their 40s have abnormalities of brain glucose metabolism and subtle cognitive changes. Success in reducing AD in the population depends on nonpharmacological interventions such as exercise or drug therapies, safe with low side effects and low cost. None of the current drug therapies in ongoing clinical trials meet these criteria. Whether E44 homozygotes develop cardiovascular disease, atherosclerosis and amyloid deposition in the brain synonymously or two processes evolve separately within individuals is unknown. Potent drugs to lower lipid levels, such as statins, will likely substantially reduce atherosclerosis and CAD in ApoE44 homozygotes. Whether such drugs, including newer drugs such as PCSK9 inhibitors, have any impact on the progression of amyloid deposition in the brain is unknown. Other drugs and nonpharmacological therapies, i.e. exercise, could be tested in factorial designed clinical trials of E44 homozygotes at younger ages before extensive amyloid deposition and coronary atherosclerosis. **Conclusions:** Identification of E44 individuals early for the treatment of their CVD, i.e. lipid lowering, will likely be of great benefit to them in reducing CAD. It would therefore be ethical for the individuals to be identified by testing for ApoE4. They provide the best opportunity to find therapies to reduce the development and progression of amyloid and dementia.

P3-216 LOW EDUCATION, BRAIN WEIGHT AND DEMENTIA: EVIDENCE FOR NEURAL RESERVE

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Background: Structural brain characteristics and educational attainment have been implicated as contributors to neural reserve. The relation of brain weight and very low levels of education to dementia has not been investigated. We conducted a clinicopathological study to determine whether elementary education and brain weight, alone or in combination, are associated with lower frequency of dementia. **Methods:** In this cross-sectional study, 510 individuals, ≥50 years of age, from the Brazilian Aging Brain Study Group were included. Subjects were classified as normal cognition if CDR=0, IQCODE<3.41 (n=346) and demented if CDR ≥1 and IQCODE≥3 (n=164). Neuropathologic examinations were performed using immunohistochemistry. Multivariate logistic regression models were conducted to determine whether the association of education and brain weight to dementia was independent of sociodemographics and neuropathologic lesions. In a subsequent analysis an interaction term for education and brain weight was added. **Results:** Mean education was 4.1±3.6 years. Individuals who received formal education had a lower frequency of

dementia when compared to the individuals with no formal education (N=90). After adjustment for sociodemographics and neuropathologic features including neuritic plaques, neurofibrillary tangles, lacunar infarctions, small vessel disease, and Lewy bodies, 1-4 years of education education had an OR=0.54, 95%CI 0.28-1.02; p=0.06; >4 years had an OR=0.38, 95%CI 0.17-0.88; p=0.02. Higher brain weight was also associated to lower frequency of dementia in adjusted analysis (OR= 0.64, 95% CI: 0.49-0.85, p=0.002). The interaction between education and brain weight was not related do dementia (p=0.37). **Conclusions:** Higher education and brain weight are associated with lower frequency of dementia. Education and brain weight may represent different domains of neural reserve.

P3-217 **EFFECT OF INTELLECTUAL LIFESTYLE AND ALZHEIMER'S DISEASE BIOMARKERS ON RATE OF COGNITIVE DECLINE: MAYO CLINIC STUDY OF AGING**

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Background: To investigate the effect of intellectual lifestyle and biomarkers of AD pathophysiology on the rate of cognitive decline in a nondemented elderly population. The biomarkers evaluated were brain Aβ-amyloid load via PIB-PET and neurodegeneration via FDG-PET and Structural-MRI. **Methods:** We studied 369 non-demented (317 cognitively normal, 52 MCI) participants in the population based Mayo Clinic Study of Aging who had a baseline 3T MRI, FDG and amyloid PET scans, baseline cognitive assessment, had lifestyle measures and at least one additional clinical follow-up. We grouped intellectual lifestyle into 2 composite variables: Education/Occupation-score and mid/late-life leisure intellectual lifestyle measures. We used a global cognitive Z-score as a measure of cognition. We used linear mixed-effects models to investigate the associations between demographic, lifestyle measures, AD biomarkers and the global cognitive Z-score trajectories. **Results:** Baseline cognitive performance was lower in those with lower education/occupation, lower baseline FDG uptake, smaller baseline hippocampal volume and males. The interaction between the two lifestyle measures was significant. Only baseline age and baseline hippocampal volumes were significantly associated with change in cognitive performance from baseline after 1.3 median years of follow-up. **Conclusions:** 1) Intellectual lifestyle measures explained variability in the baseline cognitive performance but were not associated with rate of cognitive decline. 2) Higher mid/late leisure lifestyle was associated with better baseline cognitive performance only in those with low education/occupation-score. 3) While baseline FDG uptake, hippocampal volume, and sex were associated with baseline cognitive performance only higher age and smaller hippocampal volume were associated with faster rate of cognitive decline.

P3-218 **A 6-MONTH AEROBIC EXERCISE PROGRAM IS ASSOCIATED WITH INCREASED HIPPOCAMPAL VOLUME IN OLDER AFRICAN-AMERICANS**

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Background: Alzheimer's disease (AD) is increasingly an epidemic in the United States (US) and worldwide; yet, an efficacious treatment is unavailable, and amyloid-directed therapies have not produced encouraging results. Because of the understanding that cardiovascular disease (CVD) risks may catalyze Alzheimer's disease (AD) development, there is now a heightened interest in determining whether proven CVD risk reduction measures can similarly attenuate AD risk.Converging evidence from cross-sectional and

prospective studies including the CVD Health Cognitive Study and others; now suggests that exercise-training can slow cognitive deterioration. Whereas the relationships of training effects are progressively linked to improvements in markers of neurodegeneration including brain volume, data is lacking on African Americans (AA)s who are relatively sedentary and also harbor significant CVD and AD burdens. Therefore, we investigated the effects of a 6-month aerobic-exercise on markers of neurodegeneration in a mild cognitively impaired (MCI) AA sample. **Methods:** After obtaining informed consent, initial screening, qualifying treadmill, dietary stabilization on American Heart Association (AHA) Step 1 diet, and baseline tests that included MRI of the brain, volunteers were randomized into aerobic versus stretch exercise control. They then underwent supervised 3-times per week 6-month aerobic exercise training, after which all baseline tests were repeated. **Results:** In 7 older AAs, mean age 70 years, randomized into aerobic exercise versus stretch (control), completed baseline and after-training brain MRI, and then regions of interest analysis (ROI) analyses; the aerobic-exercise group had more increases in hippocampal and parahippocampal volumes (P =0.01; and corrected threshold of FDR=0.08). Such findings in a relatively small sample of MCI subjects may indicate significant favorable effects of exercise adaptation on markers of neurodegeneration. **Conclusions:** We conclude that 6-month aerobic exercise training is likely associated with increased hippocampal volume in relatively sedentary older AAs. We plan to confirm these findings in relatively larger sample and also correlate same with the cognitive phenotype.

P3-219 **A MACHINE-LEARNING APPROACH FOR INTEGRATION OF COMPUTERIZED COGNITIVE DATA IN THE NEUROPSYCHOLOGICAL ASSESSMENT OF OLDER ADULTS**

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Background: In progressive conditions like dementia, it is important to detect subtle cognitive changes early and initiate intervention to slow or even halt disease progression. Essential to early detection is comprehensive cognitive assessment. Computerized neuropsychological batteries offer rapid, standardized, and precise assessment, as well as automatic scoring, but it remains a formidable task to optimally integrate the information. This study aims to identify a machine learning (ML) algorithm that optimally and automatically integrates all available computerized cognitive testing scores to improve neuropsychological assessment of older adults. **Methods:** A dataset of 6136 individuals over age 50 who completed a computerized cognitive testing battery for mild impairment was used. 5108 individuals had a primary diagnosis of one of 81 neurological or psychiatric conditions ("neurological condition" group), and 1028 were cognitively healthy (control group). Four ML algorithms (Naive Bayes, multi-layer perceptron [MLP] neural network, support vector machine [SVM], decision tree) were compared in separating the neurological condition and control group using 65 raw cognitive scores, age and education. For the best performing algorithm, confidence in individual classifications and separation among diagnostic groups were evaluated. **Results:** The MLP neural network approach best separated neurological condition and control group (area under the curve [AUC]=0.89; compare with AUC=0.70 for a single global cognitive score). In a test sample, maximum confidence (from MLP output node activity) was assigned in 76% of individuals classified as "neurological condition", with 85% of these correctly classified. Maximum confidence was assigned in 71% of individuals classified as cognitively healthy, with 87% of these correctly classified. MLP performed well in separating the control group from mild cognitive impairment (MCI) (AUC=0.82), dementia (AUC=0.89), Parkinson's disease (AUC=0.91), multiple sclerosis (AUC=0.94), stroke (AUC=0.89), and traumatic brain injury (AUC=0.93), and showed good separation between amnestic MCI and Alzheimer's disease (AUC=0.75). **Conclusions:** ML algorithms may greatly improve the accuracy and efficiency of the neuropsychologist or cognitive expert in integrating the wealth of computerized cognitive scores with other clinical information in assessing older adults. Future work should evaluate ML