P3-183 THE IMPACT OF LORAZEPAM ON COGNITION ON APOE-ϵ4 CARRIERS VERSUS NONCARRIERS

Cynthia M. Stonnington[1], Peter J. Snyder[2,3], Joseph G. Hentz[1], Eric M. Reiman[4,5], Richard J. Caselli[1], *[1]Mayo Clinic, Scottsdale, AZ, USA; [2]University of Connecticut, Storrs, CT, USA; [3]Yale University School of Medicine Child Study Center, New Haven, CT, USA; [4]University of Arizona, Tucson, AZ, USA; [5]Banner Alzheimer's Institute, Phoenix, AZ, USA. Contact e-mail: stonnington.cynthia@mayo.edu*

Background: The apolipoprotein E (APOE) ϵ4 allele is a common Alzheimer's disease (AD) susceptibility gene. Previously, sleepiness was negatively correlated with memory in an exploratory cross-sectional study of cognitively normal APOE-ϵ4 homozygotes. If the induction of acute somnolence by lorazepam were to expose neuropsychological deficits in at-risk individuals, then it could be applied to a pharmacologic challenge for prediction of subsequent cognitive decline. **Methods:** Eighteen ϵ3/4 heterozygotes (HTZ) and 18 ϵ4 noncarriers (NC), 50 to 65 years of age, all healthy and cognitively normal, participated in the study. In a double blind, crossover design, we performed neuropsychological testing before, 2.5 hours, and 5 hours after participants received a single 2 mg dose of lorazepam or placebo. Main outcome measures were the Groton Maze Learning Test (GMLT), Rey Auditory Verbal Learning Test (AVLT), and 1-Back test. NC were matched to HTZ by age and years of education. **Results:** At 2.5 hours after the dose of lorazepam, the GMLT total errors score ($P=.04$) and the AVLT long-term memory ($P=.01$) and percent recall ($P=.005$) measures of verbal memory were more impaired in HTZ than NC. A MANOVA comparing the vector of all six GMLT and AVLT measures for HTZ versus the vector of all six measures for NC yielded $P=.003$ for 2.5 hours and $P=.58$ for 5 hours. No differences between HTZ and NC were observed for measures of somnolence, speed, attention, or performance on the 1-Back test at any of the time points. At 5 hours, HTZ continued to make substantially more errors than NC ($P=.17$) only on the GMLT. **Conclusions:** Our study suggests that somnolence induced by lorazepam impairs verbal and visuospatial memory more in healthy middle-aged APOE ϵ4 carriers than noncarriers. The results warrant further research with a larger sample to determine if lorazepam induces an even greater effect in ϵ4 homozygotes, whether substantial lorazepam-induced memory impairment predicts subsequent onset of cognitive decline and conversion to mild cognitive impairment or AD, and whether adverse effects of clinical lorazepam administration are greater in ϵ4 carriers.

P3-184 CORRELATION BETWEEN MEDIAL TEMPORAL ATROPHY MEASURED BY A VOXEL-BASED MORPHOMETRY SYSTEM AND SPECIFIC DOMAINS OF COGNITIVE FUNCTION IN ALZHEIMER DISEASE

Hajime Takechi[1], Yoshiyuki Hamakawa[1], Atsuko Kokuryu[1], Seiichi Furuya[2], *[1]Department of Geriatric Medicine, Kyoto University, Kyoto, Japan; [2]Louis Pasteur Center for Medical Research, Kyoto, Japan. Contact e-mail: takechi@kuhp.kyoto-u.ac.jp*

Background: Recent advance in volumetric MRI technique provide occasion to measure brain atrophy in routine clinical practice. To study correlation between specific area of brain atrophy and cognitive impairment would be useful to understand pathophysiology of Alzheimer disease (AD). **Methods:** Twenty AD, 10 MCI and 12 patients who were finally diagnosed as normal were recruited to this study. Mean (SD) age of each group was 75.9 (6.1), 74.3 (9.7) and 75.2 (7.0), respectively. All of the patients underwent volumetric MRI measurement on a 1.5-T system and neuropsychological examination. The voxel-based morphometry for MR images were performed using a voxel-based specific regional analysis system for AD (VSRAD, Hirata Y et al. Neurosci. Lett. 2005) in which specific voxel of interest, mainly in bilateral entorhinal cortex, was determined by group comparison of gray matter images for patients with very early AD at the MCI stage with those for healthy volunteers using SPM. **Results:** Mean (SD) of MMSE were 21.0 (3.3) for AD, 26.5 (2.1) for MCI and 28.9 (1.3) for normal. Mean (SD) of VSRAD z-score were 3.23 (1.45) for AD, 1.77 (1.08) for MCI and 1.38 (0.70) for normal. For the analysis of correlation, data of AD and MCI were combined. The analysis of correlation between VSRAD z-score and neuropsychological examination revealed the correlation between VSRAD z-score and MMSE ($r= -0.433$, $p<0.05$), word fluency (vegetables, $r= -0.538$, $p<0.005$) and a subscale of MMSE (orientation for place, $r= -0.518$, $p<0.01$). Correlation was not observed between VSRAD z-score and other tests including category-cued memory test (16 words), Trail Making Test A and B, Block design test of WAIS-R, Clock drawing test and subscales of MMSE related to recent memory (orientation for time, 3 words delayed recall). **Conclusions:** Medial temporal atrophy measured by voxel-based morphometry was correlated with MMSE and word fluency, but not with recent memory test, which is usually thought to reflect the function of medial temporal lobe. Slight atrophy in medial temporal lobe in very early stage of the disease may be responsible for memory loss and the additional atrophy in it may predict decline in language and general cognitive function.

P3-185 PREDICTORS OF LONGITUDINAL COGNITIVE DECLINE IN A COMMUNITY-BASED SAMPLE OF SPANISH- AND ENGLISH-SPEAKING OLDER ADULTS

Sarah Tomaszewski Farias[1], Dan Mungas[1], Ladson Hinton[1], Mary Haan[2], *[1]University of California, Davis, Sacramento, CA, USA; [2]University of Michigan, Ann Arbor, MI, USA. Contact e-mail: sarah.farias@ucdmc.ucdavis.edu*

Background: The identification of older adults who are at an elevated risk of future decline in cognitive function is often difficult, particularly in individuals of an ethnic minority. We prospectively evaluated which baseline demographic, neuropsychological and functional variables were most strongly associated with future longitudinal decline in global cognitive function. **Methods:** Participants were part of the Sacramento Area Latino Study on Aging (SALSA) (N = 696) and included cognitively normal, mildly impaired, and demented cases. 63% were tested in Spanish. Average follow-up was five years. Latent growth modeling of longitudinal data assessed the effects of age, gender, education, language (Spanish or English-speaking), acculturation, measures of neuropsychological function (i.e. verbal memory and confrontation naming) and functional status (as measured by the IQCODE) at baseline, on rate of change in global cognitive impairment (measured by the 3MS). **Results:** Lower education, Spanish-speaking status, lower scores on the neuropsychological tests and more impaired everyday function at baseline were all associated with greater global cognitive impairment at baseline. In terms of predicting change, the only baseline demographic variable associated with a faster rate of decline was older age. Poorer baseline memory and naming were associated with global cognitive decline but this relationship did not remain significant after including age in the model. More functional impairment at baseline was associated with a faster rate of decline and this effect was independent of age. **Conclusions:** Education and language of test administration were associated with baseline cognitive performance but not change over time, highlighting the importance of longitudinal follow-up in understanding the effects of neurodegenerative disease in ethnically and educationally diverse populations. Baseline functional status but not neuropsychological variables were independently associated with both baseline and change in global cognitive impairment, suggesting functional problems may be a more sensitive indicator of disease presence and progression than cognitive test performance in ethnically and educationally diverse samples.

P3-186 SUBJECTIVE MEMORY COMPLAINT IN ALZHEIMER'S DISEASE

Francisco A. C. Vale, Ari P. Balieiro Jr, José H. Silva-Filho, *Behavioral Neurology Goup of Clinics Hospital of the Ribeirão Preto Faculty of Medicine, Ribeirão Preto, SP, Brazil. Contact e-mail: facvale@hcrp.fmrp.usp.br*