IC-P1-035 LOWER CORTISOL AWAKENING RESPONSE IS ASSOCIATED WITH SMALLER HIPPOCAMPAL VOLUMES

Arnoud J. G. Knoops[1], Yolanda van der Graaf[1], Willem P. Th M. Mali[2], Mirjam I. Geerlings[1], *[1]University Medical Center Utrecht , Julius Center for Health and Primary Care, Clinical Epidemiology, Utrecht, Netherlands; [2]University Medical Center Utrecht, Department of Radiology, Utrecht, Netherlands. Contact e-mail: a.j.g.knoops@umcutrecht.nl*

Background: Although it has frequently been hypothesized that high levels of glucorticoids have deleterious effects on the hippocampus and may contribute to increased risk for Alzheimer's disease, this study is among the first to investigate the effect of changes in HPA axis activity on hippocampal volume by assessing the diurnal cortisol profile. **Methods:** Within the SMART-MR study, a prospective cohort study among patients with manifest arterial disease, cross-sectional analyses were performed in 278 patients (mean age 62 ± 9 years) with available data on cortisol and hippocampal volume. Circadian cortisol rhythm was assessed with 6 saliva samples, collected at awakening and 30, 45 and 60 minutes thereafter, and at 10 PM and 11 PM. A low dose of dexamethasone (0.5 mg) was administered at 11 PM and saliva was sampled the next morning at awakening. The diurnal cortisol profile was defined as the cortisol awakening response (CAR), a distinct and dynamic part of the cortisol circadian rhythm (mean cortisol secreted within the first hour after awakening); resting evening values (mean of the two evening measurements); and the suppressibility of the HPA axis (cortisol after 0.5 mg dexamethasone). Volumetric measurements of the hippocampus was performed on a 3-dimensional TFE T1-weighted MRI scan with isotropic voxels. The left and right hippocampus were manually traced and corrected for head size by dividing hippocampal volume by intracranial volume, which was obtained by automatic brain segmentation. **Results:** Mean total hippocampal volume relative to intracranial volume was 6.2 ± 0.7 ml. Linear regression analyses, adjusted for age and sex, showed that subjects with a lower CAR had smaller hippocampal volumes (β per nmol*h/l increase=0.014 ml; 95% CI 0.001 to 0.028). Evening levels and cortisol levels after dexamethasone were not significantly associated with hippocampal volume. **Conclusions:** In this population, a lower cortisol awakening response was associated with smaller hippocampal volumes, but evening cortisol levels and cortisol levels after dexamethasone suppression were not. Future studies should determine to what extent lower cortisol secretion after awaking associated with smaller hippocampal volumes increases risk for Alzheimer's disease.

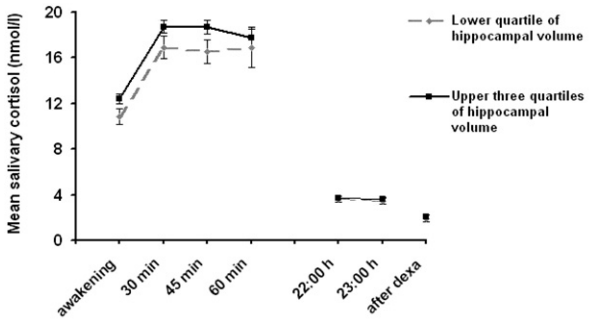

Figure 1 Cortisol profiles (mean ± SEM) of all participants (n=278) divided in the lower quartile and upper three quartiles of hippocampal volume. Shown are the awakening response, evening levels and mean cortisol levels after ingestion of 0.5 mg dexamethasone.

IC-P1-036 CATEGORICAL AND CORRELATIONAL ANALYSES OF BASELINE FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY IMAGES FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

Wendy Lee[1,2], Jessica B. S. Langbaum[1,2], Kewei Chen[1,2], Cole Recshke[1,2], Daniel Bandy[1,2], Gene E. Alexander[2,3], Norman L. Foster[4], Michael W. Weiner[5], Robert A. Koeppe[6], William J. Jagust[7], Eric M. Reiman[1,2], *[1]Banner Alzheimer's Institute, Phoenix, AZ, USA; [2]Arizona Alzheimer's Consortium, Phoenix, AZ, USA; [3]University of Arizona, Tucson, AZ, USA; [4]University of Utah, Salt Lake City, UT, USA; [5]University of California, San Francisco, CA, USA; [6]University of Michigan, Ann Arbor, MI, USA; [7]University of California Davis, Davis, CA, USA. Contact e-mail: Wendy.Lee@bannerhealth.com*

Background: Alzheimer's disease (AD) is characterized by regional reductions in fluorodeoxyglucose positron emission tomography (PET) measurements of the cerebral metabolic rate for glucose (CMRgl), which are correlated with clinical severity, progressive and apparent before the onset of dementia or mild cognitive impairment (MCI). We have been using statistical parametric mapping (SPM) to analyze PET data from probable AD patients, amnestic MCI (aMCI) patients and normal controls (NC) from the AD Neuroimaging Initiative (ADNI). Our objective was to characterize patterns of cerebral hypometabolism in probable AD and aMCI, and correlate lower Mini-Mental State Examination (MMSE) scores with lower regional CMRgl in both the overall cohort of probable AD, aMCI and NC subjects and the probable AD group. **Methods:** Baseline PET images from 298 subjects, including 74 probable AD (age 70±10, MMSE 23.5±2.2), 142 aMCI (age 67±12, MMSE 27.1±1.7) and 82 NC (69±10 years old, MMSE 28.9±1.1), were analyzed on a voxel-by-voxel basis using SPM5. ANOVA with pair-wise comparisons contrasted regional CMRgl in the three subject groups. Linear regression correlated lower MMSE scores with lower CMRgl in the overall cohort and probable AD group. **Results:** Compared to NC, the probable AD and aMCI groups each had lower CMRgl bilaterally in previously characterized posterior cingulate, precuneus, and parietotemporal regions ($P<0.05$ corrected for multiple comparisons), and occipital cortex, hippocampus, parahippocampal gyrus and fusiform gyrus (uncorrected $P<0.005$). Compared to NC, the probable AD group had lower CMRgl in frontal regions (corrected $P<0.05$). In the overall cohort, lower MMSE scores were correlated with lower CMRgl in the posterior cingulate, precuneus, parietotemporal and frontal regions ($P<0.05$, corrected for multiple comparisons). In the probable AD group, lower MMSE scores were correlated with lower CMRgl in left frontal and temporal regions (uncorrected $P<0.001$). **Conclusions:** Findings from this large multi-center study confirm the previously characterized pattern of regional hypometabolism in AD and aMCI and implicate additional brain regions. Furthermore, they confirm the previously characterized correlation between severity of clinical impairment in a combined group of patients and controls, but suggest strongest correlations between clinical severity of frontal and temporal regions by the time AD patients satisfy criteria for dementia.

IC-P1-037 FUNCTIONAL MAGNETIC RESONANCE IMAGING ACTIVATION PATTERNS IN COGNITIVELY NORMAL ELDERLY, AMNESTIC, AND NON-AMNESTIC MILD COGNITIVE IMPAIRMENT DURING A RECOGNITION MEMORY TASK

Mary M. Machulda, Matthew L. Senjem, Glenn E. Smith, Robert J. Ivnik, Bradley F. Boeve, David S. Knopman, Ronald C. Petersen, Clifford R. Jack, *Mayo Clinic, Rochester, MN, USA. Contact e-mail: machulda.mary@mayo.edu*