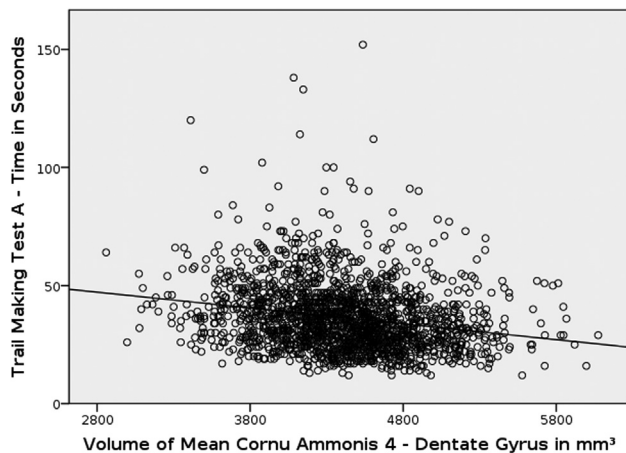


aged 19-82years with MRI and neuropsychological tests (mean-age=57.61,  $\pm$ 15.08SD). **Exclusion:** stroke, major-brain-pathologies, central-nervous-medication. **Independent Variables:** Volume of hippocampus and its subfields (CornuAmmonis1, 2-3, 4-DentateGyrus, (Pre-)subiculum). **Dependent Variables:** Verbal word-list learning, verbal-fluency, TrailMakingTask-(TMT)-A&B. **Covariates:** sex, age, years-of-education, total grey-matter-volume **Image Analysis** on high-resolution T1-images assessed at 3T. Hippocampal volumes were estimated using automatic segmentation analysis implemented in FreeSurfer ([www.freesurfer.net](http://www.freesurfer.net)). **Statistical Analysis:** Independent and dependent variables were first entered into Pearson Correlations. Variables with a correlation coefficient of  $r > 0.1$  were entered into multiple linear-regressions and adjusted for potential confounding (forward inclusion-model). **Results:** According to bivariate correlations, better performance in verbal-learning, verbal-fluency and TMT-A&B correlated moderately with larger whole-hippocampal volume and the volumes of all subfields (all  $|r| > 0.102$ , all  $p < 0.002$ ; Fig.1) except CA1 showing a weak positive correlation with TMT-A&B only (all  $|r| > 0.046$ , all  $p < 0.046$ ). Linear regressions controlling for age, sex, education and total grey matter volume indicated that whole-hippocampal volume significantly explained 0.2% variance of verbal-learning performance ( $p = 0.01$ ,  $\beta = 0.054$ ) and CA4-DG volume explained 0.5% of the variance in TMT-A performance ( $p = 0.001$ ,  $\beta = -0.054$ ). Verbal-fluency, TMT-B, as well as other subcortical structures such as the thalamus were not associated with cognitive performance after controlling for confounders ( $p > 0.5$ ). **Conclusions:** Using a large cross-sectional cohort of healthy adults we found that volumes of the whole-hippocampus and subfields covering the CA4/dentate-gyrus region were weakly, yet specifically associated with verbal-learning and spatial processing-speed. Our preliminary results are in line with previous studies presuming a differential involvement of the hippocampus in tasks of verbal-learning and spatial processing (Oosterman, 2010). Upcoming analyses implementing parcellation along the anterior-posterior-axis and random-effect-models might help to further disentangle these effects.



Scatterplot of Trail Making Test A Performance in Seconds and Volume of Mean Cornu Ammonis 4 - Dentate Gyrus in  $\text{mm}^3$ . Less time needed to complete Trail Making Test A equals a better performance.

P3-358

#### SELECTIVE AGE-ASSOCIATION OF HIPPOCAMPAL SUBFIELDS IN COGNITIVELY HEALTHY ELDERLY

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**Background:** Hippocampal volume (HV) is the most robust MRI marker of neurodegeneration predicting dementia. However, the hippocampus is a heterogeneous brain structure composed of various subfields with distinct histological characteristics that can now be accurately segmented thanks to new developments in high field MRI. Due to their differential anatomy and functionality, some of these hippocampal subfields (HS) have been shown to be specifically associated with AD with higher sensitivity than HV. This study investigates the age-related changes in the volume of HS as well as the entorhinal cortex in cognitively healthy elderly. **Methods:** Thirty-two cognitively healthy elderly individuals (aged  $67 \pm 8$ , 62% Males) underwent a turbo spin echo 7T MRI scan on two different sites using the same sequence and same scanner model. The hippocampus subfields were segmented with ASHS software based on the 7T UMC Utrecht atlas. Linear regressions between HS and age with gender and intracranial volumes (ICV) as covariates were computed. **Results:** The volumes of the *cornu-ammonis* (CA,  $p < 0.02$ ), the dentate gyrus (DG,  $p < 0.001$ ) and the entorhinal cortex (ERC,  $p < 0.005$ ) were negatively and significantly associated with age. The rates of atrophy were  $-3.4 \text{mm}^3/\text{yr}$  in the DG,  $-3.8 \text{mm}^3/\text{yr}$  in the CA1,  $-0.5 \text{mm}^3/\text{yr}$  in the CA2,  $-0.9 \text{mm}^3/\text{yr}$  in CA3 and  $-2.3 \text{mm}^3/\text{yr}$  in the ERC. No age-association was found with the subiculum volume. HS volumes were also associated with ICV but not with gender. **Conclusions:** In cognitively healthy elderly subjects, HS volumes are differently associated with age suggesting a selective vulnerability which may be due to the distinctive molecular and cellular composition of the different fields. Differential age-related HS atrophy should then be taken into account when modelling the atrophy due to neurodegenerative diseases. Future studies will also allow us to better understand the link between this specificity volume damage and cognitive deficit observed in aging.

P3-359

#### BETA-AMYLOID ACCUMULATION HURTS AND CRYSTALLIZED KNOWLEDGE HELPS BRAIN MODULATORY CAPACITY: AN FMRI STUDY



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**Background:** We have previously demonstrated that crystallized knowledge, as a typical neural enrichment factor, confers protection of brain modulation to task difficulty across the adult lifespan (Jingting et al., in preparation), although modulatory capacity declines with age (Kennedy et al., 2015). Here we investigated (1) whether beta-amyloid, as a typical risk factor for Alzheimer's disease, might affect modulatory capacity; and (2) whether the protective effects of crystallized knowledge on modulation remain with the accumulation of beta-amyloid. **Methods:** We studied 274 cognitively normal participants (40-89 years) who completed an F-18 Florbetapir PET scan and an fMRI scan, where participants judged

ambiguous (“Hard”) and unambiguous (“Easy”) words for animacy. Modulatory capacity was measured by contrasting hard vs. easy in functional activation. Age, amyloid and crystallized ability were entered in a multiple regression model for each of the 8 brain regions in the frontoparietal cognitive control network to assess whether amyloid and crystallized knowledge accounted for variance in modulation beyond age. **Results:** We first replicated our previous findings that older adults had decreased modulatory capacity in the frontoparietal network. After controlling for age, amyloid accumulation was related to declined modulatory capacity in parietal and right prefrontal but not left prefrontal cortex, and such depletive effects were found in middle-aged (40-60 years) but not older (60-69 years) adults. After controlling for age and continuous accumulation of amyloid, better crystallized knowledge predicted higher modulation in the frontoparietal network. Because we were particularly interested in whether the facilitating role of crystallized knowledge in modulatory capacity was related to amyloid positivity status, in a second analysis, we conducted multiple regressions with age and crystallized knowledge predicting brain modulation for amyloid negative and positive individuals, respectively. We found that better crystallized knowledge predicted higher modulatory capacity in prefrontal regions and left angular gyrus for amyloid negative individuals but only mildly ( $p = 0.057$ ) in medial superior frontal gyrus for amyloid positive individuals. **Conclusions:** Our findings suggested that brain modulatory capability is impaired with age and amyloid. Crystallized knowledge protects modulatory capacity, which seems to have stronger effects for amyloid negative individuals, compared to amyloid positive individuals.

P3-360

#### DEVELOPMENT OF A PROGRAM FOR QUICK BRAIN VOLUMETRY



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**Background:** Brain atrophy is one of the reliable markers for the evaluation of neurodegenerative change of brain and severity of dementia. FreeSurfer and other surface morphology based volumetric programs took much time and require high performance computer system. **Methods:** We developed a volumetric analysis program that can measure 26 regional volumes of brain with high feasibility to use in clinical practice. **Results:** Based on the SPM8 and MATLAB, we developed a tool box to measure the 26 regional brain volumes in both hemispheres with segmented masks. The regions were frontal (anterior, antero-medial, dorso-lateral, dorso-medial, inferior, orbital), temporal (anterior, lateral, medial), parietal (medial, lateral), occipital and central. We also calculated ventricle volume, brain volume and total intracranial volume (TIV). We validate the program with T1 high resolution 3D MRI data from 25 AD 20 MCI and 36 normal control subjects. **Conclusions:** The average running time for single data analysis was 5 minutes and 36 seconds. Test-retest reliability of this program was perfect, ICC=0.994. AD and MCI patients showed decreased brain volume and increased

ventricle volume compared to normal controls ( $p < 0.0001$ ,  $P < 0.001$ ). TIV was similar between three groups. 25 regions except orbito-frontal region showed atrophy in AD. Proportional regional brain volumes corrected with TIV showed more significance than the absolute value in comparison. **Discussions:** This automatic brain volumetric program was reliable and feasible for the researchers in clinical practice who require fast and reliable results. We will obtain more brain volume data of normal controls with different age and sex to complete normative data set.

P3-361

#### DIFFERENCES BETWEEN HEALTHY AND AMNESTIC MILD COGNITIVE IMPAIRMENT ADULTS IN EVENT-RELATED POTENTIALS DURING MEMORY ENCODING IN A VISUOSPATIAL WORKING MEMORY TASK



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**Background:** Individuals with amnesic mild cognitive impairment (aMCI) show a decline in memory capacity, which can be difficult to differentiate early on from an age related decline. Event related potentials (ERPs) are psychophysiological indexes of the time course of different cognitive processes. Thus, they could be used to identify brain electrical activity changes in aMCI adults relative to healthy adults during working memory encoding. **Methods:** Participants included 25 healthy controls and 17 aMCI adults, both homogeneous in age, education and vocabulary score. They performed a visuospatial delayed matching to sample task with 103 trials while the EEG activity was recorded. In each trial a sample stimulus, three domino tiles, was presented on screen (encoding phase) followed by a maintenance period of 3s and a probe stimulus (three domino tiles, recognition phase). Participants were asked to compare both sets and indicate whether they were identical or not. ERPs were obtained from EEG activity to sample stimuli. We analyzed P1 latency and amplitude at PO7 and PO8 electrode sites; P2 mean amplitude at Cz electrode site for two time intervals: 170 to 210 ms and 210 to 250 ms; and N2 mean amplitude from 275 to 350 ms at Cz electrode site. As no ERP component was clearly identifiable from 400 ms onwards, the mean amplitude at Cz of the following four time windows was analyzed: from 400 to 550 ms; 550 to 700 ms; 800 to 1000 ms, and from 1000 to 1200 ms. **Results:** Healthy controls showed a larger N2 ( $p = .001$ ) and larger negative mean amplitudes for the time windows: 800 to 1000 ms ( $p = .02$ ) and 1000 to 1200 ms ( $p = .01$ ) compared with aMCI participants. The mean amplitude for the 400 to 550 ms time window was significantly more positive ( $p = .03$ ) for aMCI than for controls. **Conclusions:** The results support that healthy controls allocated more processing resources for stimulus evaluation (N2, post-stimulus interval: 275 to 350 ms) than aMCI participants; furthermore, the larger negative amplitude from 800 to 1200ms might be reflecting a greater allocation of processing resources to the maintenance and refreshing of stimulus representation in working memory for controls.

P3-362

#### PTSD AND RISK OF ALZHEIMER'S DISEASE IN AUSTRALIAN VIETNAM VETERANS: AMYLOID AND TAU PET FINDINGS FROM AIBL-VETS



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