Future works include similar experiments on different scanners and scanning protocols.

IC-P-153 WHOLE CORTICAL AND DMN MEAN FUNCTIONAL CONNECTIVITY AS POTENTIAL BIOMARKERS FOR MILD ALZHEIMER'S DISEASE

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Background: The search for an Alzheimer's disease (AD) biomarker is one of the most relevant contemporary research topics due to high prevalence and social costs of the disease. Functional connectivity alterations of the Default Mode Network (DMN) are a plausible candidate for such task, since AD dementia is among the main conditions that can disrupt the functional organization of cognitive functions. **Methods:** We evaluated 22 patients with mild AD (mean age: 73.4 years-old; 15 women) and 26 healthy controls (mean age: 71.03 years-old; 19 women) matched for gender and age. All subjects underwent a 10 minutes task-free fMRI at 3.0T MRI PHILIPS InteraAchieva scanner. Images were pre-processed by applying slice-time and motion corrections algorithms and removing linear trends in these data. Data pre-processing also included smoothing with a 6 mm FWHM Gaussian kernel, bandpass filtering (0.008 to 0.1 Hz) and spatially normalized to standard space (MNI152). Six parameters of head motion as well as cerebrospinal fluid and white matter time series were regressed as nuisance variables. To identify the DMN, seed-based functional connectivity was calculated by placing a seed in the posterior cingulate cortex (PCC; 0,-51,15; seed radius = 3 mm), and later calculated a Fisher's r-to-z transformation to obtain whole cortical statistical z-scoremaps. Then, we calculated an average z-scorefor each subject, and compared the results between the groups by using an independent two-sample t-test. We also calculated the sensitivity and specificity of the method, as well as a ROC curve analysis. **Results:** We found a significant statistical difference between mild AD and controls considering positive average z scores (z score > 0, $p = 0.005$) and absolute z-scores values ($p = 0.01$). Considering individual values, we found a sensitivity = 76.2% and a specificity = 72%, when using a cutoff value = 0.195. Area under ROC curve = 0.794, standard error = 0.67. **Conclusions:** We showed that individual measures of whole cortex connectivity in relation to DMN's PCC could be considered a promising method to differentiate AD, even at an early phase, from normal aging. Further studies with large sample size as well as validation of normal values are needed for safer conclusions.

IC-P-154 DECLINE OF FIBER TRACT INTEGRITY OVER THE ADULT AGE RANGE: A DIFFUSION SPECTRUM IMAGING STUDY

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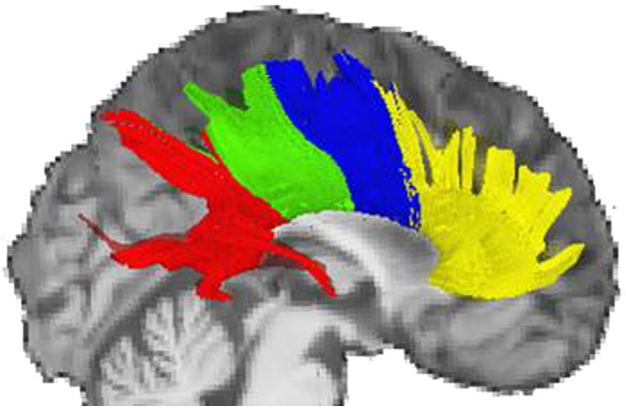
Background: Aging is associated with morphological brain changes. Diffusion spectrum imaging (DSI) is a powerful in vivo technique to determine structural connectivity in the living human brain. Here, we assessed the use of a novel DSI acquisition to determine associations between aging and subcortical fiber tract integrity. **Methods:** We studied 35 cognitively healthy subjects (17 women) spanning the adult age range between 23 and 77 years using high resolution anatomical MRI and a novel DSI acquisition at 3 Tesla. We determined effects of age on global fractional anisotropy (gFA) in selected fiber tracts as well as in a whole brain voxel-based analysis. For comparison, we studied effects of age on regional grey and white matter volumes. **Results:** We found significant decline of anterior corpus callosum fiber tract integrity with age, as well as significant gFA decline in widespread areas of subcortical white matter. GFA decline was accompanied by significant grey matter atrophy in frontal and temporal association cortex. ApoE4 genotype had a significant effect on anterior corpus callosum tract integrity, but on no other brain areas. **Conclusions:** Our data suggest that healthy aging leads to decline of fiber tract integrity. DSI appears to be more sensitive to detect these changes than common volumetry and may become a useful biomarker in healthy and pathological aging in the future.



IC-P-155 ASSOCIATION BETWEEN THE ALZHEIMER'S DISEASE-RELATED HYPOMETABOLIC CONVERGENCE INDEX AND CLINICAL RATINGS IN COGNITIVELY NORMAL OLDER ADULTS WITH AND WITHOUT SIGNIFICANT FIBRILLAR AMYLOID BURDEN: FINDINGS FROM THE ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE

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Background: We previously developed a voxel-based hypometabolic convergence index (HCI) to characterize, in a single measurement, the extent to which the pattern and magnitude of hypometabolism in a person's flourodeoxyglucose positron emission tomography(FDG PET) image corresponds to that in patients with the clinical diagnosis of Alzheimer's dementia (Chen and Ayutyanont et al., 2010). In this study, we characterized and compared HCIs and their relationship with poorer clinical ratings in cognitively normal "fibrillar Aβ positive and negative" older adults from the Alzheimer's disease Neuroimaging Initiative (ADNI). **Methods:** Florbetapir PET scans from 225 cognitively normal subjects 76$\pm$6 years of age were used to characterize mean cortical-to-cerebellar standard uptake value ratios (SUVRs) and classify the images as fibrillar Aβ positive and negative using an SUVR threshold previously found to be associated with moderate or frequent neuritic plaques (Fleisher et al., 2011). FDG PET scans from 71 Aβ positive and 154 Aβ negative subjects were used to generate HCIs, compare this index, and relate them to lower MMSE and higher ADAS-Cog scores (i.e., measures of clinical severity) in the

two subject groups. **Results:** Aβ positive groups had significantly higher HCIs than the Aβ negative groups (p=0.0024). HCIs were significantly associated with poorer MMSE and ADAS-Cog scores in the Aβ positive group (r=-0.38, p=0.001 and r=0.36, p=0.002, respectively) but not in the Aβ negative group (r=0.007, p=0.936 and r=0.06, p=0.458, respectively). **Conclusions:** Fibrillar A b burden in cognitively normal older adults is associated with an AD-related index of cerebral hypometabolism, and this index is associated with poorer clinical ratings in those who are Aβ positive.

IC-P-156 ASSOCIATION BETWEEN HIGHER FASTING SERUM GLUCOSE LEVELS AND THE PATTERN OF LOWER REGIONAL GRAY MATTER VOLUMES IN COGNITIVELY NORMAL ADULTS

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Background: Insulin resistance, as seen in type 2 diabetes, has been shown to increase the risk of late onset Alzheimer's Disease (AD) by as much as two-fold. In AD patients, characteristic findings are seen with structural magnetic resonance imaging (MRI) including global atrophy as well as regional reductions in gray matter volume (GMV) in the hippocampus, precuneus, posterior cingulate gyrus, parietotemporal, prefrontal, and orbitofrontal cortices. Additionally, negative correlations between peripheral insulin levels and regional GMV are seen in insulin resistant subjects in the middle temporal gyrus.The current study investigated whether elevated fasting glucose (FSG) levels were associated with lower GMV in brain areas that have been preferentially affected by AD. This association difference was further investigated between carrier and non-carrier (NC) groups of the apolipoprotein E (APOE) ε4 allele, a genetic risk factor for late onset AD. **Methods:** Statistical Parametric Mapping (SPM), an automated brain imaging analysis computer package, was used to spatially normalize individual brains to a standard brain template, to obtain GMV maps from structural MRI, and to examine the correlations between higher FSG levels and lower structural MRI GMV measurements in 118 cognitively normal, non-diabetic individuals 64±6 years of age (59ε4 carriers and 59 NCs). A significance threshold of p = .005 was set for all imaging related analyses. **Results:** As predicted, significant correlations were seen between higher levels of FSG and lower GMV in AD-affected regions including the left inferior orbitofrontal cortex, parietal, and occipital lobes and the left and right frontal and temporal lobes. Negative correlations between FSG and regional GMV in the middle temporal gyri confirmed findings seen in insulin resistant subjects. Additionally, these associations in AD-related areas are seen in both carriers and NC. **Conclusions:** Higher FSG levels in cognitively normal, non-diabetic, older adults are associated with lower GMV in AD related brain areas, confirming that elevated FSG may be associated with AD risk, independent of APOE ε4 status. Lastly, this study encourages the consideration of elevated FSG and other indicators of glucose control as targets for AD prevention trials, complementing the findings previously established with fluorodeoxyglucose positron emission tomography neuroimaging.

IC-P-157 HIPPOCAMPAL SUBFIELD ATROPHY IN PRECLINICAL AND PREDEMENTIA ALZHEIMER'S DISEASE IS DIFFERENT FROM ATROPHY OBSERVED IN NON-ALZHEIMER'S PATHOLOGY

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Background: Hippocampus volume has proved to be reduced in various neurodegenerative diseases including Alzheimer's disease (AD). The new diagnostic criteria for the preclinical and predemential stages of AD allow distinguishing between AD and non AD pathology since the earliest stages. In this study, we inquired whether hippocampus subfields atrophy may arise differently in AD and non-AD pathology. **Methods:** Seventy-four non-demented elderly subjects (71.2y +/- 6.9) were included in this study: Forty-three patients complaining about their memory attended our Memory Clinic and 31 not complaining volunteers were recruited by advertising. All participants underwent a full neuropsychological examination and carried out 3T brain MRI, brain PET F18-FDG and F18-flutemetamol. Subjects were consequently classified in three groups, whatever how they were initially recruited: - Preclinical and predemential AD (pAD) (n=22) had amyloid deposits on the F18-flutemetamol scan (above pc90 of volunteers). - Patients suffering from non-AD pathology (non-AD) (n=18) had no amyloid deposits but global hippocampus atrophy or F18-FDG hypometabolism (below pc10 of volunteers).- Healthy elderly (HE) (n=26) had normal cognition and none of the 3 biomarkers positive. Eight subjects could not be classified as they had abnormal cognition without evidence of neurodegeneration. Global hippocampus and subfields volumes were assessed using FreeSurfer. **Results:** Non-AD (3054 +/- 497 mm^3 - p=0.000) and pAD (2841 +/- 447 mm^3 - p=0.000) had both global hippocampus atrophy when compared to HE (3583 +/- 321 mm^3). Global hippocampus atrophy in pAD was not significantly more important than in non-AD (p=0.162). Right and left subiculum and right and left presubiculum were atrophic in non-AD as in pAD (all p-values < 0.000). Similarly, right (p=0.028 in non-AD - p=0.000 in pAD) and left (p=0.009 in non-AD - p=0.000 in pAD) fimbria were atrophic in both groups. However, right CA1 (p=0.029), right (p=0.001) and left (p=0.002) CA2-3 and left CA4-DG (p=0.001) were atrophic in pAD while they were not in non-AD. **Conclusions:** Although both pAD and non-AD present reduced global hippocampus volumes, CA subfields atrophy seems to be specific of preclinical and predemential AD. Hippocampus atrophy in non-AD seems to be mainly driven by reduced presubiculum and subiculum volumes.

Hippocampus subfields volume (mm^3) in healthy elderly (HE), in patients suffering from non-Alzheimer pathology (Non-AD) and in preclinical and predemential Alzheimer's disease (pAD)

	HE (n=26)		Non-AD (n=18)		pAD (n=22)	
	Mean	SD	Mean	SD	Mean	SD
Right CA1	325	42	313	49	*296*	*46*
Right CA2 3	948	110	877	151	*831*	*125*
Right CA4 DG	528	53	*486*	*79*	*457*	*71*
Right Fimbria	60	15	*46*	*26*	*41*	*17*
Right presubiculum	433	55	*346*	*57*	*343*	*48*
Right subiculum	601	68	*509*	*93*	*483*	*78*
Left CA1	313	27	296	51	296	58
Left CA2 3	883	78	834	147	*781*	*136*
Left CA4 DG	502	41	472	81	*441*	*77*
Left Fimbria	72	26	*50*	*28*	*41*	*21*
Left Presubiculum	441	57	*358*	*68*	*355*	*64*
Left Subiculum	604	62	*505*	*104*	*488*	*91*
Global Hippocampus	3583	321	*3054*	*497*	*2841*	*447*

NB: *Italic* values are significantly atrophic (p<0.05) in comparison with HE.

NB2: Hippocampus subfields in **Bold** are significantly atrophic in pAD but not in Non-AD.