IC-P-111 COMPARATIVE LONGITUDINAL CHANGE OF FUNCTIONAL CONNECTIVITY, DIFFUSION AND STRUCTURAL MRI MARKERS IN A PRODROMAL/ MILD AD POPULATION

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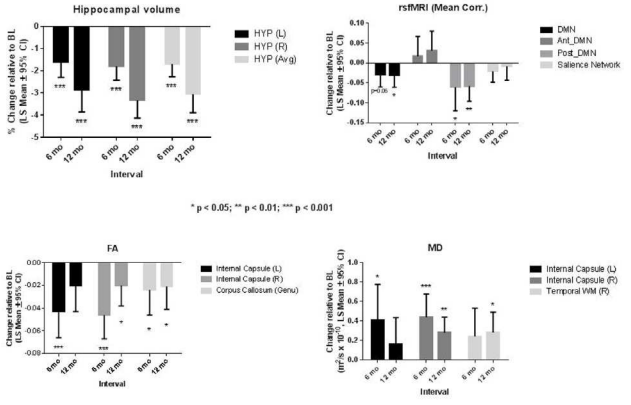
Background: Volumetric MRI (vMRI) measures are widely used as metrics of Alzheimer's disease (AD) progression. Measurements of white matter (WM) integrity by diffusion tensor imaging (DTI) and functional connectivity by resting state functional MRI (rsfMRI) represent potential biomarkers of AD progression, but their utility is less well established. The purpose of this multi-site study was to compare the precision of longitudinal changes in vMRI, DTI and rsfMRI parameters in subjects with mild or prodromal AD over a 12 month period. **Methods:** Clinical entry criteria included objective evidence of significantly impaired episodic memory, clinical dementia rating of 0.5 or 1, memory box score $>$ 0.5 and amyloid positivity. 3T MRI scans were obtained across 10 imaging sites in France at baseline (N=56), 6 months (N=45) and 12 months (N=33). Whole brain and ventricular changes were measured by K-means Brain or Ventricular Boundary Shift Integral (BSI). Hippocampal volume (HV) was measured by learning embeddings for atlas propagation (LEAP). Acquisition parameters for DTI and rsfMRI were derived from ADNI2. For each predefined imaging measure, the longitudinal change and statistical signal-to-noise ratio (SNR) were calculated using a mixed effects model. **Results:** vMRI measures were highly significant at both time points ($p<0.001$; Figure). Average HV decreased by 1.7% (SNR=0.8) and 3.0% (SNR=1.3) at 6 and 12 months. Weaker changes in some rsfMRI and DTI measures were also observed. The mean correlation within the posterior default mode network exhibited decreased connectivity relative to baseline at both 6 months (-0.061, SNR=0.33, p=0.04) and 12 months (-0.058, SNR=0.61, p=0.004). Reductions in fractional anisotropy were observed in the corpus callosum (genu), internal capsule, temporal WM, and the uncinate fasiculus (SNR $\sim$ 0.3 to 0.6, $p<0.05$), and increases in mean diffusivity were observed in the internal capsule, the posterior cingulum bundle, and temporal WM (SNR $\sim$ 0.2 to 0.5, $p<0.05$). **Conclusions:** Robust 6 and 12 month changes in vMRI metrics were observed. RsfMRI and DTI changes were detected for certain metrics but yielded lower statistical precision over the time scale of this study.



IC-P-112 RISK FACTORS ASSOCIATED WITH DECREASED CORTICAL THICKNESS IN DEMENTIA FREE OKINAWAN ELDERLY

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Background: Cortical gray matter (GM) decline is a hallmark of neurodegenerative disease; however, its etiology and implication in dementia-free aging is unclear. The aims of this study were to: 1) investigate the impact of cortical thickness on cognition, and, 2) examine systemic inflammation and cerebrovascular disease (CVD) as potential risk factors for GM degeneration. **Methods:** 91 dementia-free Okinawan participants (mean age 83.6) from the Keys to Optimal Cognitive Aging (KOCOA) Project underwent MRI, cognitive, and physical evaluation. Mean cortical thickness (MCT) was derived using FreeSurfer. Serum markers of inflammation and CVD risk were obtained. CVD risk status was calculated based on $>$2 of the following: ever smoked, glycosylated hemoglobin $>$5.6, systolic blood pressure $>$ 139, taking anti-hypertension medication, serum triglyceride $>$150, and high density lipoprotein

Table 1
Regions in which VBM identified significantly reduced GM density in comparison with increased IL6 ($p<0.01$)

	Coordinates				Cluster size	
Talairach Region	side	X	Y	Z	Voxels	Volume (cm^3)
Inferior and Middle Temporal Gyrus*	L	61.8	13.9	-18.7	238	1.904
Inferior and Middle Temporal Gyrus	R	-42.8	61.2	-0.3	64	0.512
Superior Temporal Gyrus	R	-49.6	-7.8	-12.3	57	0.456
Insula and Claustrum	R	-38.6	5.2	-2.3	56	0.448

*remained significant after cluster thresholding

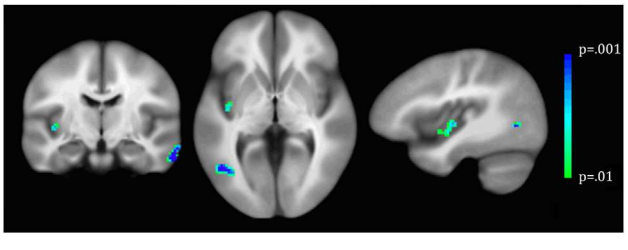

Figure 1. VBM analysis with threshold-free cluster enhancement and permutation testing to correct for multiple comparisons. Colored voxels indicate regions of decreased GM density significantly associated with higher IL6, age and gender adjusted.

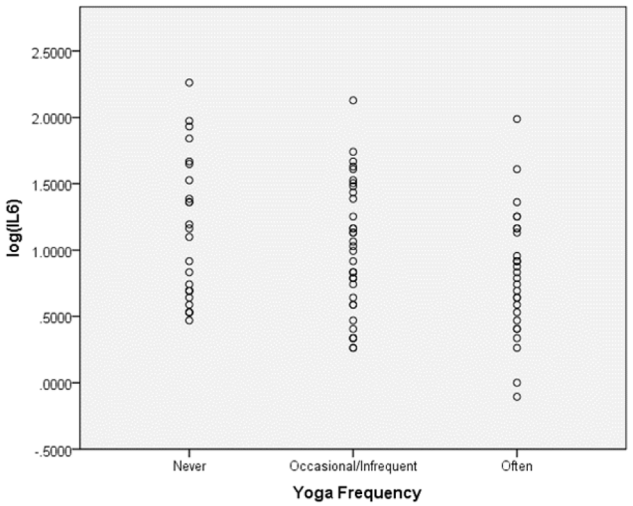

Figure 2. Serum IL6 in relation to yoga frequency ($p = 0.02$ in final model adjusted for age and gender).

< 40 in men, or < 50 in women. Inflammatory markers included: interleukin-6 (IL6) and high-sensitivity C-reactive protein (hsCRP). Subjects were surveyed regarding physical activities (PA), including walking and yoga. Multivariate analyses examined relationships between MCT and memory (mini mental word recall) and executive function (verbal fluency). Spearman's rank order correlation or t-tests examined the relationships between MCT and: age, PA, CVD risk, and inflammatory markers. Voxel based morphometry (VBM) examined relationships between regional GM density and factors significant in the previous univariate analysis. Exploratory analyses examined systemic inflammation in relation to PA. **Results:** After adjusting for age, gender, and %hippo volume, decreased MCT was associated with worse memory, but not executive function. In univariate analyses, decreased MCT was associated with increased IL6 (0.04), but not with age, PA, hsCRP or CVD risk. VBM analysis demonstrated greater IL6 to be associated with decreased cortical density in the inferior and middle temporal cortex, bilaterally. After adjusting for age and gender, greater yoga participation ($p = 0.02$), but not walking, was associated with lower IL6 levels. **Conclusions:** Decreased MCT is associated with worse memory performance in dementia free-Okinawans. Greater IL6 was related to decreased temporal lobe cortical thickness, and decreased PA. Low-impact stretch activities, such as yoga, should be further explored as potential ways to decrease systemic inflammation and prevent cortical thinning and memory loss in older individuals.

IC-P-113 HYPOMETABOLISM PATTERNS USING FDG-PET IN TYPICAL AND ATYPICAL SPORADIC FORMS OF EARLY-ONSET ALZHEIMER'S DISEASE

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Background: Non memory or atypical presentations are much more frequent in EOAD than in late-onset AD. As far as we know, no previous study showed distinct metabolic pattern according to typical or atypical presentation of sporadic EOAD, and this study aimed to assess it. **Methods:** Patients fulfilled research diagnostic criteria for AD including CSF, and were classified as typical (amnestic presentation) or atypical (non amnestic presentation, i.e. language, visuospatial and executive dysfunction) by consensus. Clinical characteristics and acquisition parameters are reported in Table 1 and Table 2. T1 images were processed with the FreeSurfer suite using the cortical reconstruction process. Rigid-body boundary-based registration was used to coregister PET to T1 subject's image. PET data were then processed by global normalization of the acquired intensity and partial volume correction with help of MRI.

Table 1
Characterization of typical and atypical EOAD patients

	Typical (n = 29)	Atypical (n = 25) (5 language - 10 visuospatial - 10 executive dysfunctions)	*P*
Gender (woman/man)	18/11	15/10	0.876[a]
Age (mean ± SD, in years)	59.31 ± 4.19	58.04 ± 3.45	0.233[b]

SD: standard deviation
[a]Pearson chi-square
[b]Two-sample t-test

Table 2
Detailed FDG-PET (GE Discovery RX scanner) and MRI (Philips Achieva 3T scanners) parameters used

	3D FDG-PET [a]	3D T1-weighted Turbo Field Echo
Matrix	256×256	256x256
Slices	47 transverse slices	160 sagittal slices
Voxel size	1.17x1.17x3.27 mm3	1×1×1 mm3
Spatial resolution	~ 6 mmFWHM	-
TR/TE	-	9.9/4.6 ms
Flip angle	-	8°

[a]Corrections for dead time, tissue attenuation using the transmission scan, decay, scatter and randoms were applied and 3D Iterative Reconstruction was used

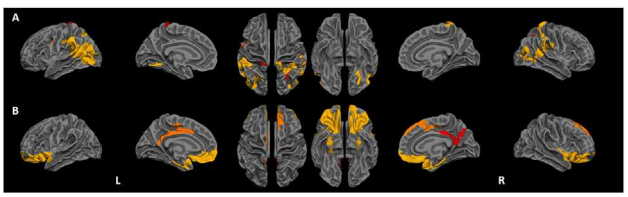

Figure. Hypometabolism patterns in atypical as compared to typical EOAD patients (A) and in typical as compared to atypical EOAD patients (B) mapped on common cortical surfaces; A modified Müller-Gärtner method proposed by Roussed was used for partial volume correction; Color distinguish significance strength of clusters revealed by statistical analysis: color scale is defined from red (less significant) to yellow (more significant) (All visible clusters have corrected p-value < 0.05)