COMPARISON OF NEUROIMAGING BIOMARKERS IN ALZHEIMER'S DISEASE

Pablo Garcia-Polo[1,2], Daniel Garcia-Frank[3], Alicia Quiros[4], Zhongmin Lin[5], Litao Yan[5], Gopal Avinash[5], Roberto Garcia-Alvarez[6], Juan Álvarez-Linera[7], and Juan Antonio Hernandez-Tamames[1,2]

[1]DTE, Universidad Rey Juan Carlos, Móstoles, Madrid, Spain, [2]CIBERNED, Alzheimer's Project Queen Sofia Foundation, Madrid, Madrid, Spain, [3]IDIPAZ, FIBHULP, Madrid, Madrid, Spain, [4]Universidad Rey Juan Carlos, Fuenlabrada, Madrid, Spain, [5]GE Healthcare, Waukesha, WI, United States, [6]GE Healthcare, Madrid, Madrid, Spain, [7]Hospital Ruber Internacional, Madrid, Madrid, Spain

Target audience: Physicians, psychologists, radiologists and MR researchers.

Purpose: This piece of work compares structural, metabolic and physiological biomarkers in order to characterize the Alzheimer's disease with neuroimaging methods.

Introduction: In this work, we focus on Alzheimer's disease (AD) that is the most common cause of dementia; and which biomarkers allow the most complete picture of the brain injury in this pathology. Anatomical [1], perfusion [2] and metabolic [3] differences in this disease have been previously reported. To measure perfusion, Arterial Spin Labeling is a non-invasive MRI technique, which allows the quantification of regional cerebral blood flow (rCBF) without contrast agents by labeling a small bolus of blood at the level of the carotid arteries with a radiofrequency pulse. In contrast, Positron Emission Tomography with FDG (FDG-PET) is considered the gold standard for mapping brain metabolism and task-induced brain activity in normal and pathologic states. Prior ^{15}O-water PET and FDG-PET studies have shown an important decrease of perfusion in rCBF maps and cerebral metabolic rate of glucose in regions such as parietal lobes and posterior cingulate [2,3]. Finally, to measure anatomical differences [1] we use a voxel-based morphometry method and a cortical thickness analysis over a structural 3DT1 image.

Methods: 20 subjects (10 healthy subjects with a mean age of 73.2±6.7 years and 10 AD patients with a mean age of 69.9±9.5 years) underwent an MR and a FDG-PET scan. FDG-PET data were acquired with a GE Discovery STE PET machine using a 128x128 acquisition matrix, 47 slices, with 2x2x3.27mm voxel resolution and a 3D-IR reconstruction method. All MR imaging was performed on a 3T Signa HDx MR scanner (GE Healthcare, Waukesha, WI) using an eight-channel phased array coil. The first sequence was a 3DT1 with a TR=6s, TE=134.65ms, TI=1.847ms, NEX=1, matrix size=256x256, 170 slices, resolution=1.0156x1.0156x1, flip angle=90. The second sequence was a 3D PCASL pulse sequence with a matrix size= 128x128, resolution=2.3x2.3x4mm, flip angle =155, transit time=1.5s, TR=9.34s and a TE=1.9ms was used to generate the rCBF maps.

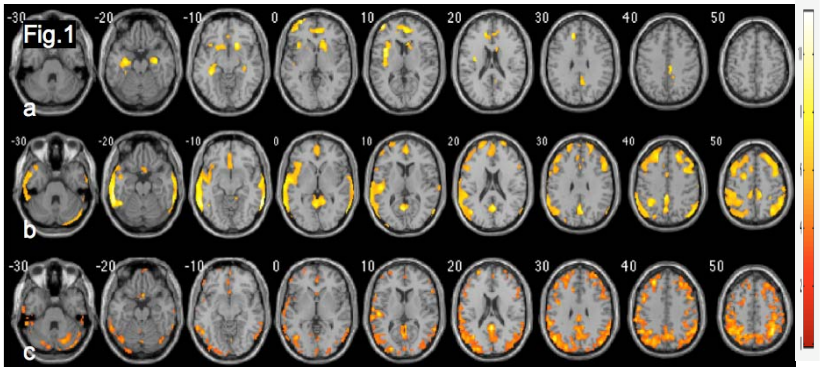
Corregistration, normalization and smoothing (FWHM=4mm) of ASL-rCBF and FDG-PET maps were performed with Statistical Parametric Map (SPM8) software. To analyse the structural image, three software packages were used: DARTEL-SPM8, FreeSurfer and CorThick (software prototype, GE Healthcare).

Statistical maps, using a Multiple Regression Analysis within the General Linear Model, for rCBF, FDG-PET and DARTEL differences, were obtained.

For cortical thickness values obtained with FreeSurfer [http://surfer.nmr.mgh.harvard.edu/] and CorThick a group means comparison t-test was performed.

Results:

DARTEL (p_{FWE}<0.05)	FDG-PET (p_{FWE}<0.002)	ASL (p_{FWE}<0.02)	FreeSurfer (p<0.01)	CorThick (p<0.05)
Gray matter atrophy in AD patients is found in posterior cingulate, mid cingulate, anterior cingulate, caudate, left insula, putamen hippocampus and parahippocampal gyrus (Fig.1a).	Reduced metabolism in AD patients is found in frontal lobe, parietal lobes, cingulum (anterior, middle and posterior) and left temporal lobe (Fig. 1b).	Reduced perfusion in AD patients is found in frontal lobe, parietal lobes, posterior cingulate, anterior cingulate and left temporal lobe. (Fig. 1c).	Reduced thickness in AD patients is found in cingulate, frontal lobes, occipital lobes, parietal lobes and temporal lobes (Fig. 2a).	Reduced thickness in AD patients is found in posterior cingulate and temporal lobes (Fig. 2b).



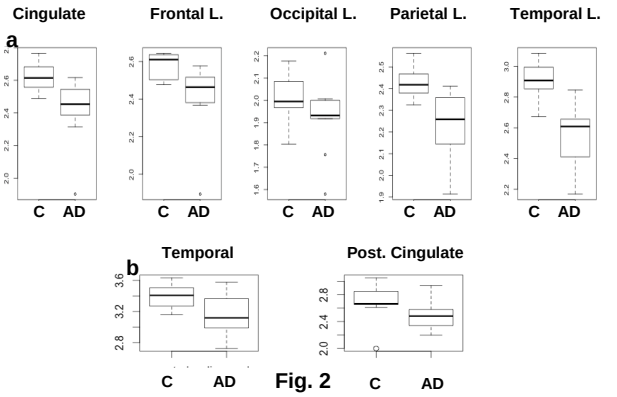


Fig. 2

Discussion: A reduction in volume and thickness in cingulate is found with DARTEL and with both cortical thickness methods. DARTEL-VBM is capable of distinguishing AD patients from controls in subcortical regions such as caudate, insula, putamen and hippocampus; however, cortical thickness methods are not capable of studying differences in these regions. On the other hand, ASL differences overlap with cortical thickness differences in cingulate, frontal lobes, occipital lobes and parietal lobes. Also, FDG-PET differences overlap with cortical thickness differences in cingulate, frontal lobes, parietal lobes and temporal lobes. These results show high overlapping in difference-regions between cortical thickness, FDG-PET and ASL, as seen in [1,2,3].

Conclusion: The results reveal that cerebral blood flow, metabolism, gray matter density and gray matter thickness are related. Some key regions in AD such as temporal lobes, cingulate and frontal lobes are well depicted by cortical thickness, FDG-PET and ASL. Nevertheless multivariate analysis with DARTEL-VBM and CorticalThickness over an anatomical image 3DT1 may be capable of replacing FDG-PET and ASL in the cheapest and less invasive way to monitor AD and other dementias.

References:

[1] *Focal decline of cortical thickness in Alzheimer's disease identified by computational neuroanatomy.* J. P. Lerch et al.; Cerebral Cortex; July 2005; 15: 995-1001.

[2] *Assessment of cerebral blood flow in Alzheimer's disease by spin-labeled magnetic resonance Imaging*. D. C. Alsop, et al.; Annals of Neurology; Jan 2000; Volume 47; 1:93-100.

[3] *Normal and pathological aging: findings of positron-emission-tomography.* R. Mielke, et al.; J. Neural Transm.; 1998; 105:821-837.