HBM 2004 Poster # WE379

rCBF in Alzheimer`s disease versus Mild Cognitive Impairment: a SPECT study with Partial Volume Effect correction

[1]Mario Quarantelli, [1]Sabina Pappatà, [1]Andrea Varrone, [2]Carmine Mollica, [2]Valeria Sansone, [2]Elisa Lorè, [3]Alfredo Postiglione, [4]Sergio Carlomagno, [5]Alessandro Iavarone, [1]Bruno Alfano, and [2]Marco Salvatore

[1]Biostructure and Bioimaging Institute, National Council for Research
[2]Department of Diagnostic Imaging, University "Federico II"
[3]Department of Clinical and Experimental Medicine, University "Federico II"
[4]Department of Neurology, University "Federico II"
[5]Institute of Neurological Sciences, Second University of Naples
Naples, Italy

Introduction

The progression from Mild Cognitive Impairment (MCI) to Alzheimer's Disease (AD) is characterized by the increase in severity and extension of cerebral hypometabolism and regional cerebral blood flow (rCBF) [Nestor 2003], which are already detectable in posterior cingulate, hippocampus and temporal neocortex in MCI patients.
Concurrently, gray matter (GM) loss, essentially limited in MCI to hippocampal cortex [Chetelat 2002], progresses into a more widespread cortical loss.
It is not currently known weather this pattern of progression is characterized by a strict coupling of these two phenomena (i.e. GM loss explains the metabolism reduction as detected by FDG-PET and rCBF-SPET studies), or if metabolic impairment exceeds the rate of GM loss.
Aim of our study was to compare rCBF decrease independently of GM loss in two groups of MCI and AD patients, using a ROI-based method for partial volume effect (PVE) correction which takes into account both WM and CSF.

Material and Methods

12 subjects with Mild Cognitive Impairment (MCI, mean age 74.8 yrs, MMSE 27.8+/-2.0 range 24.9-30.0) and 10 AD patients (NINDS-ADRDA criteria; mean age 79.5 yrs, MMSE 21.2+/-2.4, range 16.9-24.0) underwent rCBF-SPECT and volumetric MRI.
SPECT studies were carried out 20-30 min after an intravenous injection of 740-1110 MBq of [99mTc]HMPAO (Ceretec®, Nycomed Amersham Sorin), using a 64-slice brain-dedicated camera equipped with a circular LEHR collimator (Ceraspect, Digital Scintigraphics, D.S.I, Waltham, MA, USA). Studies were acquired for 30 min in step-and-shoot mode (120 steps, 3° angular step, 15 sec per step, 128 x 128 matrix). Images (pixel size 1.673mm) were reconstructed using a Butterworth filter (cut-off = 0.9 cm-1, order=10) and were corrected for attenuation assuming uniform attenuation within the skull, applying a zero order attenuation factor (0.120 cm-1) and the Chang's algorithm [Chang, 1987].
Corresponding MRI volume data (magnetization-prepared 3D T1-weighted fast-GrE images, TR/TE/TI 11/2/600ms, 1.5T, voxel size 0.98x0.98x1.2mm) were segmented into GM, WM and CSF maps by probabilistic MRI segmentation [Ashburner J, 2000] and co-registered to SPECT studies [Friston KJ, 1995].
A set of cortical volumes of interest (VOI) including cerebral lobes and hippocampus for each side, and a single region for cerebellum and posterior cingulate, was defined in the MNI space and adapted to each co-registered segmented GM (figure 1) using normalization parameters derived from the SPM99 affine normalization matrix [Berkouk 2003].
For each VOI, uncorrected and PVE-corrected mean tracer concentrations were calculated [Rousset OJ, 1998; Quarantelli M, 2003] and normalized by corresponding cerebellum values.
Comparison between MCI and AD groups was carried out for each region by Student's T-test.
Significance level was set to $P<0.05$.

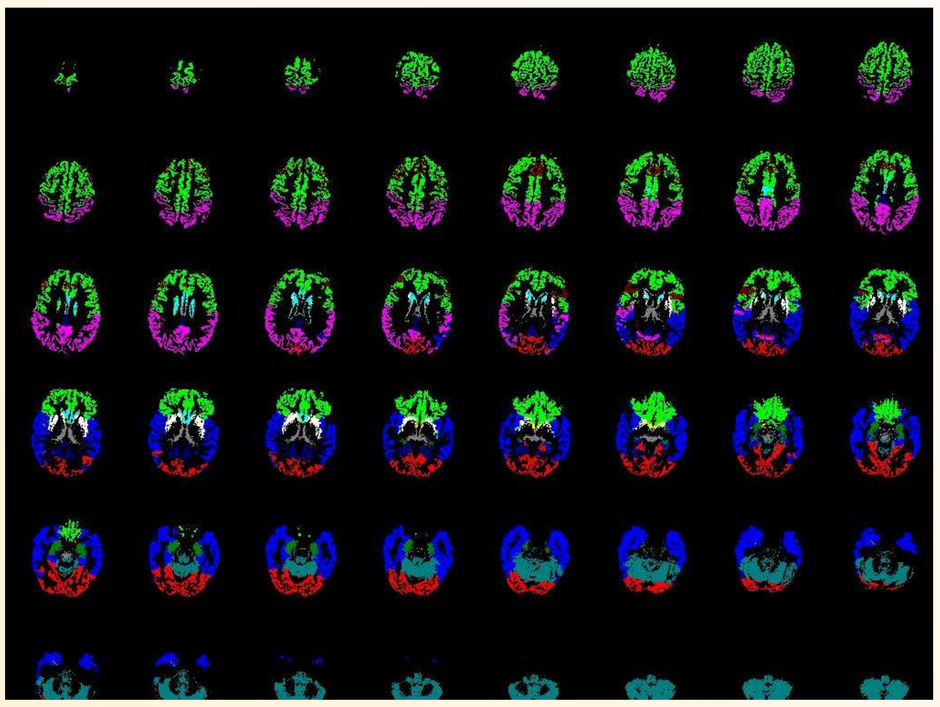

Figure 1: VOI definition
- Labeling of segmented GM voxels is obtained by wharping the MNI space onto the patient's SPET space.
- Wharping coeffcients are derived using the normalization matrix calculated by SPM (affine components only).
- For the present analysis the deep GM structures were not used.

Results

Before PVE-correction, temporal lobes (both hippocampus and lateral cortices) and posterior cingulate ($P<0.01$), as well as left dorso-lateral prefrontal cortex ($P<0.05$), showed a significantly reduced CBF in AD as compared to MCI studies. After PVE-correction, only CBF decreases in posterior cingulate remained significant ($P<0.05$).

	Left Occipital	Left Frontal	Left Temporal	Left Parietal	Left DLPF	Left Hyppocampus
Uncorrected	-1%	-4%	-7%	-4%	-8%	-13%
Corrected	3%	-1%	0%	-1%	-4%	-1%
	Right Occipital	**Right Frontal**	**Right Temporal**	**Right Parietal**	**Right DLPF**	**Right Hyppocampus**
Uncorrected	-1%	-5%	-8%	-4%	-7%	-16%
Corrected	2%	-1%	-1%	1%	1%	-2%
	Posterior Cingulate					
Uncorrected	-7%					
Corrected	-7%					

Mean percentage reduction in AD compared to MCI patients. Data are reported before (uncorrecetd) abd after (corrected) correctionfor partial volume effects.
Significant differences ($P<0.05$) are in yellow.

Discussion

As compared to normal subjects, metabolic/CBF changes in AD are paralleled by GM loss [Baron JC, 2001a; Karas GB, 2003]. Accurate voxel-based comparisons of these changes have shown that the atrophy explains the GM hypometabolism with the exception of the posterior cingulate [Baron JC, 2001b], an area known to be affected precociously in AD [Minoshima S, 2000].

Our results integrate these findings, showing in PVE-corrected rCBF-SPET data from AD patients, as compared to MCI, the same pattern of posterior cingulate involvement independent of GM loss.
Reduced metabolism in these regions may be related to remote functional disruption.
While larger cohorts are needed to confirm these preliminary findings, longitudinal studies are needed to confirm this pattern of progression of the disease.

Figure 2
Final video output from the PVE-correction software:
Each SPECT image is displayed along with the corresponding segmented MRI smoothed to the SPECT resolution.
Relative regional proportions of GM volumes and CBF can be visually compared.

References

Ashburner J, Friston KJ, NeuroImage 2000; 11:805-21
Baron et al, NeuroImage 2001b; 13:S771
Baron JC, et al. Neuroimage 2001a ; 14:298-309
Berkouk K, et al. 2003 HBM meeting; Abs. 1017
Chang, L. IEEE Trans Nucl Sci 1987;25: 638-643.
Chetelat G, Baron JC. Neuroimage. 2003;18:525-541.
Chetelat G, et al. Brain 2003; 126:1955-1967
Chetelat G, et al. Neuroreport 2002; 13:1939-1943
Friston KJ, et al. Hum Brain Map 1995; 2:165–189
Karas GB, et al. Neuroimage 2003; 18:895-907
Minoshima S, et al. Ann Neurol 1997, 42 :85-94.
Nestor PJ, et al. Ann Neurol 2003;54:343–351
Quarantelli M, et al. J Nucl Med. 2004;45:192-201
Rousset OG, et al. J Nucl Med 1998;39:904-911

Acknowledgment:
EU fifth framework program QLG3-CT2000-00594 has funded the project.