Significantly asymmetric patterns of periventricular atrophy in Alzheimer Disease, Mild Cognitive Impairment, and Memory Complainers detected on Clinical MR images

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Introduction

Magnetic Resonance Imaging (MRI) is a valuable tool to assess structural brain changes in subjects with neurodegenerative diseases. Several studies have investigated atrophy by segmenting the parenchyma into gray and white matter, and subsequently applying volume measurements to structures of interest (SOI) [1]. Local analyses based on shape changes of SOI have also been successfully applied to highlight subtle brain changes [2]. The contrast between gray and white matter in clinical MR images tends to decline with age [3], while the contrast between Cerebrospinal fluid (CSF) and the rest of the parenchyma remains sharp. Consequently, the brain ventricles are an optimum choice to investigate changes in periventricular structures [4]. In this work, after having quantified local ventricular shape changes in patients with (1) memory complaints (without cognitive impairment, MC), (2) Mild Cognitive Impairment (MCI) and (3) Alzheimer Disease (AD), we investigated the right-left asymmetry of atrophy in periventricular structures.

Material and Method

The study included 63 patients with probable AD, 28 patients with MCI, 21 subjects with MC, and 28 healthy volunteers. Clinical MR images were acquired on a 1.5 Tesla MR-system (Philips Medical Systems, Best, The Netherlands): DUAL fast spin-echo (proton density and T2 weighted): TE 27/120 ms, TR 3000 ms, 48 contiguous 3 mm slices with no gap, matrix 256x256, FOV 220 mm. FLAIR (fluid attenuated inversion recovery): TE 100 ms, TR 8000, 48 contiguous 3 mm slices with no gap, matrix 256x256, FOV 220 mm. Automatic segmentation of CSF was performed according to [5] and the ventricular CSF was semi-automatically re-labeled as *ventricles*. Spatial normalization to a T2 brain template for geriatrics [6] was performed with affine 12-parameters registration. Automatic shape modeling and analysis for all brain ventricles was performed using growing and adaptive meshes (GAMEs) [7]. Using permutation tests, we compared corresponding mesh locations of the control group to all the other groups to highlight the locations on the ventricular surface found to be significantly different between groups (Fig 1). Subsequently, for each significantly different location on the surface, we evaluated the displacement vector needed to locally deform the average shape of one group into the average shape of the other (Fig. 2). Finally, in order to relate local ventricular changes to adjacent periventricular structures, a trained radiologist manually parceled the ventricular surface of an average (template) ventricle into regions according to the adjacent structures (see Fig. 3). This parceled mesh was then mapped back automatically on every single ventricular mesh.

Considering two groups (e.g., *controls vs. AD*), we compared the probability distribution (pdf) of the p values in a given area (e.g. *left* inferior temporal horn) with the corresponding pdf in the symmetric area (e.g., *right* inferior temporal horn), by means of the Kolmogorov-Smirnov (KS) test. In the areas presenting a significant asymmetry, the regional mean p value was used to establish which side of the ventricular system was more affected (showing a lower mean p value). A similar analysis was performed on the displacement vectors. The distribution of the p values is an indication of the *extent of area* presenting atrophy, while the distribution of displacement vectors represents the *focal severity of atrophy*.

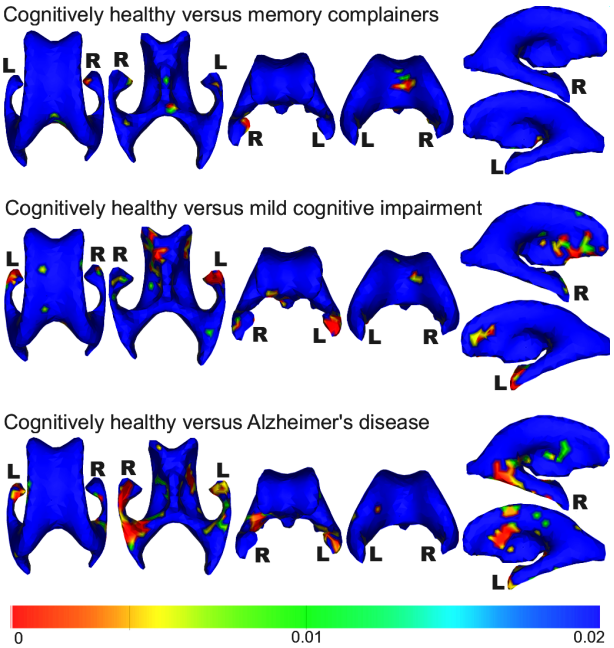

Figure 1 Results of the permutation tests showing significant shape differences between controls and the other groups. Each location is color-coded with the corresponding p value: values higher than 0.01 are color-coded in blue (not significantly different).

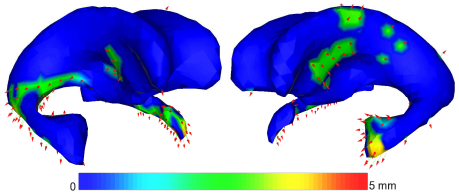

Figure 2 Displacement vectors for *controls vs. AD*: a general ventricular enlargement is needed to move from an average control to an average AD. The amount of displacement is color-coded.

Table 1 KS test results: the asymmetry between left and right regions was tested (per group-comparison) both for the extension (p values) and the severity (displacements) of atrophy (α level set at 0.01).
$^{R\ or\ L}$ = significantly asymmetric: ^{R} = more affected on the right side (in RED). ^{L} = more affected on the left side (in GREEN)

Ventricular Regions	Controls vs. MC		Controls vs. MCI		Controls vs. AD	
	Extension	Severity	Extension	Severity	Extension	Severity
Corona Radiata	0.9040	0.0062^{R}	0.2622	0.0070^{R}	$< 0.0001^{L}$	0.4973
Corpus Callosum	0.0464	0.0037^{R}	$< 0.0001^{R}$	$< 0.0001^{R}$	0.1438	0.1179
Caudate Nucleus	0.1936	$< 0.0001^{R}$	0.0004^{R}	0.0877	0.1866	0.0009^{L}
Thalamus	0.0001^{R}	0.8836	0.0000^{R}	0.4931	0.5911	0.1706
Sup. Med. Temp. Lobe	$< 0.0001^{R}$	0.0070^{R}	0.5137	$< 0.0001^{R}$	$< 0.0001^{R}$	0.0003^{R}
Inf. Med. Temp. Lobe	0.5125	$< 0.0001^{L}$	0.0001^{L}	0.0009^{L}	$< 0.0001^{L}$	$< 0.0001^{L}$

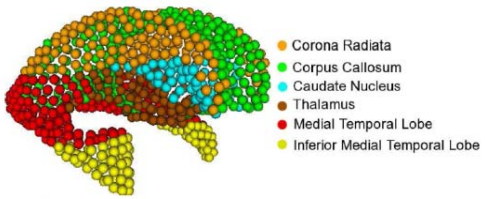

Figure 3 An expert manually delineated symmetric regions on the ventricular surface, each corresponding to an adjacent periventricular structure.

Results and Discussion

The permutation tests showed different patterns of shape variation in the different populations (as compared to healthy volunteers): an increased extent of periventricular atrophy (as reflected in ventricular shape changes) through the spectrum from memory complainers to severe AD is notable (see Fig. 1). The focus of this work, however, was on the asymmetry (per pathology) between left and right ventricular system. Results are summarized in Table 1, and show that both MC and MCI tend to affect mostly right periventricular structures, while AD affects mostly left periventricular structures. Particularly interesting are the temporal horns: both the superior and inferior medial temporal horns presented significant asymmetry in all the pathological cases, with the superior being mostly affected on the right side, and the inferior on the left. This study demonstrates the potential of MR combined with adequate post processing technique in the discrimination between AD, MCI or MC. It also highlights the periventricular brain areas where biomarkers of AD might be found.

References: [1] *L.G. Apostolova et al., Brain 129, 2006*; [2] *P.M. Thompson et al., NeuroImage 22(4), 2004*; [3] *S. Magnaldi et al., Europ. Radiology 3(6), 1993*; [4] *L. Ferrarini et al., Magnetic Resonance in Medicine (accepted for pub.), 2007*; [5] *F. Admiraal-Behloul et al., NeuroImage 8(23), 2005*; [6] *F. Admiraal-Behloul et al., ISMRM, 2004*; [7] *L. Ferrarini et al., Medical Image Analysis 11(3), 2007*.