Ventricular Shape Biomarkers for Alzheimer's disease in Clinical MR images

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Introduction

Alzheimer's disease (AD) and Mild cognitive Impairment (MCI), are often associated with atrophy of periventricular structures, such as the hippocampus and the amygdala. Clinical MR images of elderly are often characterized by low contrast between white and gray matter, making the analysis of gray matter structures very difficult: on the other hand, the contrast between cerebrospinal fluid (CSF) and white/gray matter remains good, making the brain ventricles an optimum choice for studying the effects of AD and MCI on periventricular structures. Biomarkers for early detection of the diseases are highly desirable: aim of this work was to investigate clinical MR images of the brain, and detect local shape differences between populations to be used to discriminate between healthy subjects and patients affected by AD and MCI.

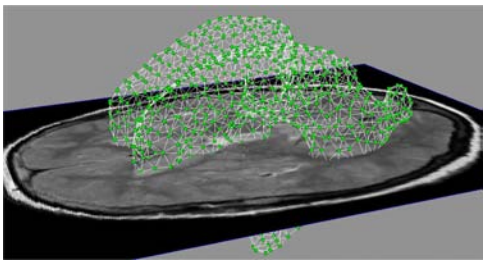

Fig. 1 Mesh modeling a brain ventricle

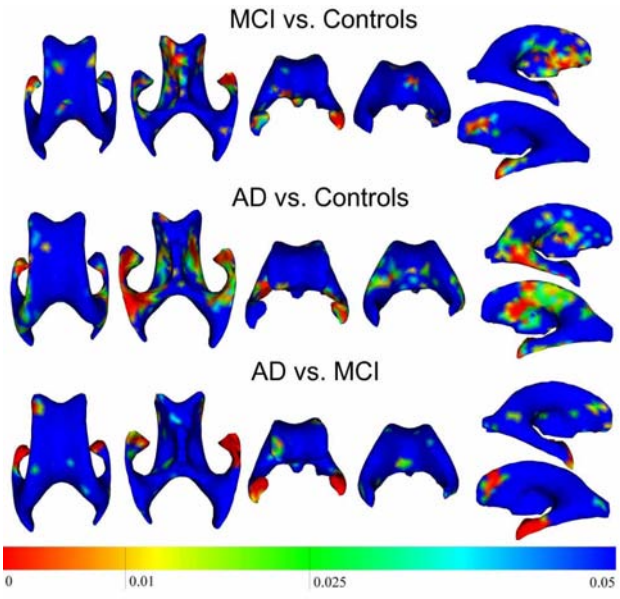

Fig. 2 Color-coded p-values showing local shape differences between groups

Material and Method

Fifty-eight patients with probable AD (27 men, mean age 74 years, age range 60-95 years), 26 patients with MCI (11 men, mean age 75 years, age range 61-85 years), and 28 volunteers with normal cognitive functions (12 men, mean age 74 years, age range 64-89 years) were included in the study. MRI was performed on a 1.5 Tesla MR-system (Philips Medical Systems, Best, The Netherlands): DUAL fast spin-echo (proton density and T2 weighted): TE 27 ms, TR 3000 ms, 48 contiguous 3 mm slices with no gap, matrix 256x256, FOV 220. FLAIR (fluid attenuated inversion recovery): TE 100 ms, TR 8000, 48 contiguous 3 mm slices with no gap, matrix 256x256, FOV 220.

We first automatically extracted the intra-cranial cavity, the CSF, and white matter hyperintensities, as described in [1]: semi-automatic region growing was used to re-label the ventricular CSF as *brain ventricles*. All the images have then been spatially normalized using affine 12-parameters registration to the LUMC T2-weighted brain template for geriatrics [2]. Using the shape modeling method described in [3], we obtained meshes of all the brain ventricles (see Fig. 1): permutation tests were then applied to identify local differences between populations [3] (see Fig. 2).

Locations with a *p value* below 0.01 were chosen as characterizing features for the brain ventricles' shapes, and were used to train three classifiers: *controls vs. MCI*, *controls vs. AD*, and *MCI vs. AD*. We used Support Vector Machines [4] with radial basis functions kernel for classification: for each classifier, the best kernel's parameters were chosen performing leave-1-out tests on the training set, avoiding the over-fitting problem. Cross-validation was performed using the AD group, since its size was twice the size of the others: for 100 times, the group was equally divided in two subgroups, AD1 for training and AD2 for testing.

Results and Conclusion

Results are reported in Tables 1 and 2. The shape-related features, selected through permutation tests, allowed us to successfully train different classifiers to discriminate between healthy subjects, and patients with MCI and AD. The best results were obtained for *controls vs. AD* (success rate > 80%) and *controls vs. MCI* (success rate ~ 80%). Discriminating between MCI and AD proved to be more challenging (success rate in [62% - 65%]), but still possible. The features used to train the classifiers are potential biomarkers for AD and MCI. In order to discriminate between controls and AD, one should look not only at the left and right inferior medial temporal horns, but also at the ventricles' areas close to the left corona radiata and left thalamus. What mostly differentiate controls from MCI are the tips of the temporal horns, and the areas close to the left and right caudate nuclei. Finally, MCI and AD seem to differ mainly in the tips of the temporal horns and in the area close to the left caudate nuclei. To the best of our knowledge, this is the first study using local shape analysis of brain ventricles in clinical MR to assess AD and MCI potential biomarkers.

Table 1 Leave-1-out tests: a classifier is trained on N-1 elements, and tested on the remained one, going through all the possible permutations

Model based on	Leave-1-out accuracy
Contr. & MCI	79.6 %
Contr. & AD1	82.5 %
MCI & AD1	65.6 %

Table 2 Cross-validation: for 100 times, the AD group was randomly split in training (AD1) and testing (AD2) datasets

Model Based on	Model Tested on	Accuracy mean ± SD
Contr. & AD1	Contr. & AD2	88.8% ± 3
Contr. & AD1	AD2	78.0 % ± 6
MCI & AD1	MCI & AD2	78.3 % ± 6
MCI & AD1	AD2	58.8 % ± 11

References

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4. V. Vapnik, The Nature of Statistical Learning (1995)