Significant local shape differences of the brain ventricles in Alzheimer's patients compared to healthy elderly

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Introduction

The brain ventricles are surrounded with sub-cortical gray and white matter structures that are often affected in dementia in general and AD in particular. In these conditions, atrophy may occur in these structures. Any change of volume or shape occurring in these structures must have an impact on the volume and shape of the ventricles. It is well known that brain ventricle volume is significantly higher in AD patients compared to age matched healthy subjects. However, the large overlap between the two volume distributions makes the measurement unsuitable as a biomarker of the disease. The purpose of this work was to assess whether local shape differences of the ventricles can be detected comparing AD patients and controls. If such differences could be identified they could be the target of further studies aimed at the identification of early signs of pathological changes.

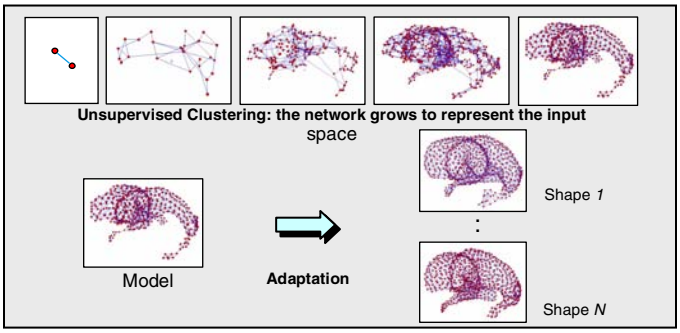

Fig. 1: The Shape Modeling Algorithm: *unsupervised surface point clustering* and *adaptation phase.*

Material and Method

Twenty-nine patients with probable AD (12 men, mean age 73 years, age range 60-83 years) and 25 volunteers with normal cognitive function (11 men, mean age 74 years, age range 64-89 years) were included. Out of 29 AD patients, 2 patients had an MMSE < 10, 20 had an MMSE between 9 and 21, and 7 had an MMSE > 21. MRI was performed on a 1.5 Tesla MR-system (Philips Medical Systems, Best, The Netherlands) using the following pulse sequences: 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 3mm slices with no gap, matrix 256x256, FOV 220.

In-house developed automated segmentation software (SNIPER, Software for Neuro-Image Processing in Experimental Research) was used to pre-process the images. Using the method described in [1], the software extracted fully automatically the intra-cranial cavity, the cerebrospinal fluids (CSF) and the white matter hyper-intensities. Brain-ventricles (the lateral and third) were semi-automatically extracted by re-labeling, with minimal manual interaction and automatic region growing, from the ventricular CSF to ventricles.

Next, all images were corrected for head-size and orientation using affine 12-parameters registration to the LUMC T2-weighted brain template for geriatrics [2].

The shape modeling was performed using the method described in [3]. This method is based on growing cell neural networks and is briefly described in Fig1. A first mesh model is generated on the average brain ventricles of the control group using the unsupervised growing phase of the algorithm. After convergence, the shape is adapted to every instance of the data set (healthy and AD subjects). The point correspondence is established during the adaptation phase (deformation) of the mesh.

We performed permutation tests for every single node of the mesh and mapped the corresponding p-values with a color code to highlight the local areas with significant differences (see Fig. 2). For these areas, we computed the displacement vectors that would move a node from an average control shape to an average AD shape (see Fig3).

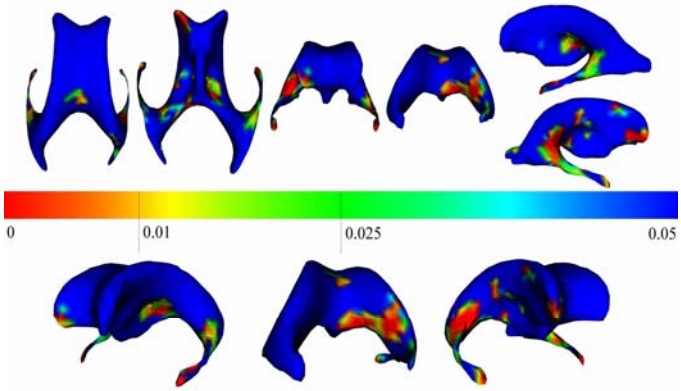

Fig. 2: Color-coded maps showing the p value associated with each node when comparing Controls and Alzheimer's disease patients.

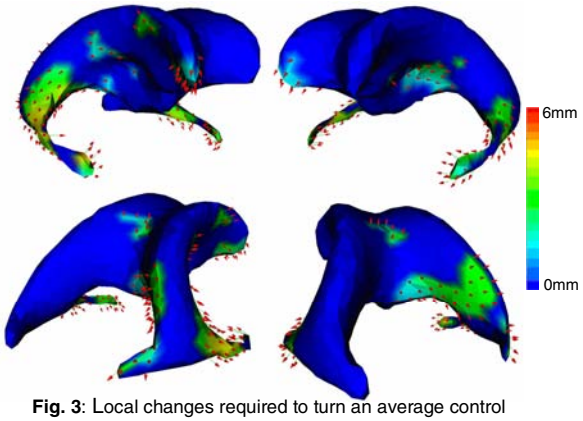

Fig. 3: Local changes required to turn an average control shape into an average Alzheimer shape. The direction of movement is indicated by the arrows; the amplitude of movement is color coded.

Results and Conclusion

Our results, showed in figure 2, suggest that in patients with Alzheimer disease, not only the lateral horns were significantly affected by AD, but also the areas adjacent to the anterior corpus callosum, the splenium of the corpus callosum, the amygdala, the thalamus, the tale of the caudate nuclei (especially the right one), and the head of the right caudate nucleus. The right lateral ventricle presented more significant different areas as compared to the left ventricle. At a global level, 22% of total brain ventricles surface was significantly different with $p < 0.05$ and 9 % of total brain ventricles presented a significance at $p<0.01$.

To our knowledge, this is the first report on shape differences of the whole cerebral ventricular system in AD patients; this may be of great importance in identifying early signs of pathological changes.

References

1. F. Admiraal Behloul et al., NeuroImage 8 (23), 2005.
2. F. Admiraal-Behloul et al., ISMRM, 2004
3. L. Ferrarini et Al., MICCAI, 2005.