4D Deformation modeling of Cortical Disease Progression in Alzheimer’s Dementia

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Introduction

Linear registration, region of interest analysis, and voxel-based morphometry methods have all been employed to elucidate the changes observed at discrete intervals during a disease process. Deformation field mapping can be used to extract additional information regarding the temporal characteristics of disease progression. To extract the changes associated with neurodegeneration in AD, both dilation and translation were modeled from perturbations in the deformation maps. In this study, dilation and translation are representative of local volume increase (CSF increase); decrease (atrophy); and local volume translation. In this context, translation relates to an area undergoing change spatially with little growth or atrophy.

Methods

21 subjects (68.7 ± 8.4 yr., MMSE 1-21) who met NINCDS and DSM-IV criteria were scanned at 3 to 6 month intervals by clinical examination and with the MMSE. A probable AD subject was only included if their MMSE declined over a period of observation of 1-2 years. Imaging was performed on a 2T Bruker Medspec S200 whole-body scanner using an inversion recovery segmented 3D GE sequence [MP-RAGE] with the following parameters. TI/TR/TE/flip angle/phase encoding steps per segment/FOV, 850/1000/8.3 ms/20deg/32/23cm. Images were acquired in an oblique plane perpendicular to the plane of the hippocampus, with an acquisition matrix of 256x256x256 and zero filled to 256x256x256. Data was cropped, intensity corrected (1) and linearly registered to the ICBM-152 model (2,3). 3D deformation maps with a step size of 2mm were then built to describe the changes between patient data sets (2,4). Deformation maps were then linearly distributed along a time-scale axis dependent upon initial degree of Alzheimer’s as measured by MMSE z-score (5). The time-line is corrected for education and age. The deformation maps are then concatenated and blurred along the z-score time dimension with a FWHM of 2.5 standard deviations. Local volume increase and decrease measurements were then calculated via the trace of the deformation field at each of the blurred resampled time-points (6). In addition, local volume translation is calculated (Figure 1).

\[ \text{Translation} = \arccos \frac{A \cdot B}{||A||_2 ||B||_2} + \frac{||A - B||_2}{||A||_2} \]

Figure 1 - Equation for Translation

Results

The average deformation map can now be classified into three mutually related classes: volume decrease, increase and translation. Areas of strong positive dilation (bright red) are predominately representative of CSF volume increase, likewise, areas of strong negative dilation (bright blue) represent atrophied tissue. Regions undergoing translation with little or no volume change (bright green) represent tissue that has been displaced as a result of the neurodegenerative processes. Significant negative dilation was observed in medial temporal lobe structures including the hippocampal formation and entorhinal cortex, and parietal lobe regions. These results are consistent with the reported atrophy of these structures. In the early stages of the disease process, perturbation of the deformation field was more extensive in the left hemisphere (Figure 2).

Conclusion

In neurodegenerative diseases, such as Alzheimer’s disease, deformation field modeling of atrophic processes has a number of advantages over traditional discrete modeling methods. The principal advantage is the ability to model longitudinal changes in a continuous manner. Correlation between structural change and the degree of disease progression can therefore be probed.

In this work, care has been taken during this reduction so that only information pertinent to the atrophic disease process is selectively enhanced; that being volume decrease, increase and translation. It is possible to extract further information from the deformation map such as local rotation. However, a logical criterion should be that a physiological process is easily inferable from the chosen metric. The changes in deformation maps produced in this study are consistent with the structural changes previously reported in studies using a variety of methods, such as voxel-based morphometry and analysis of cyto-architecture.

References