Introduction

The global impact of Alzheimer’s Disease (AD) on the cerebral cortex is still not fully understood. The ability to analyze the changes in cortical thickness across the whole cortex thus provides an exciting opportunity to gain further insight into the spatial distribution and extent of cortical atrophy in the disease. In the present work, we were able to use deformable models to fit the inner and outer cortical surfaces of 42 T1 MRI scans (25 AD, 17 controls) and compute the cortical thickness at every vertex of the surface. Statistical analysis was then performed comparing both clinical state and Mini-Mental State Exam (MMSE) scores against cortical thickness.

Methods

42 scans (25 AD, 17 controls) were investigated. These scans were acquired from patients with the clinical diagnosis of probable AD according to the NINCDS-ADRDA criteria. Subjects were recruited from the Department of Psychiatry, Alzheimer Memorial Center, Dementia and Imaging Research Group, University of Munich, Germany. Cognitive impairment in the AD patients was assessed using the Mini Mental State Examination. The average MMSE score in the Alzheimer group was 21.13, ranging from 10 to 29. In the control group, MMSE scores showed a ceiling effect, with an average score of 29.30 (range 28 to 30).

The ability to analyze the changes in cortical thickness across the whole cortex thus provides an extensive analysis of the disease in the present work. We were able to use deformable models to fit the inner and outer cortical surfaces of 42 T1 MRI scans (25 AD, 17 controls) and compute the cortical thickness at every vertex of the surface. Statistical analysis was then performed comparing both clinical state and Mini-Mental State Exam (MMSE) scores against cortical thickness.

Results

The average thickness across the whole cortex is significantly thinner in AD patients (3.21 mm) than controls (3.74 mm) (t = -4.8089, p = 0.000023), amounting to an average change of 0.53 millimeters. The most affected parts of the cortex are the medial temporal lobes, the temporal gyri, the dorsal lateral prefrontal cortex (slightly dominant effect in the left hemisphere), the inferior parietal lobules, the left insula, the orbitofrontal cortex, and some associative visual areas. In the most severely affected parts of the cortex, the parahippocampal gyrus (PHG), losses exceeded over 1.2 mm of cortical thickness.

The most affected parts of the cortex are the medial temporal lobes, the temporal gyri, the dorsal lateral prefrontal cortex, and the orbitofrontal areas. The effect is stronger in the left hemisphere than the right, especially when considering the MMSE analysis. The orbitofrontal cortex appears not as affected in the MMSE regression when compared to clinical state.

Discussion and Conclusions

The method shown in this paper introduces a fully automated analysis of cortical thickness analysis derived from MR images, which provides a meaningful metric (millimeter thickness loss) along with maps of statistical significance. The primary site of impact of AD is, as expected, found in the medial temporal lobes, with some spread to the posterior cortex, the cingulate, and frontal areas. The MMSE regression is a little more difficult to interpret. The areas of effect appear to have shifted to the anterior. One possible and appealing interpretation is that the MMSE analysis shows the areas of the human cortex that deteriorate along with the progression of AD. Care should be taken, however, not to overlook the possibility that the MMSE investigates functional differences among the subject population not purely related to AD.

References


Changes in Cortical Integrity in Alzheimer’s Disease

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Figure 1: Methods: each scan was registered to Talairach space, classified (1), fit with an inner and outer surface (2,3). Cortical thickness was determined at each vertex (4), then blurred using a 20 mm surface based kernel (5).

The native MRIs were registered into standardized MNI-talairach space using a linear transformation [1]. Simultaneously, the images were corrected for non-uniformity artifacts [2]. The thus registered and corrected volumes were segmented into white matter, gray matter, cerebro-spinal fluid and the associative visual areas, especially in the left hemisphere. Moreover, the entire posterior cortex appears to be mildly affected (t-values between 2.5 and 4.4), not just those areas mentioned above. The one exception here is the primary visual cortex, which is spared.

Figure 2: Frontal Lobes in MMSE (left) and clinical state (right): The effect in the frontal lobes is comprised of three distinct areas: the anterior cingulate gyrus, the dorsolateral prefrontal cortex, and the orbitofrontal areas. The effect is stronger in the left hemisphere than the right, especially when considering the MMSE analysis. The orbitofrontal cortex appears not as affected in the MMSE regression when compared to clinical state.

Figure 3: Lateral views, MMSE on left, clinical state on right: The ventral stream of the visual pathway atrophies in AD, along with a left dominant decline in the insula and dorsolateral prefrontal cortex. The superior temporal gyrus, with the exception of Heschl’s gyrus, is mostly spared.

Figure 4: Posterior views, MMSE on left, clinical state on right: Several distinct regions in the posterior cortex decline with AD: the posterior cingulate, the inferior parietal lobules, and the associative visual areas, especially in the left hemisphere. Moreover, the entire posterior cortex appears to be mildly affected (t-values between 2.5 and 4.4), not just those areas mentioned above. The one exception here is the primary visual cortex, which is spared.

Figure 5: The parahippocampal gyrus in AD. The middle figure represents the probabilistic anatomical locations of the entorhinal cortex (EC, blue) and the perirhinal cortex (PRC, green). The PHG has long been cited as the origin of AD related atrophy [6], in our study the anatomical correspondence between the EC and PRC reaffirm that conclusion. The left EC, moreover, is strongly affected when regressed against MMSE scores.

Figure 6: Posterior views, MMSE on left, clinical state on right: Several distinct regions in the posterior cortex decline with AD: the posterior cingulate, the inferior parietal lobules, and the associative visual areas, especially in the left hemisphere. Moreover, the entire posterior cortex appears to be mildly affected (t-values between 2.5 and 4.4), not just those areas mentioned above. The one exception here is the primary visual cortex, which is spared.