Determination of Age-Related Loss of Cerebral Cortical Thickness using a Novel Technique

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Introduction

The estimation of regional human cerebral cortical thickness has potential clinical importance in the assessment of the processes of normal brain ageing. Normative MR studies [1] often use Voxel-Based Morphometric (VBM) methods to quantify age-related change in grey matter density (a surrogate for thickness). However, the great variation in topological structure in the brain renders VBM unable to differentiate true change (due to age) from high variability, so we have developed a robust, data-driven approach which we apply in this abstract to investigate the changes in cortical thickness with age, head size and sex.

Methods

T2 inversion-recovery MR scans (1.5T Philips ACS PT 6000 NT , TI/TR/TE = 300/6850/18ms, pixel size = 1.8x1.8mm, 51 slices) were taken of the entire cerebrum in 119 normal volunteers (52 male, mean age = 70.3 years, range = 19-86 years). 110 scans had axial slices (thickness = 3.0mm), 9 had coronal (thickness = 4.0mm)

The MR image volumes were initially pre-processed to convert the data into a form suitable for estimating cortical thickness. The mean and standard deviation of the grey-level image values of the grey matter (GM), white matter (WM) and CSF were determined and were used in the up-interpolation of the images to produce a volume at twice the resolution in the through-plane direction. This volume was then registered to the Talairach stereotaxic atlas[2], to define the 31 sub-lobar regions in which cortical thickness was later obtained. The GM in the images was segmented to produce a volume of GM probability maps, again using the estimated tissue mean values.

The GM cortical thickness was then estimated as follows. The GM/WM boundary in the registered images was found using an iso-contour detector which picked out those edges consistent with the average of the GM and WM mean values. The 3D surface normal to the boundary was determined, and a search performed in this direction (away from the WM) on the segmented GM images until an opposing GM edge was found. The distance traversed was recorded as the cortical thickness. This edge may be a true edge, a transition from greater than to less than 50% probability or may be due to partial voluming of the GM with other tissue. In both cases, the edge may be with either WM or CSF. If it was WM, it was assumed that 2 gyral banks, of approximately equal width with no intervening CSF, had been traversed, and the cortical thickness length was duly halved. A robust estimate of regional cortical thickness was obtained by taking the median of the cortical thickness lengths in each gyral region of the cortex, as determined by the registration to the Talairach atlas. The statisical error on the determination of the median for the majority of regions has been assessed and presented in [4] and is between 0.05 and 0.3mm

ANOVAs were performed for each region over the entire dataset, correlating cortical thickness against sex, head size (using the bounding box of the interior of the skull as a surrogate for intra-cranial volume [3]) and age.

Results

There were no significant correlations between age and sex or age and head size. Sex was highly significant in predicting head size ($p<<0.0001$,Adj R-sq=0.305); females having smaller heads than males.

Using a probability significance value of $p = 0.05$, sex was significant in predicting cortical thickness in the following 10 regions: the rectal and superior frontal gyri; anterior cingulate; angular and cingulate gyri and superior lobule of the parietal lobe and in the fusiform, parahippocampal, middle and superior gyri of the temporal lobe. In all 31 regions except the uncus, females have a greater cortical thickness than males. In the 10 significant regions, the average difference due to sex was 0.18mm. Once the effects of sex have been accounted for, head size is only significant in predicting thickness in the uncus and fusiform gyrus, with a negative correlation for both; on average a decrease of 0.59mm/litre of bounding box. Having accounted for both sex and head size, age was highly significant in predicting cortical thickness in all regions except the rectal frontal and inferior temporal gyri, with an average loss over all regions of 0.02mm/year.

Conclusions

A novel data-driven cortical thickness estimation has been introduced and successfully used to demonstrate global cortical thickness loss with ageing in normal subjects. This supports the notion that the processes of atrophy with normal ageing are not specific to a few key areas. Cortical thickness appears largely invariant to head size, and the effects of sex are region specific.

References

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