CORTICAL THICKNESS IN PATIENTS WITH MAJOR DEPRESSION AND HEALTHY VOLUNTEERS

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Introduction: Major depression is the most common psychiatric disorder. Neuroimaging studies with quantitative evaluation of anatomical structures and physiological parameters may provide increasing knowledge on the pathophysiology of the disease (1). Automatic measurements of cortical thickness in high resolution structural MRI can be performed by reconstruction of the cortical boundaries using deformable surfaces (2, 3).

Purpose: To analyse cortical thickness in patients with major depression compared to a group of healthy volunteers and secondary to evaluate the age effect on cortical thickness in healthy subjects.

Methods: *Subjects* – Prospective study of outpatients with major depression (planned 45 patients). Inclusion criteria: ≥ 18 on the Hamilton Rating Scale for Depression (HAM-D) or ≥9 on the HAM-D subscale. Use of selective serotonin reuptake inhibitor (SSRI) or other anti-depressant medication was noted. Thirteen patients (9f, 4m, mean age 35.8 yrs, age range 23-61 yrs) were included in the present study. Control group consisted of 21 healthy volunteers (10f, 11m, mean age 41.8 yrs, age range 21-63 yrs). *Image Acquisition* – T1 MRI data were obtained on a 3T system (Signa HDx, R14M5, GE Healthcare) using a 3D inversion recovery fast spoiled gradient recalled sequence with TR/TE/TI = 9/3.6/600 ms, 14º flip angle, recon. matrix 512×512, FOV = 25.0 cm, and a slice thickness of 1 mm. Whole head images were acquired with 124 - 150 axial slices using a 8-channel head coil. *Image Processing* – MRI data were registered to the ICBM152 target space (4) and intensity non-uniformities were corrected (5). A brain mask was created by iteratively fitting a deformable surface to the brain surface and the voxels inside the brain mask were classified into white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) (2). The cerebral WM was separated from the brain stem and cerebellum by stereotaxic masking. The ventricles and subcortical regions were labeled WM to obtain a solid WM component for the following surface generation and cortical segmentation. The cerebral WM was separated into two hemispheres by a mid-sagittal cut and spherical topology of each hemisphere was obtained using a topology correction algorithm. Cortical boundaries of each hemisphere were identified using deformable surfaces and a force balancing scheme. An initial WM surface defined by the topologically correct WM component was deformed iteratively to the WM/GM boundary under influence of forces derived from the fuzzy classifications and the gradient image (2). The GM/CSF boundary was found by expanding the initial surface under influence of deformation forces derived from the surface normals, a gradient vector field, and a GM/CSF edge map (3). Cortical surfaces were visually inspected for segmentation errors, both using a 3D visualization tool and by superimposing the surfaces onto the original MR images. The cortical thickness was measured as the distance between the WM and GM surface orthogonal to the GM surface. *Statistical Analysis* – Each hemisphere was divided into the main lobes based on an atlas in stereotaxic space enabling regional based analysis. To facilitate construction of statistical parametric maps (SPM) of cortical differences between the groups, cortical surfaces were mapped to a reference surface of a healthy subject using a feature based surface mapping algorithm (6). The SPMs were constructed by assumption of normally distributed measurement and presented as p-values on the reference surface. To measure the age effect on cortical thickness linear regression was performed on mean thickness of the main lobes in the healthy volunteers.

Results: Regional analysis of mean cortical thickness measurements of the main lobes showed no significant (α=0.01) differences between patients with major depression and healthy controls. In the patient group, the SPMs revealed significant focal cortical thinning ($p<0.01$) in the medial prefrontal cortex (MPFC) mostly in the right hemisphere, but also medially in the primary motor cortex (PMC) (fig. 1). Some regions were found to be significantly thicker in the patient group. These were mainly located more posteriorly in the parietal lobe mostly in the left hemisphere. Linear regression analysis of the healthy volunteers showed significant ($p<0.01$) negative correlation between cortical thickness and age in frontal and temporal lobes corresponding to a decrease in cortical thickness of 2-4% per decade in these lobes from 21-63 years of age (fig. 2). Measurements of other lobes, though decreasing, did not reach significance in the linear model.

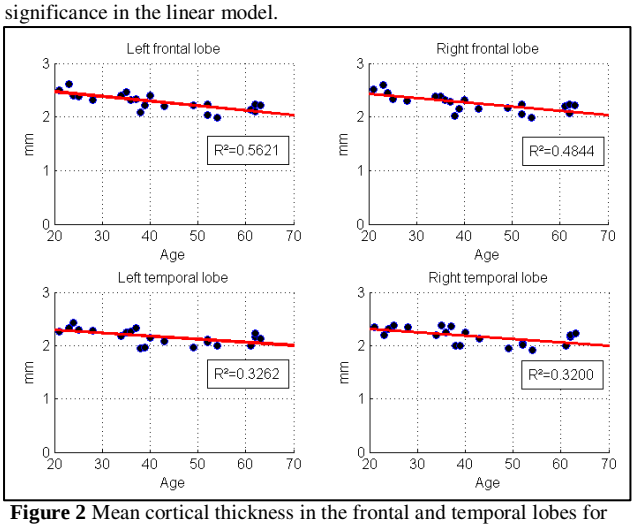

Figure 2 Mean cortical thickness in the frontal and temporal lobes for the healthy volunteers. The shown regressions are significant ($p<0.01$).

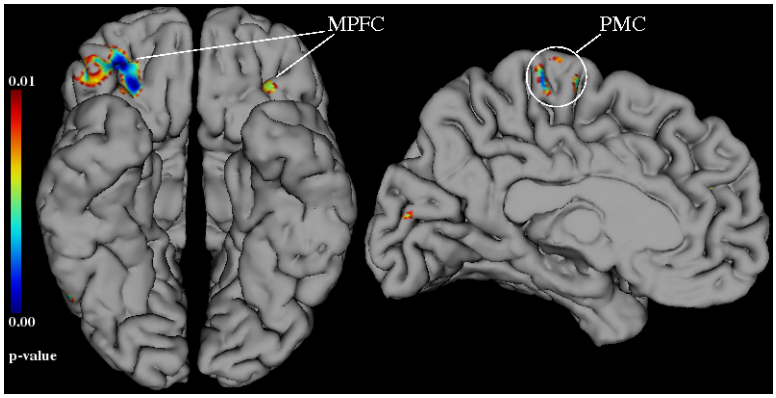

Figure 1 SPM showing areas of significantly ($p<0.01$) thinner cortex in major depression.

Discussion: The cortical thinning in the MPFC of patients with major depression is in agreement with other studies (1). However, cortical thinning in the PMC in patients with major depression has to our knowledge not previously been reported. Also, the significantly thicker regions found in the patients were surprising. Cortical thickness has been shown to differ across the sexes. In particular, the right inferior parietal and posterior temporal regions have been shown to be thicker in women (7). The main region found to be thicker in the major depression group is in the right parietal lobe. This combined with the greater female-male ratio in the patient group may explain the difference. This may be clarified with the inclusion of more patients. The decrease in cortical thickness due to age is consistent with findings of GM volume reduction (8) and indicates a high sensitivity of the cortical thickness measurements.

Conclusion: The study demonstrates that it is possible to measure differences in cortical thickness between patients with major depression and healthy controls even on a relatively small sample. Analysis of age effect on cortical thickness revealed a decrease of 2-4% per decade in the frontal and temporal lobes of healthy volunteers.

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