Regional increases of cortical thickness in untreated, first-episode major depressive disorder

Su Lu[1], Lihua Qiu[2], John A. Sweeney[3], and Qiyong Gong[2]

[1]West China Hospital, Chengdu, Sichuan, China, [2]West China Hospital, Sichuan, China, [3]University of Texas Southwestern, TX, United States

Target audience:

The target audiences for this study are psychiatrists, neurologists and radiologist.

Purpose:

Most previous structural studies of major depressive disorder (MDD) investigated volumetric changes in chronic medicated patients. However, it is increasingly recognized that gray matter volume of a cortical region represents the combination of cortical thickness and surface area and these two parameters reflect different neurobiological processes and are regulated by different genetic mechanisms. Thus, analyzing these two morphological parameters separately may help to discriminate these two genetically independent traits. In the present study, we investigate both the cortical thickness and surface area changes in first-episode, treatment-naïve, mid-life MDD which may help to elucidate the core pathophysiology of this disease and its early impact on the brain.

Methods:

In a cross-sectional case-control study, 46 first-episode, treatment-naïve, mid-life adult MDD patients and 46 matched controls were scanned employing a spoiled gradient recalled sequence. The diagnosis of depression was made using the SCID (Structured Clinical Interview for DSM Disorders) according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria. All patients had a score of at least 18 on the 17-item Hamilton Depression Rating Scale (HDRS). Constructions of cortical surface were developed from 3D SPGR images using FreeSurfer software (http://surfer.nmr.mgh.harvard.edu/, vision 4.5.0), which uses automated surface reconstruction, transformation and high-resolution inter-subject alignment procedures to measure the thickness of the entire cortex. The differences of cortical thickness between patients and controls were compared using a general linear model approach with age and sex as covariates. Partial correlations were computed to examine relationships between the mean cortical thickness in regions with altered thickness with disease duration (weeks) and HDRS. Correlations among altered brain regions were also analyzed.

Results:

The most important findings of our study were the increased cortical thickness in right hemisphere, including medial orbitofrontal gyrus, pars opercularis, rostral middle frontal gyrus, supramarginal gyrus, and the thickness of rostral middle frontal gyrus were negatively related with the HDRS (Figure 1). Furthermore, MDD patients showed significantly increased associations among the areas with increased cortical thickness. Analysis of pial area also revealed a trend toward increased surface area in left parahippocampal gyrus in MDD. In order to compare our result with the most previous gray matter volume studies, the voxel-based morphometry analysis were also performed which revealed significantly increased gray matter volume in left paracentral lobule, left superior frontal gyrus, bilateral cuneus and thalamus which belongs to limbic-cortico–striato–pallido–thalamic loops.

Discussion:

To the best of our knowledge, the current study measured the alterations of cortical thickness in by far the largest cohort of first-episode, treatment-naïve, mid-life MDD patients. In contrast to observations of volume reduction in studies of chronic patients, we observed greater rather than reduced cortical thickness at early stage of MDD. Though the exact mechanism for increased regional cortical thickness in MDD remains to be established, our findings document regional changes in cortical thickness early in the course of MDD for which further research is needed to clarify its cause, course and consequences. The enhanced correlations of changes in thickness of the right supramarginal gyrus with the three prefrontal regions in MDD patients suggest a wide scale process.

Conclusion:

These changes in first-episode, treatment-naïve, mid-life MDD patients may reflect an active illness-related cortical change close to illness onset, and thus may provide important new insight into the early neurobiological manifestations of the disorder.

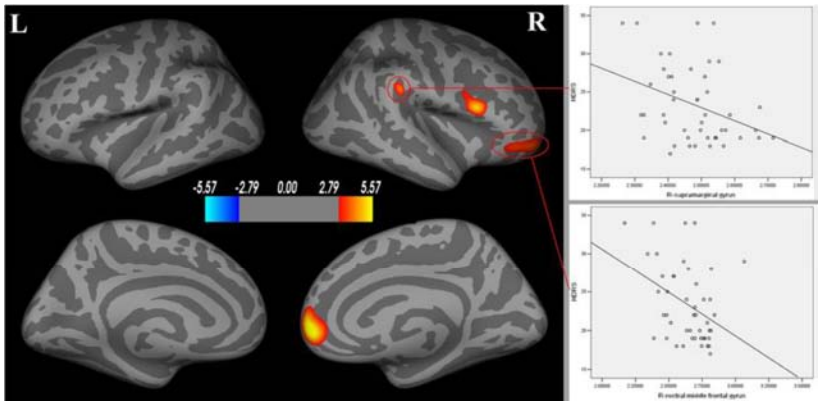

Figure 1. Areas with Cortical Thickness Differences between Healthy Controls and Patients with Major Depression (left) after FDR Correction. Scatterplots show the negative correlation between HDRS with right rostral middle frontal gyrus and right supramarginal gyrus (right). Warmer colors (positive values) represent cortical thickening; cooler colors (negative values) represent significant cortical thinning in MDD patients.

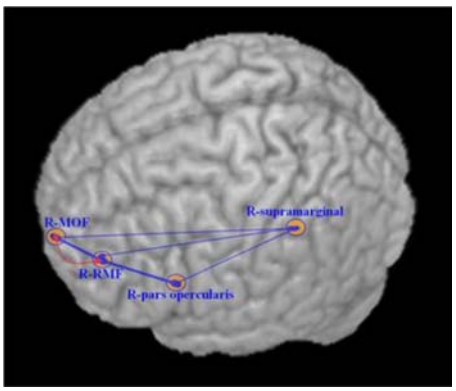

Figure 2. Correlations of Mean Cortical Thickness across Brain Regions in MDD and Healthy Controls.The heavy line represents higher correlation coefficients ($r>0.5$, $p\leq0.001$). The red line represents the significant positive correlations in healthy controls, and the blue line represents the significant correlations in MDD patients. R: right hemisphere, L: left hemisphere, MOF: medial orbitofrontal gyrus, RMF: rostral middle frontal gyrus.