Regional gray matter changes in major depressive disorder: an optimized voxel-based morphometry study

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Introduction

Voxel based morphometry (VBM) is a neuroimaging analysis technique that allows investigation of focal differences in brain anatomy, using the statistical approach of so-called statistical parametric mapping [1,2]. Major depressive disorder (MDD) is a common and serious psychiatric illness. In past study, the authors have done many researches to reveal the change in grey matter [3-7]. However, the neurobiology of MDD is largely unknown. The purpose of the present study was to identify brain regions with gray matter volume and density changes with relative large MDD subjects and controls using optimized voxel-based morphometry.

Material and Method

Fifty one patients experiencing MDD (mean age = 34.6 ± 12.7, twenty five males and twenty eight females) according to the diagnostic criterion of DSM-IV, who had a score of 18 or greater on the 17-item Hamilton Depression Rating Scale (HAMD), and fifty two age and sex matched normal controls (mean age = 37.2 ± 16.1, twenty three males and twenty eight females) were recruited. MR scanning was carried out on a 3.0 TMR scanner (EXCITE, GE Signa, Milwaukee, USA). High resolution 3-dimensional T1-weighted (T1W) images were acquired employing a spoiled gradient recalled (SPGR) sequence with TR/TE = 8.5/3.4 ms, FA = 120, 156 axial slices with thickness = 1 mm, axial FOV 24 × 24 cm^2 and data matrix = 256 × 256.

Optimized voxel-based morphometry [2] was conducted using Statistical Parametric Mapping–2 (SPM2) (Welcome Department of Imaging Neuroscience, London [*http://www.fil.ion.ucl.ac.uk/spm*]). The voxel-based morphometry–2 toolbox, which implements the optimized voxel-based morphometry approach [2], was used for data preprocessing. Voxel-by-voxel-based comparisons of gray matter density and volume were performed between groups using two-sample *t* tests. The correlation between the regional gray matter changes and clinical symptom severity was examined. A corrected *p* value of less than 0.001 was deemed to be significant.

Results

Patients with MDD exhibited higher grey matter volume than normal controls in multiple brain regions including bilateral thalamus, left and right superior parietal lobule, right frontal lobe (Table 1, Figure 1 A, B and C). MDD patients also showed higher grey matter density than normal controls in bilateral thalamus (cluster level $p < 0.001$, corrected) (Table 1, Figure 1 D). No significant correlation between regional gray matter changes and HAMD scores was found after controlling for age, years of education and duration of illness.

Table 1. Voxel-based morphometry showed grey matter volume and density changes in major depressive disorder (MDD) compared with normal controls (NC) ($p < 0.001$, corrected).

Description of extent of cluster	L/R	Cluster size[a]	T value	Peak coordinates voxel (x, y, z)
MDD > NC in Volume				
Thalamus	L	7758	4.47	14, -10, 5
Thalamus	R	6785	4.61	-10, -10, 6
Superior parietal lobule	L	9912	4.98	-28,-52, 60
Superior parietal lobule	R	7004	4.65	32, -49, 60
Frontal Lobe, Precentral Gyrus	R	3081	4.97	21, -23, 60
MDD > NC in Density				
Thalamus	L	5945	4.55	19, -26, 8
Thalamus	R	6519	4.59	-9, -11, 7

Listed are coordinates corresponding to the voxels with maximum (peak) effects sizes defined in Montreal Neurological Institute (MNI) space.

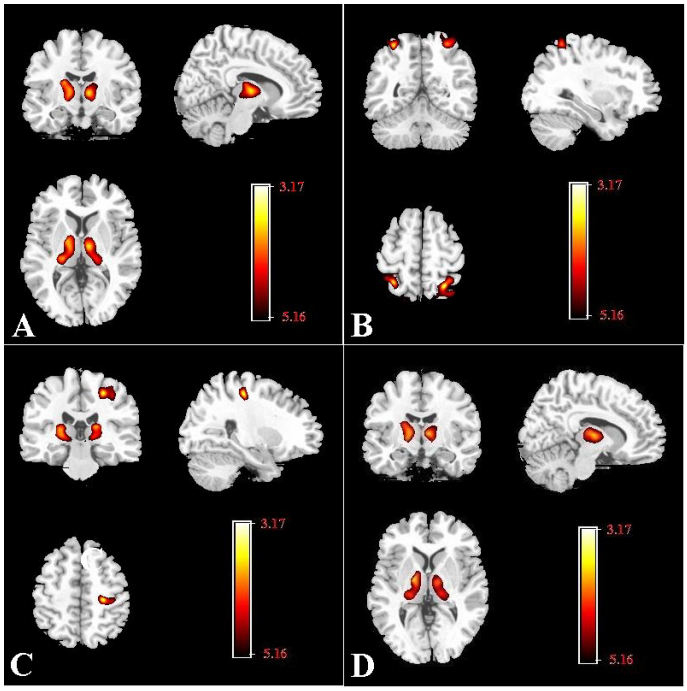

Figure 1. Volume or density changes in major depressive disorder (MDD) patients comparing with normal controls (NC)[a]

[a] Volume: MDD > NC in in bilateral thalamus (A), in left and right superior parietal lobule (B) and in right frontal lobe (C). Density: MDD > NC in bilateral thalamus (D). Images are presented in radiological orientation. Statistical inferences were made with a voxel-level statistical threshold of $p < 0.001$ (corrected) was considered significant.

Discussion and Conclusion

Present study demonstrated that MDD patients have higher volume and density of grey matter in multiple brain areas than controls, especially in bilateral thalamus. Studies of thalamic neuroanatomy or morphologic image show different results in depression. Several studies showed the volume of thalamic reduced in depression [5,6], while Neumeister *et al* found depressed patients in remission had increased thalamic metabolism after tryptophan depletion but not after sham depletion [8]. At the cellular level, a recent postmortem study demonstrated increased neuronal number (26–37% more) in the thalamus of patients with depression, and the mean total thalamus volume was 16% greater in the MDD group versus the comparison subjects, although there was not significant at the $p < 0.05$ level [4]. This is consistent with our results. Young and colleagues suggest that such elevations could reflect an abnormality in the neurodevelopmental process such as an accentuated neuronal birth rate or, alternatively, an excess survival in the numbers of neurons. However, it remains unknown as to which cell population is responsible for this increase in neuron number and whether the modulation of thalamic activity is really reduced; further study should reveal this change in thalamus using multiple methods.

Reference

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