Altered regional gray matter volume in Chinese female patients with bulimia nervosa

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Abstract

The bulimia nervosa (BN) is one of the psychiatric disorders, which pathophysiology is not clear currently. Recent studies have concentrated on brain structural and functional changes in BN patients. However, findings have been inconsistent. The aim of this study was to explore the relationships between brain structural alterations and clinical features in Chinese female patients with BN. Method A total of 34 female patients with BN and 34 matched healthy controls (HC) underwent a T1-weighted magnetic resonance imaging (MRI) scanning. VBM analysis was carried out by using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8/>) to explore the alterations of regional Grey Matter Volume (GMV). The correlation analysis was performed using Statistical Package for the Social Sciences (SPSS). Results The BN group showed reduced regional grey matter volume of the left medial superior frontal gyrus (SFGmed.L), the right superior temporal gyrus (STG.R), the right median cingulate and paracingulate gyri (DCG.R), the left median cingulate and paracingulate gyri (DCG.L) and the left dorsolateral superior frontal gyrus (SFGdor.L) compared to HC. There was no significantly regional grey matter volume increase in BN patients. The brain areas that GMV altered were uncorrelated with BMI and duration of illness ($p > 0.05$). There was a significantly negative correlation between age and GMV in the SFGmed.L ($P < 0.005$, $r = -0.516$), the DCG.R ($P < 0.005$, $r = -0.556$), the DCG.L ($P < 0.05$, $r = -0.576$) and the SFGdor.L ($P < 0.005$, $r = -0.576$). The self-esteem and self-evaluation of BN patients were uncorrelated with the structural alterations of GMV. Conclusions The results show altered regional GMV in females with bulimia nervosa in several brain areas, but it difficult to differentiate whether the GMV changes are the results of BN pathology or the consequences of binge-eating and compensatory behaviour. The structural alterations might be associated with impairments of inhibitory control and body dissatisfaction in BN patients, as well as mood disorder comorbidity.

Introduction

Bulimia nervosa (BN) is an eating disorder (ED) characterised by recurrent episodes of binge eating and inappropriate compensatory behaviors to prevent weight gain[1]

It usually occurs in young females, which may lead to severe medical complications affecting all body systems[2, 3], but the neurobiological mechanism of the BN are still unclear. Recently, a growing number of studies have focussed on exploring the neurobiological underpinnings of ED. Researchers have found structural and functional brain changes of the ED patients by using magnetic resonance imaging (MRI) technology. But findings have been inconsistent. Voxel-based morphometry (VBM) is an automated method based on voxel-wise statistical analysis of structural MRI images, which can be used to estimate regional grey matter volume (GMV) alterations. There are a few studies focus on brain grey matter changes in BN. Some suggested a greater grey matter volume of the medial orbitalfrontal cortex (mOFC) and the ventral striatum [2, 3], insula[2, 3], lingual gyri and inferior parietal lobule (IPL)[6]. Some found reductions in some brain volumes, including caudate and putamen[5], bilateral medial frontal (MFG) and precentral gyri (PreCg), right postcentral gyrus (PoCg), left superior (SFG) and inferior frontal gyri (IFG) in BN patients[6]. The results across studies are variable due to different approaches. Some studies

corrected for age and total intracranial volume (TIV), while others corrected for age and BMI. Some studies did not consider the effect of medication.

In ED patients, low self-esteem is one of the core features, which is the predictor and maintenance factor of ED pathology[7]. The negative self-evaluation is also commonly seen in ED patients, which is influenced by body shape and weight[8]. The purpose of this study was to explore the relationships between brain structural alterations and clinical features in Chinese female patients with BN.

Methods

2.1 Participants

A total of 68 female subjects participated in this study, including 34 patients with BN and 34 age-matched healthy controls (HC) in the normal weight range with no history of eating disorders or other psychiatric disorders. The patients group recruited from Mental Health Center of West China hospital of Sichuan University. The healthy volunteers were recruited through public advertisement. The structured clinical interview for DSM-V disorders (SCID) was administered by two trained psychiatrists. All subjects were female, non-medicated and right-handed with no lifetime history of major psychiatric disorders, head trauma, substance abuse or dependence and neurologic disease, without metal implants or heart pacemakers. We did not exclude the patients who have mild anxiety and depressive symptoms, as these symptoms were commonly seen in BN individuals[9, 10].

2.2 Clinical psychological assessments

All patients completed the revised version of Core Self-Evaluation Scale (CSES) and the Rosenberg Self-Esteem Scale (RSES) in Chinese. The CSES was revised by Du Jianzheng et al, with acceptable reliability and validity, which included 10 items and used a 5-point score method. The total score ranged from 10-50 points, which represent the core self-evaluation level of each subject. This scale had good reliability and validity in Chinese population, and the norm of CSES was 36.05 ± 5.21 for female college students. In this study, we compared the CSES score of BN with the national norm.

The RSES included 10 items, each item was rated on 4-point scale, and items 3, 5, 8, 9, 10 are negatively worded. The total score was the sum of the scores of each item, indicating the levels of individual self-esteem[12]. The Institute of Education of Tsinghua University investigated the self-esteem of college students in Beijing by using the RSES scale in Chinese. The research found the average RSES score of college students is 28.73 ± 4.48 , no significant gender difference was found[12]. It has good representation in Chinese population. In our study, we use this value to compare with the average RSES score of the patients group.

This study was approved by Ethics Committee of the West China hospital of Sichuan University, and all subjects provided written informed consent.

2.3 MRI data acquisition

MR images were obtained using a 3.0T Philips MR system. All subjects underwent a 3D T1-weighted volumetric scan with the following parameters: sagittal; matrix size, 256×256; field of view (FOV)=256mm×256mm; slice thickness=1mm; no gap; flip angle=7°; repetition time (TR)=8.2ms; echo time (TE)=3.8ms; voxel size=1×1×1mm. All subjects were asked to relax, keep their eyes closed without fall asleep, not think of anything and keep head motionless as possible.

2.4 Voxel-based morphometry processing

Data analysis was carried out using the voxel-based morphometry (VBM) toolbox by Christian Gaser (VBM8; <http://www.neuro.uni-jena.de/vbm/>), as part of SPM8 (Wellcome Trust Centre for Neuroimaging, Institute of Neurology, London, UK), run under Matlab R2013b. Structural images were normalized to Montreal Neurological Institute (MNI) standard space and segmented into grey matter (GM), white matter (WM) and cerebrospinal fluid (CSF) using the unified segmentation approach. Finally, the grey matter images were smoothed using a 8mm full-width half-maximum Gaussian kernel for analysis.

2.5 Statistical analysis

A two-sample t-test was conducted using SPM8 software to compare regional GMV differences between patients and HC, with age and total intracranial volume (TIV, the sum of GM, WM and CSF volumes) as covariates. Multiple comparisons were corrected using family-wise error (FWE) approach at a cluster level, with a corrected threshold of $P < 0.001$. An absolute threshold was set at 0.2 in all computations.

The Statistical Package for Social Science (SPSS) version 20.0 (SPSS Inc, Chicago, <https://www.ibm.com/products/spss-statistics>) was used to conduct statistical analysis of clinical variables and demographic data, as well as compare total GM, WM, CSF and intracranial volume between patients and control group. Comparison between two groups was conducted by two sample t-test.

Moreover, correlation analyses were conducted using SPSS 20.0. We extracted the brain regions that showed GMV alterations as region of interest (ROI), using the Region of Interest extraction tool in xjView via the SPM toolbox (<http://www.alivelearn.net/xjview8/>). Pearson correlations were conducted between ROIs and clinical variables after Bonferroni correction.

Results

3.1 Demographics and clinical characteristics of participants

The demographics and clinical characteristics of patients and healthy controls are summarized in Table 1. There were no significant differences in age, BMI and education years between two groups ($P > 0.05$). The mean RSES score of BN was lower than the college students in China, and the mean CSES score of BN was lower than the national norm for female college students.

3.2 VBM results

3.2.1 Whole brain tissue volumes

There were no significant differences in total GMV, WMV and TIV between BN and HC group ($p>0.05$). The BN group showed increased total volume of CSF when compared to healthy controls. See Table 1.

3.2.2 Regional grey matter volumes

With age and TIV as confounding covariates, the VBM analysis of regional grey matter volumes yielded five clusters after correction for multiple comparisons at the cluster level (threshold of $P<0.001$). The BN patients had lower GMV in these clusters, including the left medial superior frontal gyrus (SFGmed.L), the right superior temporal gyrus (STG.R), the right median cingulate and paracingulate gyri (DCG.R), the left median cingulate and paracingulate gyri (DCG.L) and the left dorsolateral superior frontal gyrus (SFGdor.L) when compared to healthy controls. We have found no regional GM volume increase in BN. See Table 2 Fig.1.

3.3 Correlations

We have found no significant correlations between BMI and GMV in the brain areas that GMV altered, nor any significant correlation of duration of illness, total RSES score and CSES score ($P>0.05$). There was a significantly negative correlation between age and GMV in the SFGmed.L ($P<0.005$, $r=-0.516$), the DCG.R ($P<0.005$, $r=-0.556$), the DCG.L ($P<0.05$, $r=-0.576$) and the SFGdor.L ($P<0.005$, $r=-0.576$). See Fig.2. We found both RSES and CSES score were lower in BN than Chinese college students, but the self-esteem and self-evaluation are uncorrelated with alterations of regional GMV.

Discussion

4.1 Global brain volume alterations

In our research, no alterations were observed in total GMV, WMV and TIV in BN group when compared to controls, which are in line with previous studies[12]. Previous researches have showed alterations of CSF volume in BN. Krieg et.al has found enlarged external CSF spaces in bulimic patients[16], while Joos et.al has not found alterations of CSF volume in BN patients[14], this difference most likely due to methodological difference across different studies. In our study, we found the volume of CSF increased in BN, but we have not found changes in TIV, it suggested that decreases in GMV were replaced by increases in CSF.

4.2 Regional GMV changes

In this study, we investigated global and regional brain volume alterations in BN patients by using VBM analysis. Reduced grey matter volume was observed in the SFGmed.L, the STG.R, DCG.L, DCG.R and SFGdor.L when compared to healthy controls, while we have not found increased GMV of any brain regions in BN.

Previous study reported that reduced volumes of the frontal cortex are associated with deficits in self-regulation and loss of control over eating [17], which are commonly seen in BN patients. The SFG located in the superior part of the prefrontal cortex (PFC). The PFC has been demonstrated that play essential roles in executive controls [18], including the control of attention, temporal organization of a response, task management, inhibiting behavioral responses to inappropriate stimuli and processing working memory [19, 20]. The executive functions involve in the self-regulation of eating behavior [21]. Therefore, the reduced grey matter volume of SFG might reflect impaired executive control function in BN patients. The temporal gyrus are associated with the ability of emotion processing [22] and body image perception [23]. Kambe et.al has found the symptoms of depression are inversely associated with the normalized volumes of bilateral superior temporal gyrus [22]. Previous studies also have reported reduced volume of the left superior temporal gyrus in anxiety disorders. The reduced right superior temporal gyrus volume may be associated with suicide attempt in adolescents [25]. Therefore, the alterations of temporal gyrus volume may be related to the depression and anxiety comorbidity in BN. The disturbance of body image perception would contribute to body dissatisfaction, which is one of the common symptoms of eating disorders. Kohmura et.al has found decreased GMV in superior temporal gyrus in anorexia nervosa, which is related to body dissatisfaction [23]. We have not found previous studies on the relationship between body dissatisfaction and structural MRI alterations in BN at present. The cingulate cortex involves in the perception of pain [26]. Decreased pain sensitivity is found in individuals with bulimia nervosa, and it persists after recovery [27]. Reduced grey matter volumes in this region may be relative to elevated pain threshold in BN.

4.3 Correlations between GMV and clinical variables

The brain areas that GMV altered were uncorrelated with BMI and duration of illness ($p > 0.05$), but some brain regions were negatively correlated with age in BN patients, including the SFGmed.L ($P < 0.005$, $r = -0.516$), the bilateral DCG ($P < 0.005$, $r = -0.556$), the SFGdor.L ($P < 0.005$, $r = -0.576$). Both RSES and CSES score were lower in BN patients than college students. Body image disturbance is the common symptom of BN [28], and previous study demonstrated that self-esteem was linked to concern with body shape and weight in BN patients [29], the low self-esteem associated with high levels of body dissatisfaction [30]. In our research, we assumed that the total RSES score might be correlated with regional brain volume alterations. Similarly, self-evaluation of BN patients is unduly influenced by body shape and weight [1]. We also supposed that structural alterations in the brain contributed to lower self-evaluation in BN. However, the present study indicates that both self-esteem and self-evaluation were uncorrelated with alterations of GMV. We have not found the previous studies that investigated the relationship between brain structural alterations and self-esteem in BN patients, as well as the relationship between brain structural alterations and self-evaluation. Therefore, further study is necessary to verify these results.

4.4 Limitations of the study

There are some limitations in this study. Firstly, this study only consisted of female patients, as the majority of ED patients are female, both female and male participants should be included in future

studies. Secondly, a small part of the BN patients have psychiatric comorbidities, such as mild anxiety and depressive symptoms. Although mood disorder are commonly seen in BN[9, 10], it might have some effect on results. Moreover, this study was cross-sectional, it difficult to differentiate whether the GMV changes are the results of BN pathology or the consequence of binge-eating and compensatory behaviour. Finally, the sample size of BN patients is small. In future studies, it is necessary to enlarge the sample size to increase the statistical power.

Conclusions

The present study showed regional GMV decrease in female with bulimia nervosa in several brain areas. The structural alterations might be associated with impairments of inhibitory control and body dissatisfaction in BN, as well as mood disorder commorbidity. Except for age, we have not found the relationship between these stuctural alterations in the brain and clinical symtoms of BN in this research temporarily. These findings need to be replicated in the further studies.

Abbreviations

BN: Bulimia nervosa

GMV: grey matter volume

VBM: Voxel-based morphometry

HC: Healthy controls

MRI: magnetic resonance imaging

SPSS: Statistical Package for the Social Sciences

SFGmed.L: the left medial superior frontal gyrus

STG.R: the right superior temporal gyrus

DCG.L: the left median cingulate and paracingulate gyri

DCG.R: the right median cingulate and paracingulate gyri

SFGdor.L: the left dorsolateral superior frontal gyrus

ED: eating disorder

mOFC: medial orbitalfrontal cortex

IPL: inferior parietal lobule

TIV:total intracranial volume

SCID:the structured clinical interview for DSM-V disorders

RSES:the Rosenberg Self-Esteem Scale

CSES:the Core Self-Evaluation Scale

WMV:white matter volume

CSF:cerebrospinal fluid

TIV:total intracranial volume

ROI:region of interest

NS:not significant

BMI:body mass index;

Declarations

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Authors' information

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Authors' contributions

LZ, YW and XL designed the study. LLZ, LFL, YYL and JM recruited patients and collected patient's demographic data. XL, XWL and YW collected the MRI data. XL and XWL analyzed and interpreted the patient's data. XL drafted the manuscript. LZ revised the manuscript. All authors have read and approved the final manuscript.

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Ethics approval and consent to participate

The study was approved by the Ethics Committee of West China Hospital of Sichuan University. All the participants agreed and provided signed, informed assent or consent of their own accord.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1 Demographic variables, clinical characteristics and whole brain tissue volumes of the subjects.

Characteristic	BN (N=34) Mean±SD	HC (N=34) Mean±SD	P
			Age 22.85±3.89 22.26±2.53 NS
BMI(kg/m ²)	20.46±2.80	20.52±1.52	NS
Duration of illness(years) ^a	2.92±2.35	-	-
Education(years)	15.53±2.43	16.09±2.45	NS
CSES global score ^a	33.24±3.56	-	
RSES global score ^a	25.76±5.47	-	
Whole brain tissue volumes (VBM)			
Grey matter volume(ml)	660.56±34.17	662.97±37.11	NS
White matter volume(ml)	525.68±39.46	526.02±48.38	NS
CSF volume(ml)	227.69±22.82	212.68±24.09	<0.05
Total intracranial volume(ml)	1413.94±78.41	1401.67±91.04	NS
NS=not significant; BMI=body mass index;			
CSES=the Core Self-Evaluation Scale; RSES=the Rosenberg Self-Esteem Scale			
^a at the time of scanning			

Table 2 Regional GMV changes in patients with BN compared to healthy controls

Regions	Hemisphere	Cluster size (voxels)	Number of voxels within the anatomical region	P-value (FWE cluster- level)	Peak t values	MNI coordinates (x,y,z)
BN<HC						
Cluster 1		1704		<0.001	-5.73	-1.5,52.5,7.5
Frontal_Sup_Medial_L	Left		855			
Cluster 2		767		<0.001	-4.57	52.5,-33,18
Temporal_Sup_R	Right		347			
Cluster 3		876		<0.001	-4.85	-1.5,1.5,42
Cingulum_Mid_R	Right		364			
Cluster 4		1042				
Cingulum_Mid_L	Left		512	<0.001	-4.42	-6,-42,46.5
Cluster 5		705				
Frontal_Sup_L	Left		366	<0.001	-4.69	-24,18,55.5

Figures

Figure 1

Regional grey matter volume alterations in BN (n=34) relative to HC (n=40). The statistical brain maps showed regional GMV decrease in BN, including the SFGmed.L, the STG.R, DCG.L, DCG.R and SFGdor.L ($P < 0.001$, corrected at cluster level). The color bar represents the t-scores.

Figure 2

Correlation of regional grey matter volume with age in BN patients.

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