Systematic Review

Zhenzhen Pan[1]
Hongyang Qi[1]
Jie Zhou[1]
Yuhua Xu[1,*]

Comparison of Brain Function and Structure in Patients with Major Depression: A Systematic Review and Meta-Analysis of MRI-Based Data

[1]Department of Radiological, Shaoxing Seventh People's Hospital, 312000 Shaoxing, Zhejiang, China

Abstract

Background: Depression is a common mental illness worldwide. Neuroimaging techniques, such as magnetic resonance imaging and functional magnetic resonance imaging, play an essential role in diagnosing and evaluating depression. This study is based on magnetic resonance imaging (MRI)-related research to explore the comparison of brain function and structure between patients with severe depression and normal individuals, and to conduct meta-analysis.

Methods: We conducted searches in various databases such as PubMed, Web of Science, Embase, and Cochrane Library to obtain research data on comparing brain function and structure between patients with severe depression and healthy individuals. The search keywords included "Major Depressive Disorder", "Brain Function", "Brain Structure", "Depression", "MRI", and "Magnetic Resonance". The quality assessment was conducted using the bias risk assessment tool recommended by the Cochrane Collaborative Network. Literature was screened following the predetermined inclusion and exclusion criteria, and Anisotropic Effect-Size Seed-Based Differential Mapping (AES-SDM) was used for systematic meta-analysis. Regression analysis was performed on age, gender, disease duration, years of education, and treatment status.

Results: After a thorough screening process, 10 documents were selected for subsequent analysis. These studies consisted of 477 study subjects, including 231 depression patients and 246 healthy individuals. The proportion of women was 36%–75%, and the disease duration was 3–60 months. The patients in 4 documents had first attacks, and the patients in the other 6 documents had multiple attacks. The baseline conditions of the 10 included documents were consistent and comparable. None of the studies reported blinding methods, and none of the results had incomplete data. The Regional homogeneity (ReHo) levels in the left precuneus (BA7), lentiform nucleus (BA48), and left prefrontal lobe (BA32) were significantly increased in the depression group, with voxel numbers of 358, 116, and 181, respectively. Conversely, the left postcentral gyrus (BA4), left cerebellar area (hemispheric lobule I, IV/V, lingual gyrus, fusiform gyrus), left fusiform gyrus (BA30), and right cingulate gyrus (BA23) were significantly reduced, with voxel numbers of 17, 50, and 124, respectively. Furthermore, regression analysis showed that gender, age, disease duration, years of education, and disease severity were potential influencing factors, and the disease duration demonstrated the most significant impact on the left cingulate gyrus (SDM = 2.777).

Conclusion: There are significant differences in brain function and structure between patients with major depression and healthy individuals. Furthermore, our findings reveal a substantial correlation between the severity of depressive symptoms and brain function and structure indicators. These findings provide novel research directions and ideas for the diagnosis and treatment of depression.

Keywords

major depression; brain function; brain structure; MRI; meta-analysis

Introduction

Depression is a prevalent mental illness globally. The number of patients increased from 172 million in 1990 to 258 million in 2017, representing a 49.86% rise [1]. The

*Corresponding author details: Yuhua Xu, Department of Radiological, Shaoxing Seventh People's Hospital, 312000 Shaoxing, Zhejiang, China. Email: 17815756028@163.com

primary symptoms include persistent low spirits, loss of interest, and lack of energy, with severe cases leading to suicidal thoughts [2]. According to the World Health Organization, the incidence of depression is steadily rising each year and is projected to become the leading cause of disease burden globally by 2030 [3]. Depression severely affects the quality of life and increases the risk of suicide, causing significant distress to their families and society [4]. Despite considerable progress in depression research, the etiology and pathogenesis remain unclear, diagnosis and assessment methods need improvement, and current treatment strategies still face many challenges [5].

However, the causes of depression are not yet fully understood, but current research suggests that a combination of biological, psychological, social, and other factors influences this disorder. Biological factors include genetics, neurotransmitters, and neuroendocrine disorders. Psychological factors include coping styles, personality traits, and psychological well-being. The social factors involve family environment, social support, and life stress. The pathogenesis of depression is complex, involving numerous factors, such as neuroplasticity, neural network abnormalities, and inflammatory responses. Depression can be classified into mild, moderate, and severe levels based on the severity of the condition [6].

The diagnosis of depression mainly relies on clinical symptoms, medical history, and psychological assessment results. Commonly used psychological assessment tools include the Self-Rating Depression Scale (PHQ-9) and the Hamilton Depression Rating Scale (HAM-D) [7]. However, the diagnosis of depression remains somewhat subjective and requires a combination of multiple assessment methods, such as symptom assessment, functional assessment, and quality of life assessment. Additionally, neuroimaging techniques such as magnetic resonance imaging (MRI) and functional magnetic resonance imaging (fMRI) are crucial in diagnosing and evaluating depression. In recent years, numerous studies have indicated that individuals with major depression exhibit substantial differences in brain function and structure compared to healthy people [8,9]. Patients with severe depression exhibit various brain function abnormalities, such as impaired emotional regulation and cognitive control. For instance, when processing negative emotional information, their brains display reduced activation in relevant areas. Additionally, their brain structure shows specific changes, including reduced gray matter volume and damage to white matter fiber tracts. These abnormalities can potentially impair psychological and physiological functions [10,11].

Table 1. A list of English abbreviations used in the manuscript.

Full English name	English abbreviation
Self-Rating Depression Scale	PHQ-9
Hamilton Depression Rating Scale	HAM-D
Magnetic resonance imaging	MRI
Functional magnetic resonance imaging	fMRI
Regional homogeneity	ReHo
Standardized mean difference	SMD
Confidence interval	CI
Odds ratio	OR
Electroencephalography	EEG
Computed tomography	CT
Kendall consistency coefficient	KCC

The purpose of this study is to conduct a comprehensive meta-analysis to systematically explore the differences in brain function and structure between patients with severe depression and healthy individuals. The objective is to establish a new theoretical foundation for the diagnosis, treatment, and prevention of depression, ultimately contributing to a better understanding of the underlying pathophysiological mechanisms of the disease. These outcomes will offer clinicians more precise diagnostic and treatment strategies and serve as a reference for assessing the recovery and prognosis assessment of patients with depression. Furthermore, this study may inspire further investigations in neuropsychology, fostering academic exchanges and advancements in related fields.

Treatments and Methods

Our study adhered to the PRISMA 2020 guidelines. The detailed C-PRISMA 2020 checklist can be found in **Supplementary File 1**.

Literature Retrieval Strategy

This study employed a systematic literature retrieval strategy to obtain data on brain function and structure in patients with major depression compared to healthy individuals. We performed searches in various databases, both domestically and internationally, such as PubMed, Web of Science, Embase, and Cochrane Library. The English keywords utilized were “Major Depressive Disorder”, “Brain Function”, “Brain Structure”, “Depression”, “MRI”, and “Magnetic Resonance”. The search period was extended from the establishment of each database to 2023. The abbreviations used in the article are listed in Table 1.

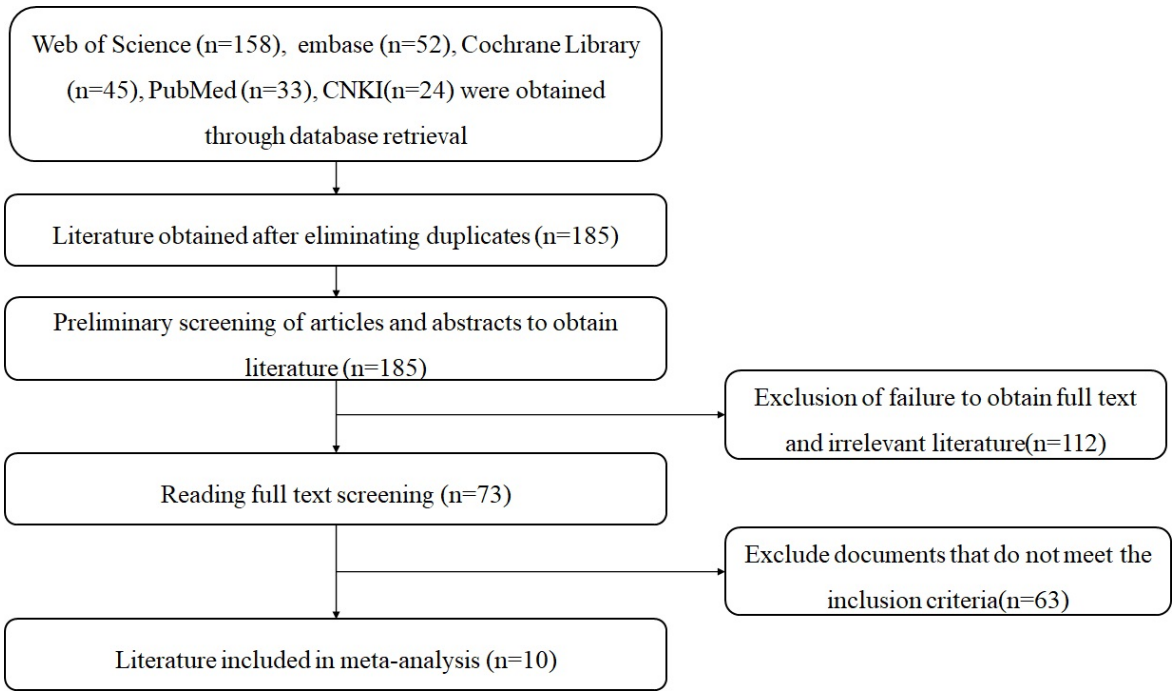

Fig. 1. Literature retrieval strategy.

Inclusion and Exclusion Criteria

This study included research manuscripts that investigated patients with severe depression and healthy individuals. Furthermore, we focused on comparing indicators of brain function and brain structure between these cases and controls. The manuscripts published in either Chinese or English languages were included.

However, duplicate publications or documents with incomplete data, those investigating study subjects with other mental or neurological diseases, reviews, case reports, and conference papers were excluded.

Data Extraction and Quality Assessment

Two experimenters used a double-blind method to perform Anisotropic Effect-Size Seed-Based Differential Mapping (AES-SDM) process operations, which included coordinate preprocessing, mean analysis, threshold test, and meta-regression. The data were extracted from the peak coordinates and T-values of activation points in each study. A permutation test for mean analysis ($p < 0.05$, voxel from k = 10) was used to measure the validity of the observed values. Furthermore, meta-regression was weighted based on the square root of the sample size, and AES-SDM utilized a Monte Carlo random algorithm to select regression variables for predicting SDM values [12,13]. Regression analysis, single or multiple, was performed, and subgroup analysis was conducted by controlling related variables. The threshold test ($p < 0.005$) was used to minimize false results. The heterogeneity of each study voxel bundle was determined utilizing Q-statistics (chi-square distribution converted to Z-value, permutation test with $p < 0.05$, k = 10) and Gaussian random field ($p < 0.001$) random effects model.

Data Analysis

Meta-analysis was conducted using RevMan 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark). For continuous variables, the effect size was expressed by the standardized mean difference (SMD) with a 95% confidence interval (CI). Categorical variables were represented using the odds ratio (OR) with a 95% CI. Heterogeneity between studies was evaluated using the Q test and I^2 statistic. If the heterogeneity was low ($I^2 \leq 50\%$), a fixed effects model was employed to merge the results. However, the random effects model was utilized if the heterogeneity was high ($I^2 > 50\%$). Sensitivity analysis was conducted using the literature elimination method one by one. Publication bias was assessed using Begg's test and Egger's test. All statistical analyses were two-sided, with $p \leq 0.05$ considered statistically significant.

Table 2. Characteristics of the selected manuscripts.

Author	Depression group	Control group	Age of onset (SD)	Female proportion (%)	Disease duration in months (SD)	Disease onset	Hamilton Depression Rating Scale 24 items (points)
Wu 2011 [14]	22	26	35 (13)	55	32 (64)	Multiple attacks	30
Yao 2009 [15]	22	22	38.2 (10.2)	55	60 (54)	Multiple attacks	48.86
Huang 2014 [16]	23	20	27.7 (10.9)	70	NA	Multiple attacks	28.7
Xue 2016 [17]	31	31	33.8 (9.2)	58	34.1 (46.8)	Multiple attacks	30.8
Yang 2015 [18]	50	50	31.12 (9.5)	62	9.84 (12.59)	First attack	30
Späti 2015 [19]	21	35	36.6 (12.3)	48	16.6 (2.8)	Multiple attacks	NA
Liang 2013 [20]	16	16	36.06 (9.43)	50	28.3 (22.68)	Multiple attacks	35.18
Liu 2010 [21]	16	16	30.38 (12.6)	75	12.1 (NA)	First attack	NA
Peng 2011 [22]	16	16	34.1 (9.2)	63	3.1 (0.7)	First attack	31.71
Wang 2014 [23]	14	14	32.93 (13.87)	36	6.12 (5.82)	First attack	35

Note: SD is the average value, NA is unclear.

Results

Literature Screening

Using PubMed, Web of Science, Embase, and Cochrane Library databases, we retrieved 312 documents. After excluding 127 duplicate documents, the remaining 185 were included in the subsequent analysis. After conducting an initial screening based on the title and abstract, a total of 112 documents that were either unavailable or irrelevant to the study were excluded. This led to a final selection of 73 relevant documents. After applying further exclusion criteria, only 10 documents were finally included in the analysis. The entire literature retrieval strategy is presented in Fig. 1.

Literature Characteristics

Literature retrieval and screening led to the selection of 10 documents, resulting in a final sample size of 477 study subjects. This included 231 patients in the depression group and 246 healthy individuals in the control group. The proportion of women in the included studies ranged from 36% to 75%. The duration of the disease varied from 3 to 60 months. Among the selected documents, 4 reported patients with first attack, while 6 reported patients with multiple attacks (Table 2, Ref. [14–23]).

Quality Evaluation of Included Studies

The baseline characteristics of the 10 included studies were consistent and comparable. Furthermore, none of the studies reported blinding methods, and none of the results had incomplete data (Table 3, Ref. [14–23]).

Meta-Analysis Results

ReHo Analysis of the Depression and Control Groups

In the depression group, the Regional homogeneity (ReHo) levels were significantly increased in the left precuneus (BA7), lentiform nucleus (BA48), and left prefrontal lobe (BA32), with voxel numbers of 358, 116, and 181, respectively. In contrast, the levels were substantially reduced in the left postcentral gyrus (BA4), left cerebellar area (hemispheric lobule I, IV/V, lingual gyrus, fusiform gyrus), left fusiform gyrus (BA30), and right cingulate gyrus (BA23), with voxel numbers of 17, 50, and 124, respectively (Table 4).

Meta-Regression Results

Gender, age, duration of disease, years of education, and disease severity are all influencing factors. Gender was found to exert significant effect on ReHo changes in the left postcentral gyrus and right anterior cingulate gyrus. Similarly, age substantially impacted ReHo in the left fusiform gyrus, lingual gyrus, and left putamen. Furthermore, the duration of the disease significantly affected ReHo in the left anterior cingulate gyrus and left cerebellar region (hemispheric lobule IV/V). Disease severity considerably influenced ReHo in the right anterior cuneate lobe, left inferior parietal lobe, right temporal gyrus, right middle frontal gyrus, and frontal box. Among these factors, the

Table 3. Quality evaluation of 10 included studies.

Included studies	Baseline situation	Stochastic method evaluation	Blinded evaluation	Result data is incomplete	Optional reporting of results	Other biases
Wu 2011 [14]	Consistent	Not sure	Not mentioned	Low risk	Not sure	Not sure
Yao 2009 [15]	Consistent	Low risk	Not mentioned	Low risk	low risk	Not sure
Huang 2014 [16]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Low risk
Xue 2016 [17]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Not sure
Yang 2015 [18]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Not sure
Späti 2015[19]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Not sure
Liang 2013 [20]	Consistent	Not sure	Not mentioned	Low risk	Low risk	Low risk
Liu 2010 [21]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Not sure
Peng 2011 [22]	Consistent	Not sure	Not mentioned	Low risk	Low risk	Not sure
Wang 2014 [23]	Consistent	Low risk	Not mentioned	Low risk	Low risk	Low risk

Table 4. ReHo analysis of the depression and control groups.

Brain area		MNI coordinates	SDM analysis Z value	*p* value	Voxel partition (voxel number)			Sensitivity analysis	Heterogeneity test	ReHo subgroup analysis
Increased ReHo value	Left precuneus	–4, –64, –52	1.904	0.000069022	BA7 (358)	BA7 (111)	BA5 (92)	25/25	None	Therapy group
	Multiple attacks of left lentiform nucleus	–24, –6, –6	1.694	0.000365325	BA48 (116)	BA34 (20)	BA48 (14)		Have	Untreated first episode
					BA35 (13)	BA36 (13)				
Left frontal gyrus		0, 34, 32	1.563	0.000543416	BA32 (181)	BA32 (100)	BA24 (53)	24/25	None	Treat multiple attacks
					BA32 (43)	BA32 (32)	BA8 (21)			
					BA9 (21)	BA24 (18)	BA4 (17)			
ReHo value decreases	Left postcentral gyrus	–18, –18, 46	–2.146	0.00001265	BA4 (296)	BA3 (253)	BA 6 (149)	25/25	None	Multiple untreated attacks
					BA3 (105)	BA6 (84)	BA2 (51)			
					BA43 (47)	BA4 (46)	BA3 (37)			
					BA2 (22)	BA48 (21)				
Left cerebellar area		–36, –76, –20	–2.027	0.000037670	BA19 (227)	BA19 (181)	BA19 (130)	24/25	Have	Untreated first episode
					BA19 (71)	BA18 (41)	BA19 (35)			
					BA18 (28)	BA18 (24)	BA 18 (17)			
Left fusiform gyrus		–18, –44, –12	–1.557	0.000796080	BA30 (50)	BA37 (33)	BA37 (25)	24/25	Have	Untreated first episode
					BA30 (21)	BA30 (16)	BA37 (16)			
Right cingulate gyrus		6, –20, 30	–1.469	0.001337469	BA23 (124)	BA30 (16)	BA37 (16)	20/25	Have	Therapy group

Note: MNI, Montreal Neurological Institute; AES-SDM, Anisotropic Effect-Size Seed-Based Differential Mapping; ReHo, Regional homogeneity.

Table 5. Meta-regression analysis of factors influencing ReHo changes in depression group.

	MNI coordinates	SDM analysis Z value	*p* value	Voxel number	Center voxel brudmann partition
Gender effect					
Left precentral gyrus	–48, 4, 20	1.780	0.00023246	119	BA6, BA44, BA48
Left medial cingulum/paracingulate gyrus	–4, –46, 40	–2.038	0.000365674	369	BA23, Left precuneus
Right anterior cingulum/lateral cingulum	4, 42, 22	–1.807	0.001116693	157	BA32, BA24
Age effect					
Left lingual/fusiform gyrus	–22, –44, –10	2.368	0.000023663	316	BA37, cerebellum lobule IV/V, BA30, BA19, BA18
Left lentiform nucleus, putamen	–28, 0, –6	–2.260	0.000008881	210	BA48, BA34
Disease duration					
Left anterior cingulum/lateral cingulum	–6, 46, 12	2.777	0.000060201	209	BA32, BA40, BA23
Left cerebellar hemisphere lobule VI	–34, –76, –22	–2.602	0.000063062	137	BA18, BA19
Years of education					
Left anterior cingulum/lateral cingulum	0, 36, 26	2.129	0.001907647	172	BA24, BA32
Left/right precuneus	4, –70, 44	–1.476	0.000451982	242	BA7
Severity of disease (HAM-D)					
Increased ReHo					
Right precuneus	2, –66, 42	1.629	0.000472963	267	BA7, BA18, BA19
Left inferior parietal gyrus	–30, –42, 48	1.983	0.000080585	132	BA40, BA3
ReHo decreases					
Right superior temporal gyrus	64, –24, 6	–1.420	0.001457393	346	BA48, BA22, BA21
Right middle frontal gyrus, box part	26, 60, –12	–1.543	0.000885069	185	BA11, BA47

Note: MNI, Montreal Neurological Institute; SDM, Seed-Based Differential Mapping.

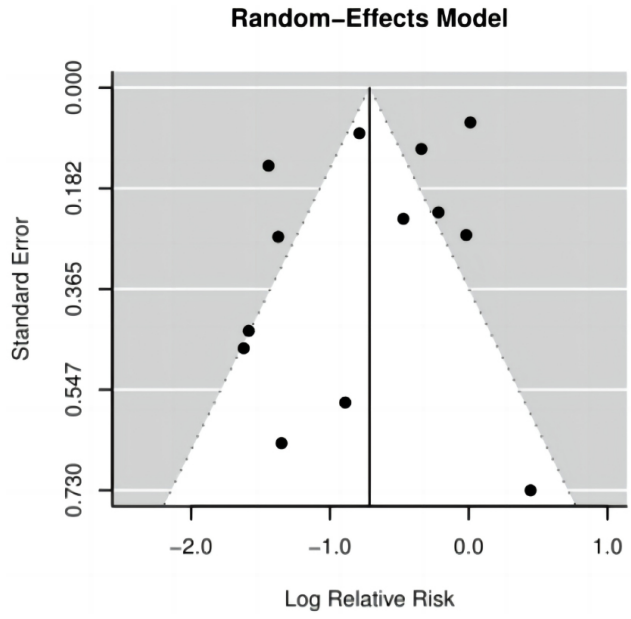

Fig. 2. Funnel chart of the bias analysis.

disease duration indicated the most significant impact on the left cingulate gyrus (SDM = 2.777). Meta-regression analysis is shown in Table 5.

Bias Analysis

The points in the funnel plot represent the studies included in this analysis. The horizontal axis represents the OR value, while the vertical axis shows the standard error of the logarithm of the effect size. The larger the sample size, the smaller the error, the smaller the standard error, and the higher the distribution. The vertical line in the middle represents the merged OR values. Ideally, with no bias, each study is evenly distributed on both sides of the vertical line, forming an inverted funnel shape. This funnel plot was used to evaluate the publication bias, and the results indicated no bias in this study (Fig. 2).

Discussion

Depression is a common mental disease that causes significant distress to patients and their families. Those with severe depression experience more intense mental symptoms, often resulting in reduced quality of life and impaired psychological functioning. With the development in neuroscience, researchers have increasingly focused on the abnormalities in brain function and structure associated with depression [24]. In recent years, advancements in neuroimaging technology have extended the range of re-

search methods for exploring brain function and structure. Common brain function testing methods include fMRI and electroencephalography (EEG). However, brain structure is commonly assessed using MRI and computed tomography (CT) techniques. Numerous studies have shown that patients with depression exhibit abnormalities in brain function and structure [25–27]. For example, depression patients exhibit changes in functional and structural connectivity in areas such as the prefrontal lobe, amygdala, and hippocampus. Additionally, the brain network topology depression patients show abnormalities, such as reduced global efficiency and enhanced local modularity. Comparative research on brain function and structure in patients with severe depression can help reveal the pathogenesis of the disease and provide new ideas for clinical diagnosis, treatment, and prevention [28]. This article seeks to explore the alterations in brain function and structure in patients with major depression and analyze their relationship with the onset, severity, and treatment effects of depression.

Abnormal connections in the precuneus network may lead to the clinical manifestations of depression. The prefrontal cortex is widely recognized as an essential brain region involved in depression. ReHo is an analytical method based on rs-fMRI that measures spontaneous brain functional activity by examining the consistency of time series between target voxels and their nearest neighbor voxels using the Kendall consistency coefficient (KCC). ReHo reflects local characteristics of spontaneous brain functional activity, with any abnormal decrease or increase in its value indicating changes in the synchronization or coordination of local brain functional activity. Such alterations may be a primary underlying cause of cognitive dysfunction in patients. Due to cognitive impairment in patients with severe depression, it is speculated that changes in ReHo may occur and could be related to the patient's cognitive function [29]. Our finding indicates abnormalities and a lack of heterogeneity in the ReHo of the left prefrontal gyrus. Previous research has shown that the prefrontal limbic system plays a crucial role in regulating depression, with its dysfunction closely associated with the development of this disorder [30]. In this regulatory network, the anterior cingulate gyrus, amygdala, and hippocampus are particularly crucial, with meta-analysis revealing abnormal ReHo in the amygdala and hippocampus. Functional connectivity studies have indicated that individuals with depression exhibit reduced activity in the dorsolateral, dorsomedial prefrontal cortex, and dorsal anterior cingulate gyrus. Conversely, they display increased activity in the ventrolateral prefrontal cortex, subgenual cingulate gyrus, and amygdala. Depression patients often experience cognitive dysfunction, such as executive deficits and emotional instability. Furthermore, it has been observed that depressed patients have smaller prefrontal cortex, amygdala, and hippocampus compared to healthy individuals. This finding suggests a potential connection to the pathogenesis of depression. Structural changes in these brain areas may affect mood regulation and cognitive functions in patients. Additionally, patients with depression have thinner left temporal cortex and right parietal cortex compared to healthy individuals, which may be related to impairments in social interaction, language, and memory. Further analysis has revealed a significant correlation between the severity of depression and both brain functional and structural indicators [31]. As depression worsens, the functional and structural abnormalities in the prefrontal cortex, amygdala, and hippocampus become more apparent. Furthermore, there is a negative correlation between the thickness of the left temporal cortex and right parietal cortex and the severity of depression [32]. These findings suggest that the abnormalities in brain function and structural indicators can be crucial for assessing the severity of depression. Furthermore, they provide valuable insights for clinical diagnosis and treatment decisions.

A previous study has reported reduced functional connections between the anterior cingulate gyrus and the amygdala, globus pallidus, striatum, and medial thalamus in patients with depression [33]. A meta-analysis demonstrated that individuals with depression exhibit significant reductions in the volume of the frontal lobes, especially the anterior cingulate and orbital cortex [34]. We observed that both regions of the anterior cingulate were significantly affected. Additionally, volume reductions were observed in the hippocampus, putamen, and caudal nucleolus, which were also abnormal in the AES-SDM meta-analysis. These findings support each other, indicating a close association between abnormalities in these regions and depression. ReHo abnormalities were identified in various brain regions, including the lentiform nucleus, postcentral gyrus of the somatosensory center, fusiform gyrus, and cerebellar regions (hemispheric lobules I, IV/V, lingual gyrus, fusiform gyrus). Recent research has demonstrated that the cerebellum plays a role in voluntary movements, language processing, learning, and related emotional experiences, aligning with the results from meta-analysis [35]. Furthermore, subgroup analysis revealed abnormal ReHo in the left precuneus, left prefrontal lobe, and cingulate gyrus in the treatment group. In patients experiencing their first attack, abnormal ReHo was found in the left putamen, left cerebellar region, and left fusiform gyrus. A possible mechanism is that the response to antidepressant drug treatment is associated with increased connectivity between frontal and limbic brain regions.

Brain functional and structural indicators have considerable value in the diagnosis and treatment of depression. Firstly, these indicators can help improve the diagnostic accuracy of depression. By testing the brain function and structure of patients with depression, we can find the differences between patients with depression and healthy people. This assessment provides an objective basis for clinical diagnosis. Secondly, these indicators are crucial to evaluate the severity of depression. Research has revealed a positive correlation between the severity of depression and abnormalities in brain function and structure in patients [36]. Monitoring these indicators can assist in assessing the patient's condition and treatment outcomes. Moreover, brain function and structural indicators offer new targets for depression treatment. By understanding the mechanisms underlying abnormal brain function and structure, researchers can develop new treatments and medications targeting these specific areas, thereby enhancing the efficiency of depression therapy. For example, for neurotransmitter disorders, drugs such as selective 5-HT reuptake inhibitors (SSRIs) can be developed; for neuroendocrine disorders, anti-inflammatory and antioxidant treatment strategies can be used; and for reduced neuroplasticity, cognitive-behavioral therapy and other interventions can be used [37].

Through a meta-analysis of brain function and structure in patients with major depression, this study revealed significant differences compared to healthy individuals. These findings provide a basis for further investigation into the pathogenesis and treatment strategies of depression. However, this study still has certain limitations. Firstly, biases may exist due to differences in sample sizes and research methods. Secondly, the study primarily focused on brain function and structure abnormalities in patients with severe depression, and there is insufficient research on those with mild or moderate depression. Finally, the study investigates a limited set of observational indicators, suggesting a need for future studies to explore the role of other brain functions and structural indices in depression. Future research could expand its scope in the following aspects: (1) Increasing sample sizes and exploring brain function and structure across patients with varying severity; (2) Using more precise neuroimaging techniques and biomarkers to delve deeper into the neurobiological mechanisms of depression; (3) Combining genetic, environmental, and behavioral factors to develop personalized treatment plans for depression patients; (4) Conducting multi-center, interdisciplinary clinical research to validate further the diagnostic and therapeutic potential of brain function and structural indicators in depression.

Conclusion

In conclusion, this study reveals significant differences in brain function and structure between patients with major depression and healthy people. It highlights a correlation between the severity of depressive symptoms and brain function and structure indicators. These results provide new research directions and ideas for the diagnosis and treatment of depression. Moreover, specific and technological progress is expected to further enhance our understanding and treatment of depression. Considering the heterogeneity within severe depression, the total sample size of 477 across 10 studies appears relatively small. Future research should aim for more extensive and diverse samples to improve the generalizability of research results. Furthermore, future studies could investigate how different treatment methods impact observed changes in brain function and structure among patients with severe depression.

Availability of Data and Materials

The datasets used and/or analyzed during the current study were available from the corresponding author on reasonable request.

Author Contributions

ZZP and HYQ designed the study; all authors conducted the study; JZ and YHX collected and analyzed the data. ZZP and HYQ participated in drafting the manuscript, and all authors contributed to critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, take public responsibility for appropriate portions of the content, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62641/aep.v52i4.1636.

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