

Analysis on International Scientific Collaboration and Research Focus on Depression Field

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Depression is one of the most prevalent psychiatric diseases and significantly negatively impacts patients' productivity, quality of life, and cognitive functions.^[1] According to a recent survey by the World Health Organization, it has been estimated that depression currently ranks the third in terms of disability-adjusted life years and will be the leading cause of disease and injury burden by 2030, surpassing cancer as well as cardiovascular and respiratory disease.^[2] This troubling situation, which has raised concern among the international field of psychiatry, challenges researchers worldwide to investigate the prevention and control of depression and identify the necessary funding to support this research. Given the expansive and interdisciplinary nature of biomedicine, no single researcher or institution can stay current on all developments within depression research. Thus, scientific collaboration becomes indispensable to make progress in biomedicine as it strengthens communication, encourages competency sharing, and facilitates the discovery of new scientific knowledge. Despite this fact, there have been few scientific publications to date regarding collaborative research within the field studying depression. Therefore, this article aimed to measure scientific collaborations at three levels – authors, institutions, and countries. By examining scientific collaboration, this article also identified hot topics in depression research, which represent the areas of focus that numerous researchers have decided to have substantial potential to prevent and cure this pervasive disease.

The data used in this article were retrieved from the Science Citation Index Expanded (SCI-Expanded) in the Web of Science. We searched for all types of documents (including articles, reviews, meeting abstracts, and papers) that contain the word “depression” in the title, abstract, or keywords, from

January 1, 2003 to December 31, 2012. We retrieved a total of 127,676 records with their titles, abstracts, author names, institutions, sources, and keywords. These records included 254,809 authors, 43,906 institutions, and 176 countries. Papers co-authored by authors from more than one institution were classified as “inter-institutional collaborations” and papers co-authored by authors from more than one country were classified as “international collaborations.”

In this article, social network analysis (SNA) was used to identify the connections and illuminate the structure of collaboration among authors, institutions, and countries. SNA has been proved useful in studies of scientific collaboration because its objective is to reveal the underlying connections between different social entities, such as people, organizations, and countries.^[3,4] The SNA used in this article was adapted for depression research from the methods of Otte and Rousseau,^[3] White,^[5] and Kretschmer and Aguillo.^[4]

Centrality, which reflects the status and rights of activities in a given social network, is one of the most important content of SNA. There are three commonly used measures of centrality: degree, betweenness, and closeness. In a collaborative network, degree centrality is the number of nodes that are connected to a central node. Thus, it follows that if an entity has a high degree centrality, it is considered the “central entity” within that collaborative network. Betweenness centrality is the number of shortest paths that pass through a given node.^[6] In this article, a high betweenness centrality indicated that an entity possessed and controlled a great deal of research resources. Finally, the closeness centrality of a node was the reciprocal of the total distance from this node to all other nodes. High closeness centrality indicated that a node was very close to other nodes, suggesting that the entity with the lowest closeness centrality was at the core of the entire network. The University of California at Irvine NET work (UCINET) and Netdraw were used to

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identify and visualize authors', institutions', and countries' collaborative network structures.^[7,8] CiteSpace, invented by Dr. Chao-Mei Chen from the School of Information Science and Technology of Drexel University in USA and based on a JAVA application, was used to analyze the research focus in this field. In CiteSpace, the nodes and lines in the network are generated automatically.^[9] Nodes of different sizes and colors, which construct the whole network represent different cited articles. Citation tree-rings represent the citation history of an article. The color of a citation ring denotes the time of corresponding citation, while the thickness is proportional to the number of citation in a given time slicing.^[10] The purple ring represents the key document that resulted in an important theory and a new concept.

ANALYSIS OF COLLABORATION AMONG AUTHORS

Publications represent achievements in scientific research while co-authorship reflects collaboration. Smith, who studied the increase of co-authorship of papers, viewed co-authorship as an important scientometric indicator of collaborative research among authors.^[11]

Of the 127,676 articles about depression retrieved from SCI-Expanded that date from 2003 to 2012, 115,257 were multi-authored papers. Co-authorship increased from 6880 articles in 2003 to 15,648 in 2012; the percentage of all papers that were co-authored rose from 81.1% to 93.3% over the last 10 years [Table 1].

To identify the main co-authorship structure of the network, we selected the 50 most prolific authors between 2003 and 2012. This criterion resulted in authors who co-authored at least 111 publications from 2003 to 2012 [Figure 1]. A co-authorship map made up of these 50 authors, illustrated the structure of authors' collaborative network. The line value and the distance between two vertices represented the collaborative strength, while thickness of the line was correlated with the quantity of co-authorship papers. The authors who were in the top 10 of centrality were mostly American demonstrated that they, with access to a significant portion of research resources, were in a position to shape the whole network. In this network, the highest degree centrality was held by Rush A. John, indicating that he

had the most direct collaborators. Fava Maurizio had the highest betweenness centrality, indicating that he possessed and controlled a great deal of research resources. Dr. Fava also had the lowest closeness centrality, indicating that he occupied a core position in this network. Sheng-Yu Lee from Taiwan, China has the second highest betweenness centrality, but his degree and closeness centrality are not among the top 10. This pattern indicated that Sheng-Yu Lee played an important bridging role, but lacked extensive and direct communication with other authors. It also suggested that in the future, he should collaborate with others, especially the core authors, directly. For Demyttenaere, Koen from Belgium, his closeness centrality was the tenth highest, but his degree and betweenness centrality were not in the top 10. This showed that Demyttenaere Koen was closely connected with the core authors. In the future, he should intensify his collaborations in the network.

ANALYSIS OF INSTITUTIONAL COLLABORATION

From 2003 to 2012, there were 90,667 papers that involved inter-institution collaboration. The number of inter-institution papers increased from 5371 in 2003 to 122,990 in 2012. These papers included 43,906 institutions that appeared 351,245 different times. The number of collaborating institutions grew significantly in 2007 and 2011, aligning with the years in which there were significant increases in publications in the field [Table 2]. This suggested that the scale of collaboration is positively correlated to the output of scientific research.

We selected the 30 institutions that appeared most frequently, each of which had more than 879 appearances, to form a map illustrating the structure of collaboration in the network of institutions involved in depression research from 2003 to 2012 [Figure 2]. As in the co-author map, the distance and thickness of the line between two nodes represented their collaborative strength and the number of collaborative papers, respectively. The institutions with the top 10 centrality were mostly USA-affiliated, suggesting that US institutions researching depression occupied a core position in the whole network. The analysis of centrality revealed that Harvard University has the highest degree and betweenness centrality

Year	Total papers (n)	Co-authored papers (n)	Percentage of co-authorship
2003	8483	6880	81.1
2004	9920	8779	88.5
2005	10,294	9203	89.4
2006	11,393	10,163	89.2
2007	12,336	11,065	89.7
2008	13,603	12,311	90.5
2009	14,190	12,913	91.0
2010	14,993	13,764	91.8
2011	15,692	14,531	92.6
2012	16,772	15,648	93.3

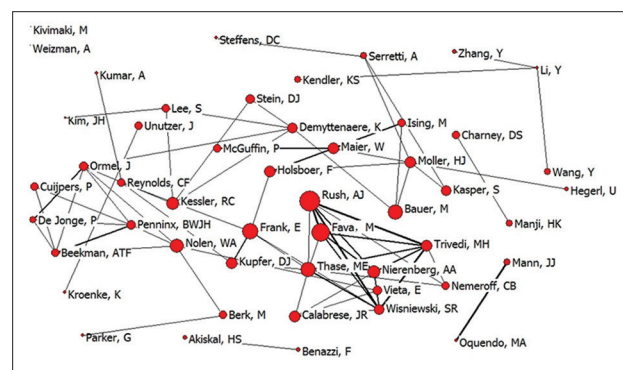


Figure 1: The structure map of the collaboration network among authors on depression research.

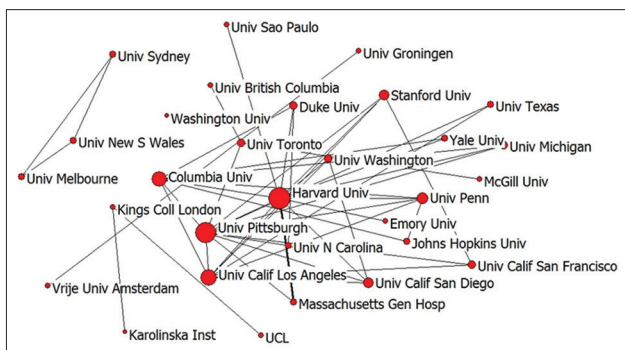


Figure 2: The structure map of the institutional collaboration network on depression research.

and the lowest closeness centrality. The betweenness centrality of the University of Toronto in Canada was third highest and the closeness centrality second highest, but its degree centrality did not appear in the top 10. This indicated that the university held an important position in the whole network and played a key communicative role among institutions. It also indicated that the University of Toronto had access to lots of research resources and was closely connected to core institutions, but lacked robust communications with other institutions. Similarly, Kings College London in England had a high betweenness and closeness centrality, indicating that it maintained an important position in the network, but its degree centrality did not make the top 10. These two institutions should establish direct connections with other institutions in the future.

ANALYSIS OF COLLABORATION AMONG COUNTRIES

From 2003 to 2012, a total of 176 countries were represented. The number of papers with international collaborations increased from 5168 in 2003 to 12,750 in 2012 [Figure 3]. The most productive countries were USA, England, and Germany; approximately 53% of all papers in depression research originated in the USA. China was in 10th place, producing 4586 papers [Figure 4].

We chose the 30 most productive countries to construct the collaboration map; each of these 30 countries appeared at least 761 times in the literature. The map [Figure 5] included 30 nodes, and the number of ties represented the collaborative strength among countries. We then selected the 20 nodes with more than 61 ties and included the country name, number of ties, and papers corresponding to these 20 nodes as shown in Table 3. Scientific collaboration was generally positively correlated with the number of papers published. However, some countries, such as France, had many ties but not many papers, while others, such as Brazil, had many papers but few ties. Finally, we found that the three countries that engaged in international collaboration most frequently – USA, England, and Germany – also have the most number of publications. This suggested that to some extent, international scientific collaboration in this field was positively correlated to the degree of productivity. USA held the highest degree of centrality, the highest betweenness

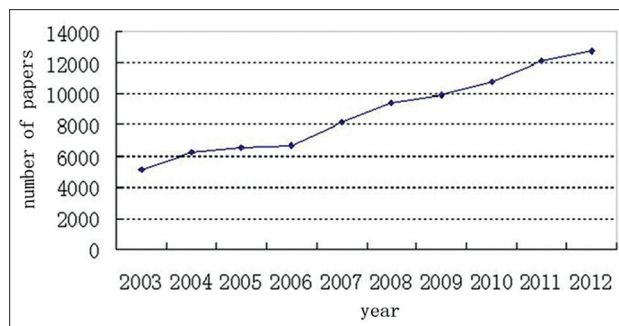


Figure 3: Distribution of papers about countries' collaboration.

Table 2: Annual institutional changes on depression research

Year	Frequency of institutions (n)	Actual institutions (n)	Number of papers (n)
2003	19,425	5155	8483
2004	23,494	5966	9920
2005	24,977	6325	10,294
2006	26,078	6287	11,393
2007	32,266	7938	12,336
2008	37,153	8972	13,603
2009	39,902	9100	14,190
2010	44,172	10,314	14,993
2011	50,387	11,008	15,692
2012	53,391	11,881	16,772

Table 3: The relation between International collaboration and scientific papers

Country	Collaboration		Production	
	Ranks	Ties	Papers	Ranks
USA	1	97	46,668	1
England	2	93	10,785	2
Germany	3	92	10,143	3
France	4	83	4814	9
Australia	5	82	6434	5
Canada	6	80	7914	4
Italy	7	80	5608	6
Spain	8	77	3625	11
Switzerland	9	76	2436	14
Netherlands	10	76	5358	7
Japan	11	72	4958	8
India	12	71	1488	16
Belgium	13	70	1644	15
China	14	69	4586	10
Austria	15	69	1251	18
South Africa	16	69	587	20
Sweden	17	67	2918	13
Scotland	18	67	1420	17
Brazil	19	66	3006	12
Ireland	20	61	1013	19

centrality, and the lowest closeness centrality. Thus, USA was in the center of the international scientific collaboration network in depression research.

ANALYSIS OF RESEARCH FOCUS IN PSYCHIATRY FIELD

In order to detect the research focus in depression field, we used CiteSpace, mapped the hierarchical clustering network of co-cited documents [Figure 6], and gained 27 sub-networks [Table 4]. We selected log-likelihood ratio and extracted the terms to identify each cluster. Using the cluster term and research direction, we identified seven research hotspots. The first research hotspot, diagnosis and assessment, was found in sub-network 0, 2, 3, 8, 9, 12, 13, 14, 15, 16, 19, 20, 25 and 26. Among these, sub-network 13 was the largest. The representative document in this sub-network, "The PHQ-9-Validity of a brief depression severity measure",^[12] was written by Kroenke K *et al.* in 2001. This study suggested that the PHQ-9 was criteria-based diagnoses of depressive disorders and also a reliable and valid measure of depression severity and a useful clinical and research tool. The second research hotspot, behavioral biology, was in sub-network 1, 4, and 5. Among these, sub-network 4 was the largest. The representative document in this sub-network was "Statement

on memories of sexual abuse" written by American Psychiatric Association Board of Trustees in 1994.^[13] The third research hotspot, neurotransmission, was in sub-network 6, 10, 17, and 18. Among these, sub-network 18 was the largest. The representative document in this sub-network, "Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants",^[14] was written by Santarelli *et al.* in 2003. The findings of this study suggested that the behavioral effects of chronic antidepressants may be mediated by stimulation of neurogenesis in the hippocampus. The fourth research hotspot, brain morphology, was in sub-network 7. The representative document, "Mechanisms of migraine aura revealed by functional MRI in human visual cortex",^[15] was written by Hadjikhani *et al.* in 2001. This study suggested that an electrophysiological event such as cortical spreading depression generated the aura in the human visual cortex. The fifth research hotspot, cognitive disorder, was in sub-network 11. The representative document, "Mini-mental

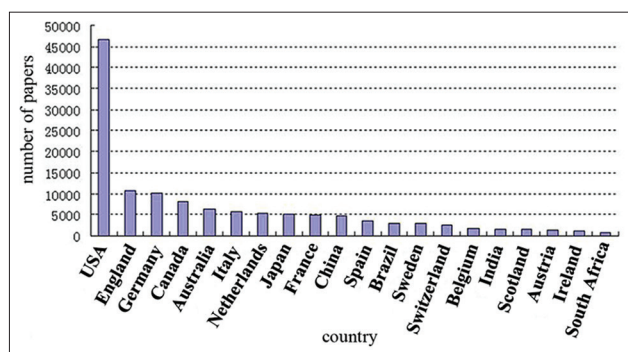


Figure 4: National distributions of papers.

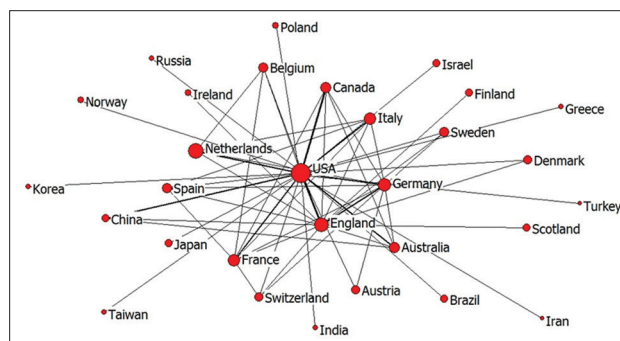


Figure 5: The structure map of the collaboration network among countries on depression research.

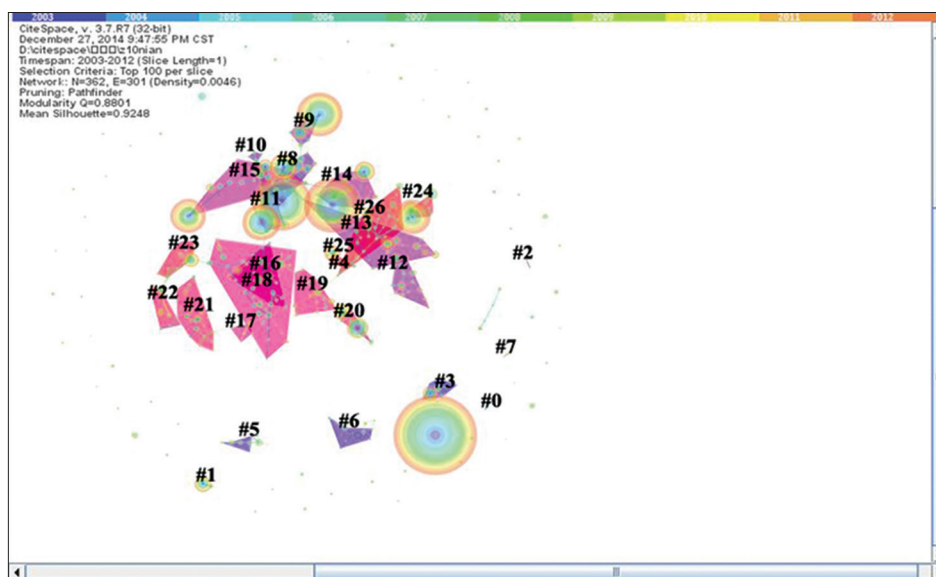


Figure 6: Research focus on depression research. Cluster top terms in each sub-network: #0: Cancer pain inventory; #1: Symptom cluster; #2: Meta-analysis; #3: Omega-3; #4: Subgroup; #5: Inbreeding depression; #6: Downstream regulatory element antagonist modulator; #7: Cortical spreading depression; #8: Antidepressant treatment trial; #9: Ecstasy; #10: Familial risk factor; #11: Cytokine; #12: Arab emirate; #13: Pain; #14: Sleep quality; #15: Medication; #16: Future research; #17: Neurotics; #18: Serum level; #19: Ketamine; #20: Treatment-seeking behavior; #21: Neuropeptide; #22: Negative emotion; #23: Presynaptic serotonin function; #24: Major depression prevalence; #25: Individual patient data; #26: Controlled trial finding.

Table 4: Information of clustering sub-network (2003-2012)

Sub-network	Number of documents	Reprehensive documents	Cluster top term	Research focus
0	2	The pain catastrophizing scale: development and validation	Cancer pain inventory	Diagnosis and assessment
1	1	Olor vision deficits in Alzheimer's disease	Symptom cluster	Behavioral biology
2	2	The Cochrane collaboration's tool for assessing risk of bias in randomized trials	Meta-analysis	Diagnosis and assessment
3	8	Detection of postnatal depression-development of the 10-item Edinburgh postnatal depression scale	Omega-3	Diagnosis and assessment
4	73	Statement on memories of sexual abuse	Subgroup	Behavioral biology
5	9	Inbreeding depression and its evolutionary consequences	Inbreeding depression	Behavioral biology
6	12	A synaptic model of memory-long-term potentiation in the hippocampus	Downstream regulatory element antagonist modulator	Neurotransmission
7	2	Mechanisms of migraine aura revealed by functional MRI in human visual cortex	Cortical spreading depression	Brain morphology
8	11	A rating scale for depression	Antidepressant treatment trial	Diagnosis and assessment
9	8	An inventory for measuring depression	Ecstasy	Diagnosis and assessment
10	4	Parkinsonism-onset progression and mortality	Familial risk factor	Neurotransmission
11	12	Mini-mental state-practical method for grading the cognitive state of patients for clinician	Cytokine	Cognitive disorder
12	14	Validation and utility of a self-report version of PRIME-MD-The PHQ primary care study	Arab emirate	Diagnosis and assessment
13	22	The PHQ-9-validity of a brief depression severity measure	Pain	Diagnosis and assessment
14	16	The hospital anxiety and depression scale	Sleep quality	Diagnosis and assessment
15	15	The center for epidemiologic studies depression scale a self-report depression scale for research in the general population	Medication	Diagnosis and assessment
16	13	Comparison of beck depression inventories IA and-II in psychiatric outpatients	Future research	Diagnosis and assessment
17	5	Deep brain stimulation for treatment-resistant depression	Neuroethic	Neurotransmission
18	37	Requirement of hippocampal neurogenesis for the behavioral effects of antidepressants	Serum level	Neurotransmission
19	15	Evaluation of outcomes with citapram for depression using measurement-based care in STAR*D: Implications for clinical practice	Ketamine	Diagnosis and assessment
20	7	Lifetime and 12-month prevalence of DSM-III-R psychiatric-disorders in the united – states-results from the national comorbidity-survey	Treatment-seeking behavior	Diagnosis and assessment
21	21	Deoression-new animal-model sensitive to antidepressant treatments	Neuropeptide	Treatment
22	9	Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region	Negative emotion	Molecular genetics
23	12	Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene	Presynaptic serotonin function	Molecular genetics
24	9	Practice guideline for the treatment of patients with major depressive disorder (revision)	Major depression prevalence	Treatment
25	5	The MINI: The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10	Individual patient data	Diagnosis and assessment
26	17	The Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II).2.multisite test-retest reliability study	Controlled trial finding	Diagnosis and assessment

MRI: Magnetic resonance imaging; PHQ: Patient Health Questionnaire; DSM: Diagnostic and Statistical Manual of Mental Disorders; MINI: Mini- International neuropsychiatric interview; ICD: International Classification of Diseases; SCID-II: Structured Clinical Interview for DSM-R Personality Disorders.

state. A practical method for grading the cognitive state of patients for clinician",^[16] was written by Folstein *et al.* in 1975. The sixth research hotspot, treatment, was in sub-network 21 and 24. Between these two, sub-network 21 was larger. The representative document in this sub-network, "Depression: A new animal-model sensitive to antidepressant treatments",^[17] was written by Porsolt *et al.* in 1977. The seventh research hotspot, molecular genetics, was in sub-network 22 and 23. Between these two, sub-network 23 was larger. The representative document in this sub-network, "Influence of

life stress on depression: Moderation by a polymorphism in the 5-HTT gene",^[18] was written by Caspi *et al.* in 2003. This study provided evidence of a gene-by environment interaction, in which an individual's response to environmental insults was moderated by his or her genetic makeup.

SUMMARY AND FURTHER PERSPECTIVE

With the recent economic developments, increasingly competitive environments, and intensifying social pressures, the number of patients with depression is growing

dramatically. Due to the complexity of this disease and the diversity of the patients that it affects, scientific collaboration plays an indispensable role in understanding and treating depression. Although previous studies have indicated that collaboration on the whole has increased at the levels of authors, institutions, and countries,^[19-21] few studies have investigated whether this held true for depression research. Thus, this article used SNA to construct and analyze the structure of scientific collaboration in depression research at the levels of authors, institutions, and countries from 2003 to 2012. It was found that, as with other fields, collaboration in depression research has increased substantially over this period.

The percentage of author-level collaborative papers increased over time, and reports of achievements in scientific research were consistent with the total output. This suggested that collaboration among authors had driven an increase in research output. The centrality analysis of the collaborative author network identified Rush A. John and Fava Maurizio as the central authors, indicating that they were the most influential persons in the field of depression research in the world. Using SNA, we can easily detect leaders in this field of learning.

In terms of inter-institutional collaboration, the number of collaborating institutions steadily increased from 2003 to 2012, in parallel with the rise in scientific research. This showed that research output kept pace with the number of inter-institutional collaborations. Certain institutions' research ability grew stronger, as they repeated greatly. Harvard University's centrality was the highest, indicating that it possessed and controlled substantial research resources and was the center of inter-institutional collaborations in the field of depression.

Finally, in terms of international collaboration, the US held the most central position in the network. The above analysis suggested that a country's degree of scientific collaboration was positively correlated with the amount of research output. However, certain countries, although prolific, should strengthen their level of international collaboration. In direct contrast, some of the more collaborative countries should work to increase the productivity of their scientific research. If we consider collaboration on all three levels simultaneously, USA unambiguously emerges as the center of depression research. This suggested that the rate of economic development affects collaborative behavior since USA has the greatest levels of international collaboration and publications. In fact, previous studies have indicated that higher income countries prefer to collaborate with each other while lower income countries prefer to collaborate with higher income countries in hopes of producing high-quality research.^[22]

Using hierarchal clustering analysis by CiteSpace, we found research focus in depression field. The diagnostic and classification criteria of depression, remaining a research focus in this field, have been continuously revised and subsequently adapted for use by clinical doctors.^[23]

Abnormal morphology of the brain was another focus of research in this field. In recent years, important applications in the study of brain image technology such as functional magnetic resonance imaging have been used to research depression as it is able to detect synchronous change of brain morphology and function. Yet another research focus was neurotransmitters. The neurotransmitters responsible for emotion and mental state, mainly 5-hydroxytryptamine, dopamine, and catecholamine caused insanity when their processes of composition, storage, release, and receptor binding were disrupted. This study laid the foundation for psychopharmacology, leading to neurotransmitters research that has guided the development of new generation psychotropic drugs. Finally, many studies have shown that mental disorders are complex polygenic diseases, so molecular genetics, more specifically susceptibility genes of mental disorders, has become a focus of research in this field. Since depression contributes most significantly to the global burden of disease, identifying genes that correspond to specific clinical symptoms and being able to tailor treatments and drug regimens to the patient's specific genotype is the ultimate goal to be achieved in the treatment of depression.^[24,25]

In conclusion, this article examined collaborative efforts in depression research at the level of authors, institutions, and countries. Collaborative research offers not only scientific knowledge, but also suggestions for changes in policy that will financially support depression research in the future. Further, identifying research focus within the field can help researchers navigate the forefront of depression research. Future studies should investigate other important mental illnesses in order to advance the development of research in the field of psychiatry as a whole.

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