Current Status of Transcranial Magnetic Stimulation for Treating Depression: A Visualization and Bibliometric Analysis

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Abstract

Background: Depression is the most disabling and prevalent psychiatric disorder; transcranial magnetic stimulation (TMS) is widely used in the treatment of depression because of its remarkable efficacy.

Objective: To investigate the current status, hotspots and frontiers of this research field, and advance the research on TMS for treating depression, this paper provides a visualization and bibliometric analysis of studies related to TMS for depression.

Methods: Literature related to TMS for depression was searched based on the Web of science core database from database creation to November 19, 2023. Cite Space 6.2.R4 and VOS viewer 1.6.20 were used to analyze the relevant literature in terms of annual publications, authors, institutions and international collaborations, co-cited literature, co-cited authors, co-cited journals, and keywords.

Results: A total of 4218 papers were included. The overall trend of the number of publications in this research area is increasing year by year. Research fervor is expected to continue to increase. The United States is in the top position both in terms of the number of publications and centrality. Although Canada ranks third in terms of the number of articles published, its centrality is not high. Based on the keyword co-occurrence analysis, the research hotspots in this field were clarified as efficacy, dorsolateral prefrontal cortex, prefrontal cortex, motor cortex and so on. In recent years, the keywords that have burst out and have continued until now are the treatment effectiveness, reliability, frequency, and theta burst treatment modality of TMS. These keywords may become hot spots for future research.

Conclusions: Conclusion: Our findings suggested that studies related to the field of TMS depression are increasingly emphasized by researchers, and the United States is an international leader in this research area. In the future, cooperation between countries should be strengthened. Meanwhile, it is important to use various imaging-assisted localization tools to carry out multi-center and large-sample clinical studies of individualized treatment parameters for TMS.

Conclusion: Our findings suggested that studies related to the field of TMS depression are increasingly emphasized by researchers, and the United States is an international leader in this research area. In the future, cooperation between countries should be strengthened. Meanwhile, it is important to use various imaging-assisted localization tools to carry out multi-center and large-sample clinical studies of individualized treatment parameters for TMS.

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Original Manuscript

Current Status of Transcranial Magnetic Stimulation for Treating Depression: A Visualization and Bibliometric Analysis

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Abstract

Background: Depression is the most disabling and prevalent psychiatric disorder; transcranial magnetic stimulation (TMS) is widely used in the treatment of depression because of its remarkable efficacy.

Objective: To investigate the current status, hotspots and frontiers of this research field, and advance the research on TMS for treating depression, this paper provides a visualization and bibliometric analysis of studies related to TMS for depression.

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Results: A total of 4218 papers were included. The overall trend of the number of publications in this research area is increasing year by year. Research fervor is expected to continue to increase. The United States is in the top position both in terms of the number of publications and centrality. Although Canada ranks third in terms of the number of articles published, its centrality is not high. Based on the keyword co-occurrence analysis, the research hotspots in this field were clarified as efficacy, dorsolateral prefrontal cortex, prefrontal cortex, motor cortex and so on. In recent years, the keywords that have burst out and have continued until now are the treatment effectiveness, reliability, frequency, and theta burst treatment modality of TMS. These keywords may become hot spots for future research.

Conclusion: Our findings suggested that studies related to the field of TMS depression are increasingly emphasized by researchers, and the United States is an international leader in this research area. In the future, cooperation between countries should be strengthened. Meanwhile, it is important to use various imaging-assisted localization tools to carry out multi-center and large-sample clinical studies of individualized treatment parameters for TMS.

Keywords: transcranial magnetic stimulation; depression; frequency; efficacy; visualization analysis

Introduction

Depression has been a clinically significant and growing public health problem in recent years [1]. It is estimated that the number of cases of depression globally increased from 172 million in 1990 to 258 million in 2017, an increase of 49.86% [2]. Depression is listed by the World Health Organization (WHO) as the leading cause of disability worldwide [3]. At present, the incidence of

depression is gradually increasing, and moving towards a younger trend; adolescents with major depression are 30 times more likely to commit suicide than normal people [4]. The onset of major depression is characterized by two temporal peaks; The majority of patients present in their 20s, while the other peak time point is around age 50 [1]. The rate of diagnosis of depression is twice as high in women as in men, but suicide after illness is three times higher in men than in women [5, 6]. It also shows the geographical characteristics of higher prevalence of depression in adolescents in the Middle East, Africa and Asia [7]. Therefore, it is particularly important to develop new and effective treatments for depression. Currently, the treatment of depression consists of three main modalities: (1) medication: antidepressants and other drugs that enhance antidepressant effects; (2) evidence-based psychotherapy: cognitive-behavioral therapy and interpersonal psychotherapy; And (3) somatic non-pharmacological treatments , including electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS) and vagus nerve stimulation [8]. TMS has been shown to be a safe, non-invasive and effective antidepressant therapy [9, 10]. TMS is used as a non-invasive form of brain stimulation by passing a brief magnetic field stimulus across the scalp and inducing a current in the cerebral cortex [11]. It has been studied for the treatment of major depression since the early 1990s [12]. The International Bipolar Disorder Association guidelines recommend TMS as a first-line intervention after a failed trial of an adequate antidepressant [13]. TMS for depression has been studied more intensively over the past decade and is emerging as a research hotspot.

Bibliometrics is the study of published literature using statistical data to describe or show relationships between published literature [14]. There has been a growing literature on TMS for depression in recent years. In contrast to traditional general reviews, bibliometrics can reveal various characteristics of published literature through quantitative and qualitative analysis. Examples include identifying countries, journals, authors, and institutions that have contributed to the field of study. Statistically analyze highly cited literature and hot keywords. Creating a mapping of collaborative relationships between countries, institutions, and authors in specific subject areas[15]. Bibliometric methods can conveniently provide researchers with an overview of the evolution and development frontiers of a given research area [16]. However, the bibliometric strategies have not yet been applied to the research field of TMS for treating depression so far. To fill this knowledge gap, this study searched the literature about TMS for depression based on Web of science core database. Bibliometric visualization and analysis were performed using Cite Space, VOS viewer software. To explore the current research status, hotspots and literature frontiers of TMS for depression, and to provide reference for future related research.

Methods

Search strategy

This study was searched based on Web of science core database. The search time: the database was searched from its construction to November 19, 2023. In order to get more comprehensive data, a comprehensive search strategy was used. We searched using the following keywords: ((Transcranial Magnetic Stimulation) OR(magnetic field therap*) OR (Magnetic Stimulation, Transcranial) OR (Magnetic Stimulations, Transcranial) OR (Stimulation, Transcranial Magnetic) OR (Stimulations, Transcranial Magnetic) OR (Transcranial Magnetic Stimulations) OR (Transcranial Magnetic Stimulation, Single Pulse) OR (Transcranial Magnetic Stimulation, Paired Pulse) OR (Transcranial Magnetic Stimulation, Repetitive) OR (noninvasive brain stimulation) OR TMS OR TBS)) AND ((depression) OR (depressions) OR (depressed) OR (despondent) OR (gloomy) OR (depressive) OR (antidepressant) OR (antidepressants)).

Literature inclusion and exclusion criteria

Inclusion criteria: ① Literature related to TMS for depression; ② Literature type of article and review; ③ Language is English.

Exclusion criteria: Conference papers, data files, editorial materials, retractions, letters and other literature.

4218 articles were included in the literature after the search.

The search details are presented as a flowchart (Fig1). The search was completed on 11/19/2023.

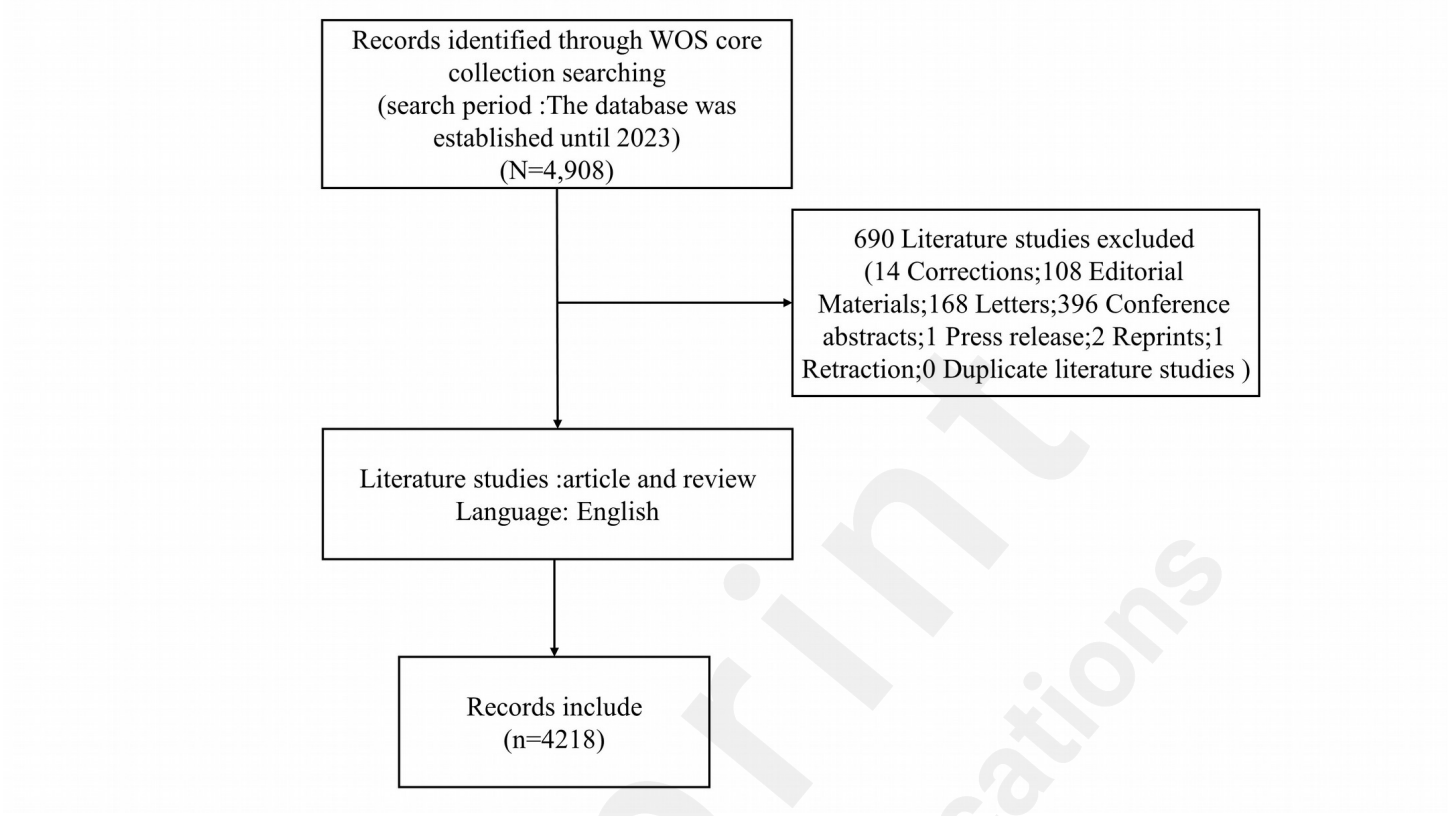


Fig 1. Flow chart for inclusion and exclusion of studies from the literature.

Data extraction and analysis

The full records with cited references that were included in the data literature were exported from Web of science in plain text format. All exported files were renamed to download_XX.txt format. The information visualization and analysis software Cite Space 6.2.R4 basic version and VOS viewer 1.6.20, which was researched and developed by Chaomei Chen's team at Drexel University, USA, were used for data analysis [17].

Results

Temporal distribution of the number of publications

The number of publications over a period of time reflects the rate and the trend of research in the field [18]. As shown in Figure 2A, research on TMS for depression began to appear in 2011, and the total number of publications in the past 13 years was 4218, with an annual average of 324.5 research publications. The number of publications increased slightly from 2011 to 2014; the number of publications about TMS for depression decreased slightly from 2014 to 2016, and the heat of its research declined slightly.2017 to 2022. The volume of literature shows an increasing trend year by year, indicating that there is a growing interest in research in this field, which may be related to the increasing incidence of depression. By looking at Figure 2B, we found that the annual cumulative volume of literature showed a linear growth trend.

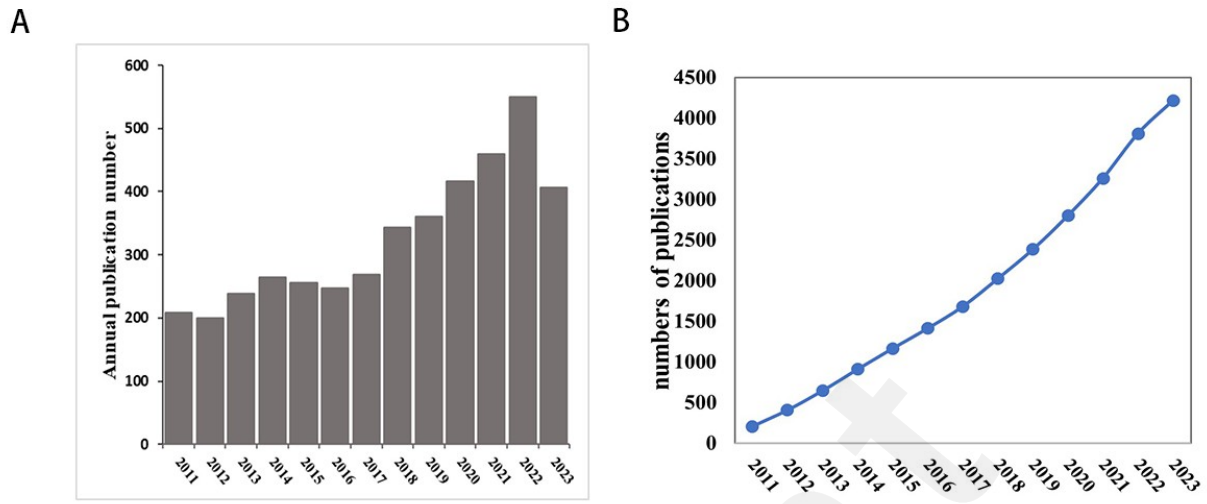


Fig 2. Fig 2 Trends in the number of publications in studies related to transcranial magnetic stimulation for depression from 2011 to 2023. (A) Number of publications per year. (B) Cumulative number of publications.

Analysis of Author, Institution, and Country/Region Collaborations

Cite Space provides 3 levels of scientific collaboration network analysis: micro-author collaboration networks, meso-institutional collaboration networks, and macro-national collaboration networks. In the collaborative networks obtained through Cite Space, the node size indicates the number of authors, institutions or countries/regions that have published [19]. The top 10 authors, institutions and countries/regions according to publication and centrality are listed in Table 1.

Analysis of author co-occurrence cooperation

In Cite Space software, "Author" was selected as a node for analysis, as shown in Figure 3, the number of nodes n = 288, the number of links E = 498, of which 10 authors with more than 40 publications in the past 13 years. The top 5 authors in terms of number of publications are Daskalakis, Zafiris J (154), Blumberger, Daniel M (114), Fitzgerald, Paul B (97), Downar, Jonathan (84), Brunoni, Andre R (66). The most prolific author is Daskalakis, Zafiris J from the University of Toronto, Canada, with an average of 11.8 publications per year. His main research interests are clinical trial studies of various forms of TMS and different treatment sites and frequencies for depression [20–24]. Through the author co-occurrence visualization mapping we found that most of the authors have some collaborative relationships with each other, interlocking to form a network of relationships. Especially, the cooperation between authors with high publication volume is very close. The top 10 authors in terms of publication volume and centrality in the last 13 years are shown in Table 1.

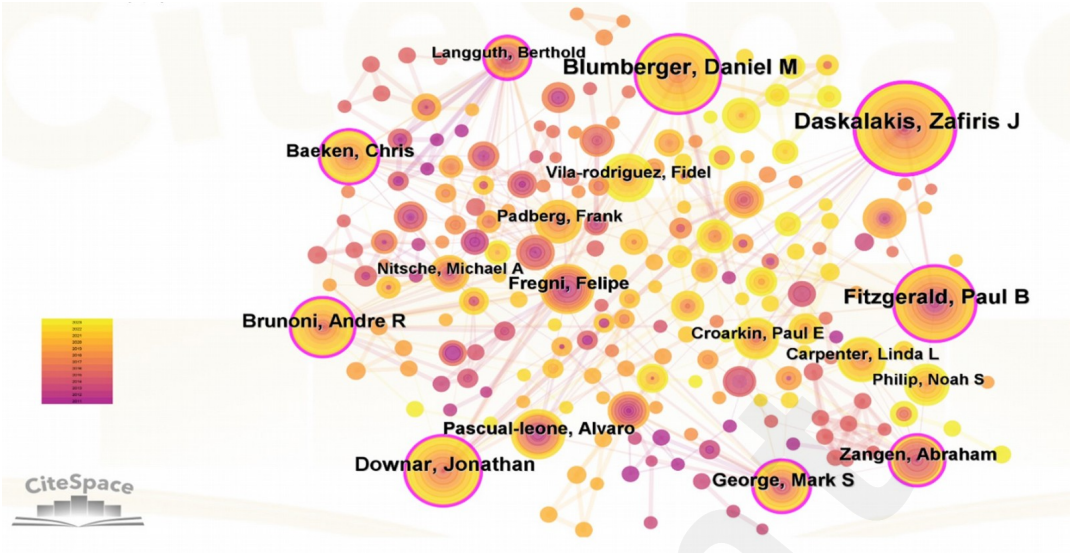


Fig 3. Author cooperation network (2011-2023).

Institutions

In Cite Space software, "Institution" was selected as a node for analysis. As shown in Figure 4, the number of nodes n = 267, the number of links = 880, and the number of organizations with more than 100 publications is 12. The most prolific organization was Harvard University (275/4218 publications, 6.5%), followed by the centre for Addiction & Mental Health - Canada (214/4218 publications, 5.1%) and Harvard Medical School (173/4218 publications, 4.1%). Five of the top 10 ranked organizations are from the United States. And the top 5 organizations in terms of centrality were University of Munich, Germany (0.17), Medical University of Vienna, Austria (0.12), Massachusetts General Hospital, USA (0.1), University of Sao Paulo, Philippines (0.09), and University College London, UK (0.09). This shows the importance of US issuing institutions in the field. The top 10 institutions in terms of the number and the centrality of publications in the last 13 years are shown in Table 1.

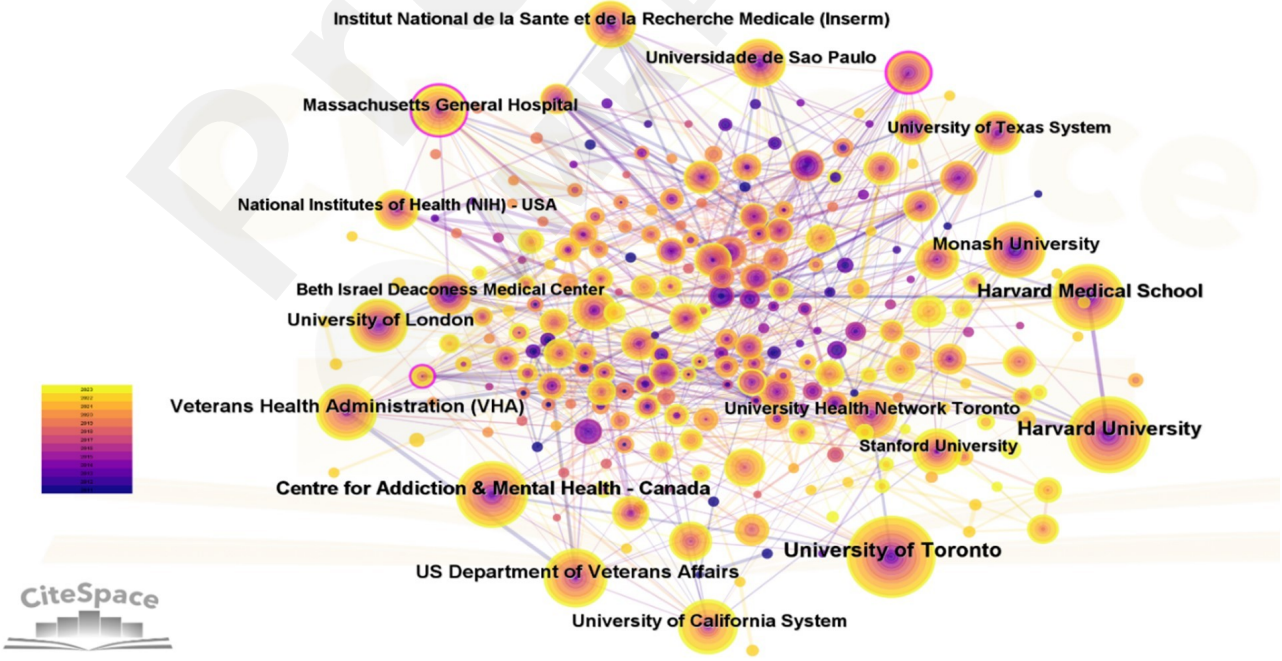


Fig 4. Institutional cooperation network (2011-2023).

Country/Region

In Cite Space software, "Country" is selected as a node for analysis. As shown in Figure 5, the number of nodes is (n = 82), and the number of links is 375, among which there are 15

countries/regions with more than 100 publications. The top one is the United States (1421 articles), accounting for 33.7% of the total published literature. It is followed by China, Canada, Germany, Australia, Italy, UK, France, Brazil, and the Netherlands. And the top 5 countries in terms of centrality are the United States (0.18), the United Kingdom (0.16), France (0.16), Australia (0.14) and Germany (0.13). The United States, the United Kingdom, France, and Germany ranked high both in terms of the number of publications and centrality, indicating that these countries play a crucial role in research in this field. On the other hand, the centrality of Canada, which ranks 3rd in terms of the number of publications, is only 0.03. Meanwhile, compared to several countries with high centrality, Canada has relatively little collaboration with other countries/regions in recent years. The top 10 countries/regions in terms of publications and centrality in the last 13 years are shown in Table 1.

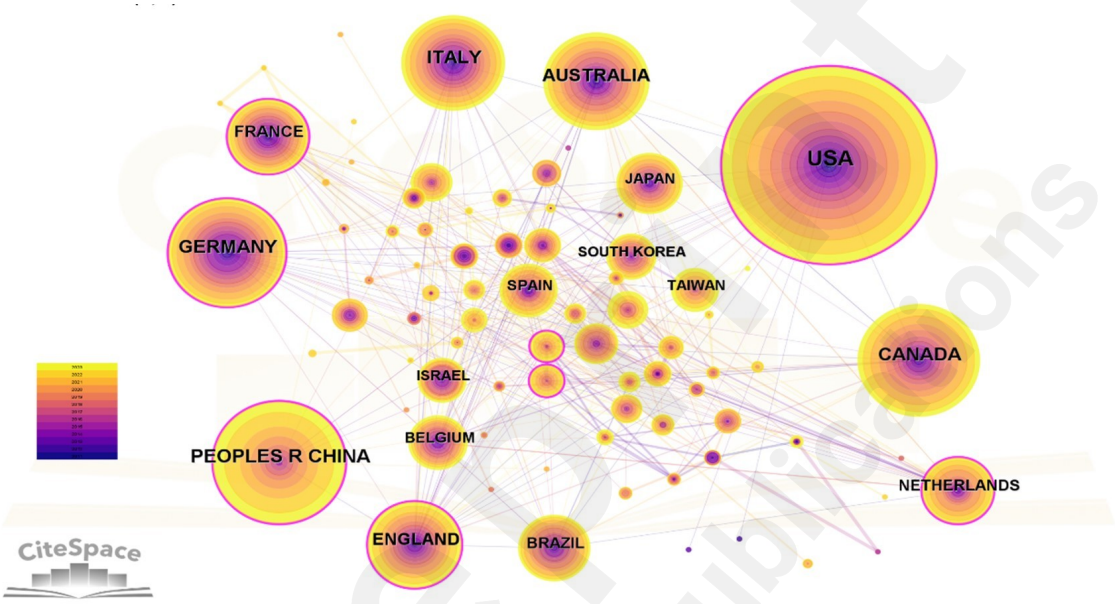


Fig 5. National/regional cooperation network (2011-2023).

Table 1. Top 10 authors, institutions and countries/regions in terms of publications and centrality.

Items	Publications			Centrality		
	Ranking	Name	Number	Ranking	Name	Number
Author	1	Daskalakis, Zafiris J	154	1	Daskalakis, Zafiris J	0.21
	2	Blumberger, Daniel M	114	2	Fitzgerald, Paul B	0.19
	3	Fitzgerald, Paul B	97	3	Brunoni, Andre R	0.18
	4	Downar, Jonathan	84	4	Baeken, Chris	0.18
	5	Brunoni, Andre R	66	5	George, Mark S	0.15
	6	Baeken, Chris	55	6	Zangen, Abraham	0.15
	7	George, Mark S	51	7	Downar, Jonathan	0.14
	8	Pascual-leone, Alvaro	48	8	Langguth, Berthold	0.14
	9	Fregni, Felipe	43	9	Blumberger, Daniel M	0.13
	10	Zangen, Abraham	41	10	Lisanby, Sarah H	0.09
Institution	1	Harvard University	275	1	University of Munich	0.17
	2	Centre for Addiction & Mental Health - Canada	214	2	Medical University of Vienna	0.12
	3	Harvard Medical School	211	3	Massachusetts General Hospital	0.1
	4	US Department of Veterans Affairs	173	4	Universidade de Sao Paulo	0.09

	5	Veterans Health Administration (VHA)	166	5	University College London	0.09
	6	University of California System	159	6	City University of New York (CUNY) System	0.09
	7	University of London	155	7	Eberhard Karls University Hospital	0.09
	8	Monash University	141	8	Beth Israel Deaconess Medical Center	0.08
	9	Institut National de la Sante et de la Recherche Medicale (Inserm)	125	9	University of California Los Angeles	0.08
	10	Universidade de Sao Paulo	124	10	NIH National Institute of Mental Health (NIMH)	0.08
Country/ Region	1	USA	1421	1	USA	0.18
	2	PEOPLES R CHINA	574	2	ENGLAND	0.16
	3	CANADA	502	3	FRANCE	0.16
	4	GERMANY	471	4	AUSTRIA	0.14
	5	AUSTRALIA	370	5	GERMANY	0.13
	6	ITALY	367	6	PEOPLES R CHINA	0.1
	7	ENGLAND	310	7	NETHERLANDS	0.1
	8	FRANCE	225	8	PORTUGAL	0.1
	9	BRAZIL	191	9	AUSTRALIA	0.09
	10	NETHERLANDS	174	10	IRAN	0.09

Citation Analysis

In Cite Space software, "Reference" was selected as a node for analysis. As shown in Figure 6, the number of nodes n = 268 and the number of lines = 468. The top 5 ranked articles in the field in terms of co-citation frequency and centrality are shown in Tables 2 and 3. More than 4 of the top 5 articles with high co-citation frequency were consensual/guidelines or reviews on TMS for depression [10, 25–27]. Only one was a clinical trial [28] (Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE -D): a randomized non-inferiority trial), ranked first in terms of total citations, with a total of 327 citations. It is likely that this study was so frequently cited because of its comprehensive coverage of the always new TMS treatment modality: intermittent theta burst stimulation (iTBS). iTBS has the absolute advantage of shortening treatment time compared to conventional TMS. There is also only one clinical trial in the top 5 of the cited literature in terms of centrality [29]. This study is the first double-blind randomized controlled multicenter study to evaluate the efficacy and safety of deep transcranial magnetic stimulation (dTMS) for Major Depressive Disorder. The study demonstrated that dTMS is a novel intervention for Major Depressive Disorder that is safe and effective in patients unresponsive to antidepressant medications; and that its effects remained stable after 3 months of maintenance treatment.

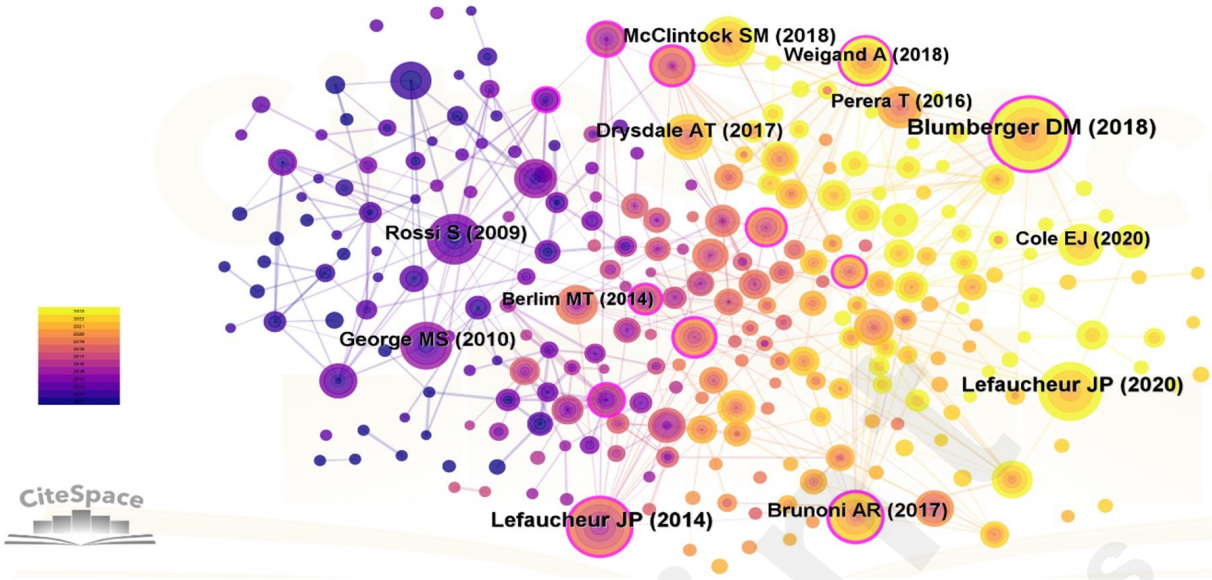


Fig 6. Co-citation analysis of references from 2011 to 2023. The size of the circle indicates the number of citations. The purple area of the circle indicates the centrality of the literature.

Table 2. Top 5 most highly cited publications.

Rank	Title	DOI[a]	Source	Publication date	Total citations[b]
1	Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial[28]	10.1016/S0140-6736(18)30295-2	Lancet	Apr 2018	327
2	Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014-2018)[25]	10.1016/j.clinph.2019.11.002	Clin Neurophysiol	Jan 2020	218
3	Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS) [26]	10.1016/j.clinph.2014.05.021	Clin Neurophysiol	Jun 2014	205
4	Consensus Recommendations for the Clinical Application of Repetitive Transcranial Magnetic Stimulation (rTMS) in the Treatment of Depression[10]	10.4088/JCP.16cs10905	J Clin Psychiatry	Jan 2018	160
5	Repetitive Transcranial Magnetic Stimulation for the Acute Treatment of Major Depressive Episodes: A Systematic Review With Network Meta-analysis[27]	10.1001/jamapsychiatry.2016.3644	JAMA Psychiatry	Fed 2017	157

Table 3. Top 5 co-cited centrality literature.

Rank	Title	DOI[a]	Source	Publication date	Centrality[b]
1	Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial[28]	10.1016/S0140-6736(18)30295-2	Lancet	Apr 2018	0.25

2	Repetitive Transcranial Magnetic Stimulation for the Acute Treatment of Major Depressive Episodes: A Systematic Review With Network Meta-analysis[27]	10.1001/ jamapsychiatry.2016.3644	JAMA Psychiatry	Fed 2017	0.24
3	Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial[29]	10.1002/wps.20199	World Psychiatry	Fed 2015	0.24
4	Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS) [26]	10.1016/j.clinph.2014.05.021	Clin Neurophysiol	Jun 2014	0.20
5	Clinically meaningful efficacy and acceptability of low-frequency repetitive transcranial magnetic stimulation (rTMS) for treating primary major depression: a meta-analysis of randomized, double-blind and sham-controlled trials[30]	10.1038/npp.2012.237	Neuropsychopharmacology	Mar 2013	0.19

[a]DOI: Digital Object Identifier.

[b]Total citations were until the November 19, 2023.

Cited Authors

Selecting "Cited Author" as the node to analyze, we found that the top 5 co-cited authors were George MS (1059 citations), Fitzgera LD PB (1043 citations), Lefauch EUR JP (1010 citations), Rossi S (803 citations) and Oreard ON JP (759 citations). The top co-cited author was George MS from the Medical University of South Carolina, U.S.A. As an expert in the clinical application of TMS, he was involved in the development of a consensus on the treatment of depression with TMS [10]. He also suggested that TMS is a safe, effective and tolerated therapy for major depression [31]. The top 5 authors with total citations in the last 13 years are shown in Table 4.

Cited Journals

Selecting "Cited Journal" as the node for analysis, we found that the top 5 co-cited journals were Biol Psychiat (2727 citations), Brain Stimul (2711 citations), Clin Neurophysiol (2475 citations), Am J Psychiat (2119 citations) and J Affect Disorders (2097 citations). Among them, Biol Psychiat was the top journal in terms of centrality, and it also found that most of the journals with a high frequency of co-cited literature were published in Clin Neurophysiol, indicating that these two journals have significant influence in the field of TMS treatment of depression. The top 5 co-cited journals in the last 13 years are shown in Table 4.

Table 4. Top 5 co-cited authors and co-cited journals

Rank	Cited author	citation frequency	Rank	Cited journal	citation frequency
1	George MS	1059	1	BIOL PSYCHIAT	2727
2	Fitzgera LD PB	1043	2	BRAIN STIMUL	2711
3	Lefauch EUR JP	1010	3	CLIN NEUROPHYSIOL	2475
4	Rossi S	803	4	AM J PSYCHIAT	2119
5	Oreard ON JP	759	5	J AFFECT DISORDERS	2097

Keywords

Co-occurrence Analysis

High-frequency keywords represent the hotspots of a research field, while high centrality keywords reflect the status and influence of the corresponding research content in that research field [32]. A total of 10,701 keywords were extracted from 4218 documents. Words with no real meaning and words related to the search strategy such as "Transcranial Magnetic Stimulation", "Depression", etc. were removed, and finally the synonyms were combined. The 173 most frequently occurring keywords that met the inclusion threshold were categorized into five clusters (Figure 7) and grouped by average publication date (between 2017 - 2019) (Figure 8). The first major cluster of keywords in Figure A is shown in red and includes major depression, efficacy, safety, double-blind and trial, etc.

This section focuses on the clinical aspects of TMS for depression. The second category of keywords is shown in green and includes neuroplasticity, theta burst stimulation, motor cortex, modulation and brain. The fourth category of keywords is shown in yellow, mainly including dorsolateral prefrontal cortex, functional connectivity and prefrontal cortex, etc. These two sections mainly explore the mechanism of TMS for depression. The third category, shown in blue, includes keywords such as noninvasive brain stimulation, Parkinson's disease, Alzheimer's disease and working memory; This section includes some other therapies for depression and complications of depression. The fifth category of keywords is shown in purple, mainly including brain stimulation, transcranial direct current stimulation, magnetic stimulation and electric-stimulation, etc. This section includes other brain stimulation therapies for the treatment of depression. An overlay of keywords grouped by average year of publication shows that research hotspots have changed over time, starting with cortex excitability, moving on to neuroplasticity, clinical efficacy, double-blind implementation, and then to functional connectivity. This also indicates that the mechanism of TMS for depression is still a hot research topic. The top 10 high-frequency keywords in the last 13 years are shown in Table 5.

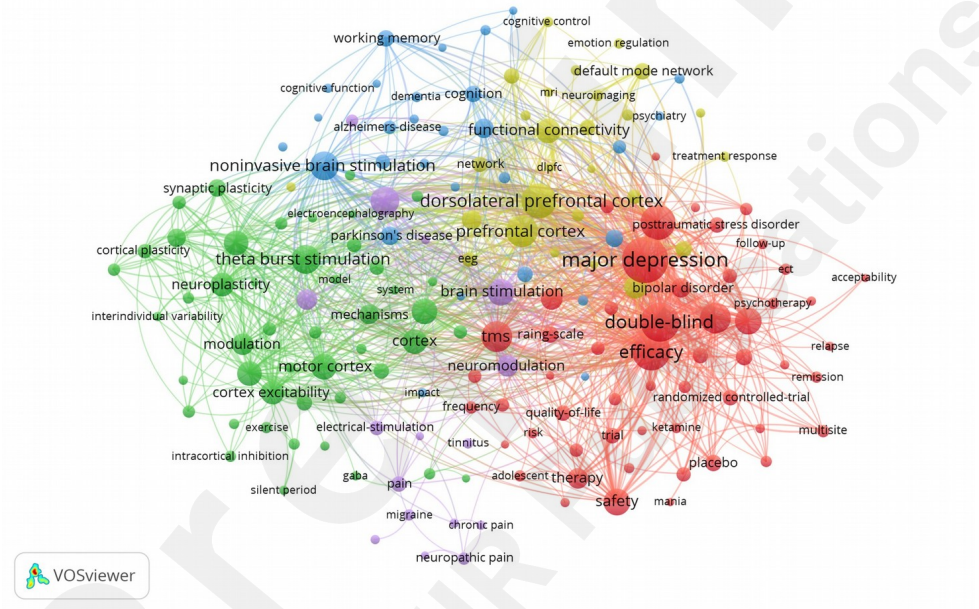


Fig 7. Keyword co-occurrence network. Shows the 173 items with the most occurrences out of 10,701 keywords, grouped into 5 clusters, with the color of the circle representing each cluster.

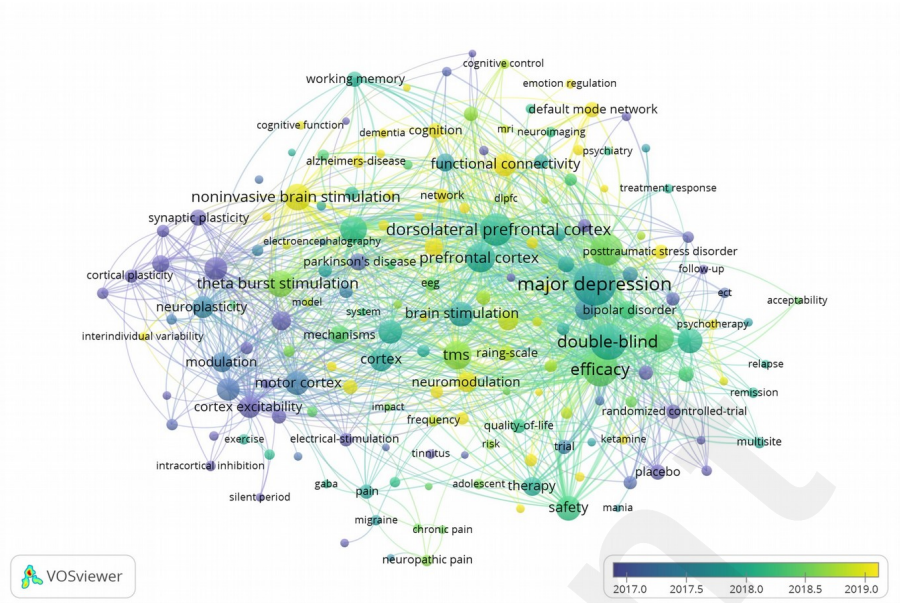


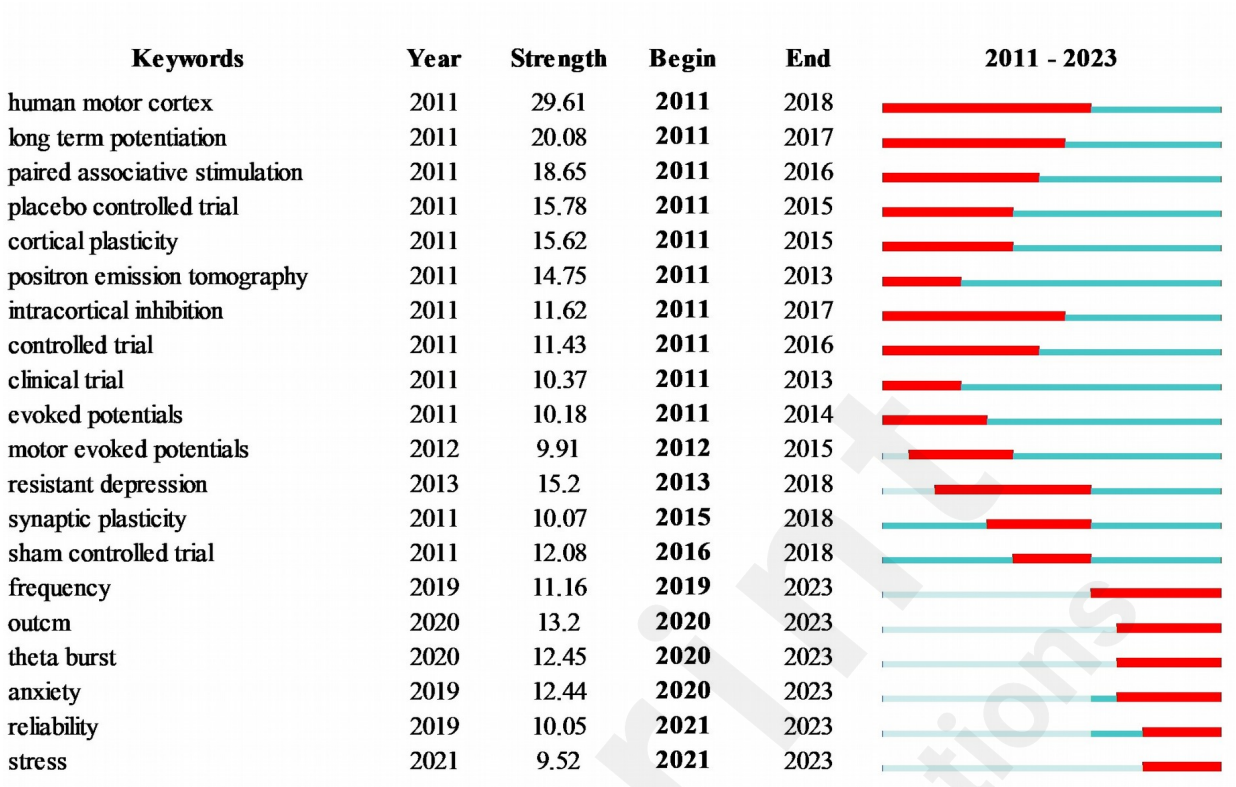
Fig 8. Overlay visualization of keyword co-occurrences. Shows keywords grouped by year of publication, with the color of the circle representing the average year.

Table 5. Top 10 high-frequency keywords

Rank	Keyword	Occurrences
1	Double-blind	731
2	efficacy	681
3	dorsolateral prefrontal cortex	587
4	prefrontal cortex	494
5	Theta burst stimulation	421
6	Noninvasive brain stimulation	402
7	safety	354
8	electroconvulsive therapy	355
9	Brain stimulation	334
10	motor cortex	326

Emergence Analysis

Keyword emergence analysis can show the year of the emergence and persistence of research hotspots in a certain field; to a certain extent, it can predict the development trend, frontier and hotspot of the discipline in this field [19].Figure 9 shows the top 20 emergent keywords with the strongest frequency bursts. Keywords such as human motor cortex, cortical plasticity and evoked potentials, which relate to the therapeutic mechanism and clinical aspects of TMS, were highlighted strongly from 2011 to 2016. However, in the past 5 years, the keywords of bursting have changed, including the terms frequency, reliability and theta burst. This suggests that the research hotspot in recent years will still continue to focus on the reliability and validity of TMS in treating depression, and further explore the treatment frequency and stimulation modality of TMS.



Keywords	Year	Strength	Begin	End	2011 - 2023
human motor cortex	2011	29.61	2011	2018	
long term potentiation	2011	20.08	2011	2017	
paired associative stimulation	2011	18.65	2011	2016	
placebo controlled trial	2011	15.78	2011	2015	
cortical plasticity	2011	15.62	2011	2015	
positron emission tomography	2011	14.75	2011	2013	
intracortical inhibition	2011	11.62	2011	2017	
controlled trial	2011	11.43	2011	2016	
clinical trial	2011	10.37	2011	2013	
evoked potentials	2011	10.18	2011	2014	
motor evoked potentials	2012	9.91	2012	2015	
resistant depression	2013	15.2	2013	2018	
synaptic plasticity	2011	10.07	2015	2018	
sham controlled trial	2011	12.08	2016	2018	
frequency	2019	11.16	2019	2023	
outcm	2020	13.2	2020	2023	
theta burst	2020	12.45	2020	2023	
anxiety	2019	12.44	2020	2023	
reliability	2019	10.05	2021	2023	
stress	2021	9.52	2021	2023	

Fig 9. The top 20 keywords with the strongest frequency bursts. Strong frequency bursts indicate a large change in the variable over a short period of time. The red bar indicates the duration of the burst.

Discussion

Current state of research

In each of the past 13 years, there have been more than 324 internationally published research publications on TMS for depression. The largest increase was from 2017 to 2018, and the overall trend of a linear increase in annual publications over time further indicates that research related to TMS for depression has become a hot topic. The analysis of the global research impact shows that for TMS for depression, there is close collaboration among countries, emphasizing that depression is a global challenge. The larger share of developed countries in the total number of publications may be related to the fact that developed countries spend more money on scientific research[19]. As well as factors such as the high prevalence of depression in developed countries[33].

Important research findings

Based on the citation frequency analysis of the literature, one of the most frequently and centrally cited is “Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomized non-inferiority trial” by Blumberger DM et al. [28] published in the Lancet in 2018. The study noted that iTBS is a newer form of TMS that can be completed in less than 3 minutes, compared to the standard 10Hz rTMS treatment time of 37.5 minutes [28]. The highest frequency and centrality of citations to this literature may be due to ① determining the clinical effectiveness, safety, and tolerability of iTBS versus standard 10hz rTMS in adult patients with refractory depression. ② And to clearly state that iTBS is not inferior to standard 10hz rTMS in terms of therapeutic efficacy [28]. ③ A thorough reading of the literature reveals that the study is a randomized, multicenter, large-sample clinical trial, published jointly by Canada, the United States, Israel, Japan and many other countries. This also makes its results more authoritative and reliable.

The expert consensus guidelines that ranked in the top 5 of cited literature for frequency and centrality of citations stated that the antidepressant effect of HF-rTMS on the left dorsolateral prefrontal cortex (DLPFC) was of grade A (definite efficacy). A grade B recommendation (possible efficacy) was made for the antidepressant effects of low-frequency (LF) rTMS in the right DLPFC [25, 26]. FDA approval of rTMS is limited to adults with major depression [10]. There is evidence of safe therapeutic use and clinical benefit of rTMS in adolescent mood disorders, perinatal depression, and other neuropsychiatric disorders (including bipolar disorder, panic disorder, obsessive-compulsive disorder, depersonalization disorder, post-traumatic stress disorder, and schizophrenia) [34–38]. However, at this time, there is insufficient evidence to support the ability to routinely use rTMS in these populations. Therefore, more clinical evidence is still needed for safety and efficacy in other age groups and psychiatric disorders.

The above findings represented important discoveries in the field of TMS for depression, and these ideas and findings were highly regarded and innovative in the field.

Research Hotspots and Frontiers

Reliability and validity of TMS in the treatment of depression

The reliability and validity of TMS, a keyword hotspot that has emerged in recent years, has also attracted a great deal of attention from researchers. There are more than 20 years of research showing that TMS is an effective treatment for major depressive disorder [10]. TMS, as a viable intervention for the treatment of depression, can normalize brain activity and reduce some psychiatric symptoms. However, TMS interventions are only moderately reliable [39]. While TMS improved depressive symptoms in some people, it was ineffective in about 50% of people with similar clinical features [40]. And a major part of this is due to the individual heterogeneity of depressed patients. The heterogeneity of TMS treatment outcomes is thought to be driven in part by the suboptimal targeting of DLPFC [41, 42]. Determining the optimal locus of therapeutic TMS in the treatment of depression remains a major goal in psychiatry.

Frequency

Repetitive TMS is one of the effective treatments for depression, but standard sessions are time-consuming. Routine TMS treatment consists of high-frequency action on the left dorsolateral prefrontal cortex (DLPFC) and low-frequency action on the right DLPFC. High-frequency stimulation (≥ 5 Hz) increases cortical excitability, whereas low-frequency stimulation (≤ 1 Hz) decreases cortical excitability [43]. Of all the TMS treatment options, high-frequency stimulation is the most clinically researched and applied method [44]. However, this conventional treatment program is not suitable for all depressed patients [45].Many new frequencies and forms of TMS for depression have emerged in recent years, including ① Theta burst stimulation (TBS): three 50 Hz pulses are emitted every 200 ms, which has a more rapid and long-lasting effect on synaptic plasticity than traditional TMS [45].② Priming transcranial magnetic stimulation (pTMS): as a variety of low-frequency TMS, a specific protocol of short bursts of low-intensity, high-frequency TMS ("priming stimulation") followed by low-frequency treatment of the right side of the DLPFC [46]. Fitzgerald et al[47] found that the antidepressant efficacy of a combined treatment regimen using 6Hz TMS initiated stimulation of the right motor cortex followed by 1Hz TMS stimulation was superior to that of the group initiating the right 1Hz TMS alone.③ Synchronized transcranial magnetic stimulation (sTMS): utilizes a rotating spherical neodymium magnet placed along the midline of the scalp to deliver low-field sinusoidal waveform stimulation synchronized to the individual alpha frequency. Following the natural resonance of the brain at an individual's alpha frequency, sTMS is thought to achieve an antidepressant effect by using a lower intensity of energy than traditional high-frequency TMS [48].④ dTMS: By using a special coil configuration (helmet-like hi-coil), dTMS can stimulate deeper and larger brain volumes than traditional high-frequency TMS [29]. However, there are no standardized criteria for which frequency form of TMS to apply for

different degrees of depressive states. Therefore, a great deal of clinical and basic research is needed in the future with a view to providing the possibility of realizing precision medicine.

TBS

Among the keyword emergences TBS started to emerge in 2021 and its popularity continues into 2023 and beyond. TBS has major advantages in terms of shorter treatment time compared to standard TMS methods [49]. The pattern-specific modulatory effects of TBS were initially demonstrated in the motor cortex and subsequently studied in prefrontal cortical regions [50]. In motor cortex studies TBS was able to induce significant and long-lasting neuronal modulatory responses, while electrophysiological and metabolic effects were also observed in prefrontal cortex [51]. TBS, which includes Intermittent theta burst stimulation (iTBS) and continuous theta burst stimulation (cTBS), is no less effective than TMS in treating depression [28]. iTBS treatment was able to reverse the decrease in mature brain-derived neurotrophic factor-related protein levels [52]. In motor areas, iTBS increases whereas cTBS mainly decreases the excitability of targeted cortical neurons [53]. The inter- and intra-individual response variability of TBS and the uncertainties associated with the mechanism of action remain and deserve continued in-depth study [51].

Limitations

In this paper, we used Cite Space 6.2R4, VOSviewer1.6.20 software to visualize and analyzed the literature related to TMS for depression in the Web of Science core database for the last 13 years. There were also some limitations. Firstly, owing to different economic strengths and population sizes, which lead to inconsistent progress in the research field among countries and may introduce bias. Second, only English literature was included in the core database of Web of Science for visualization and analysis, and future research can incorporate literature from databases such as CNKI, Scopus, and so on. Third, the visualization tools are relatively simple, and in the future, we can use the Gephi software, which can provide a more comprehensive and clearer theoretical reference for the study of TMS for depression.

Conclusions

This study is the first time to visualize and analyze the literature in the field of TMS for treating depression, which can more intuitively reflect the current status, hotspots, and future development trends in this field. In summary, there is a growing interest in TMS for the treatment of depression. The continued growth in the number of annual publications suggests that this area is becoming increasingly important globally, with the United States having the highest number of publications and a high degree of centrality in the field. The study also identified the main researchers and institutions involved in TMS for depression around the world. The results of the keywords analysis showed that TMS efficacy, treatment site and mechanism were considered popular topics. TMS treatment sites are mostly focused on the DLPFC and its subregions. However, traditional treatment site localization methods ("5cm localization method" and "Beam F3 method") ignore the variability of individual brain anatomy and function. Therefore, as far as the treatment site is concerned, structural magnetic resonance imaging, functional magnetic resonance imaging, and positron emission scanning magnetic resonance imaging, which have emerged in recent years to assist in individual localization of TMS treatment, are recommended. These individualized targeting modalities can undoubtedly improve the efficacy of TMS for depression. A study of the global field of TMS for depression in the last 10 years found that the frequency, validity, and reliability of TMS, as well as TBS, may be a key direction for future research. However, there is a lack of clinical studies on individualized treatment parameters of multicenter, large-sample TMS for depression, which makes the evidence of its validity and reliability insufficient. Therefore, in the future, it is particularly important to use various imaging-assisted localization tools to conduct multicenter, large-sample clinical studies of individualized therapeutic parameters of TMS for depression.

Acknowledgments

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Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

Multimedia Appendix 1

Comprehensive searching strategy.

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Supplementary Files

Figures

Flow chart for inclusion and exclusion of studies from the literature.

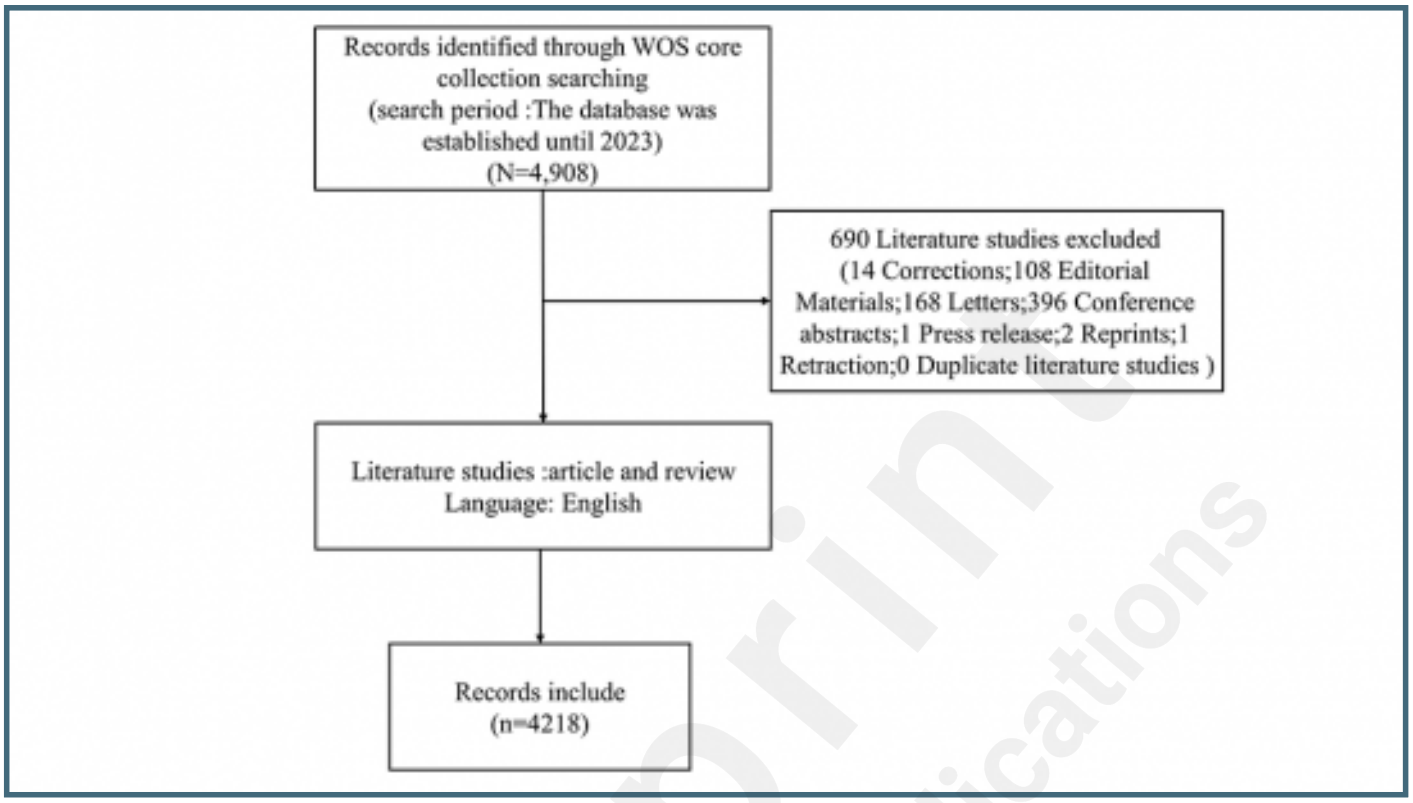
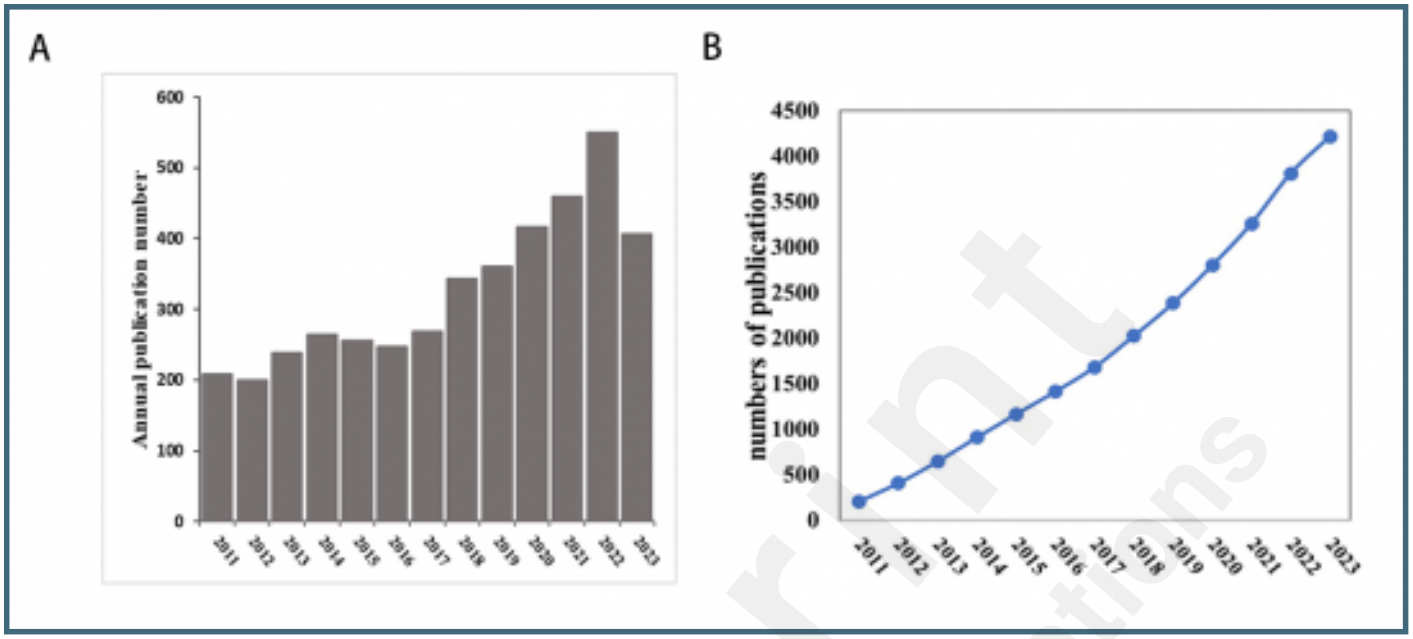
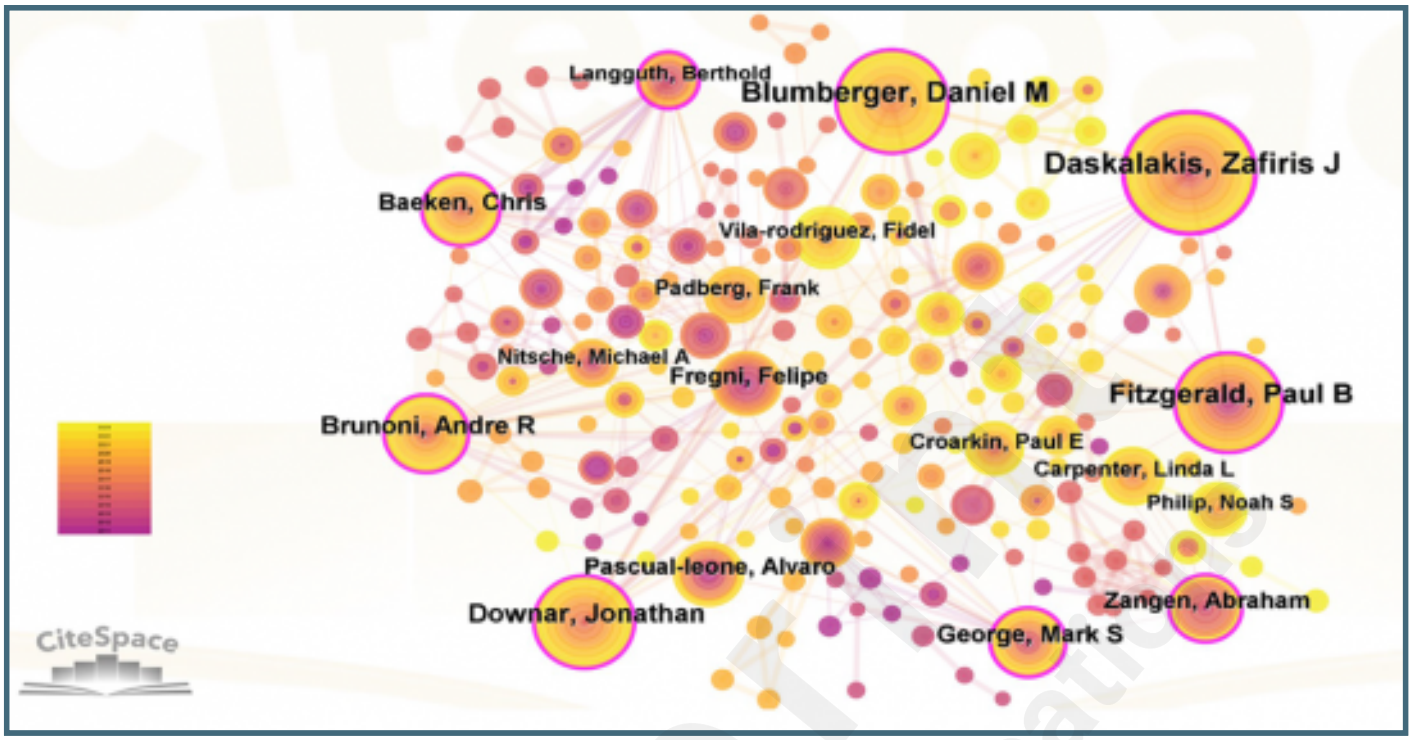


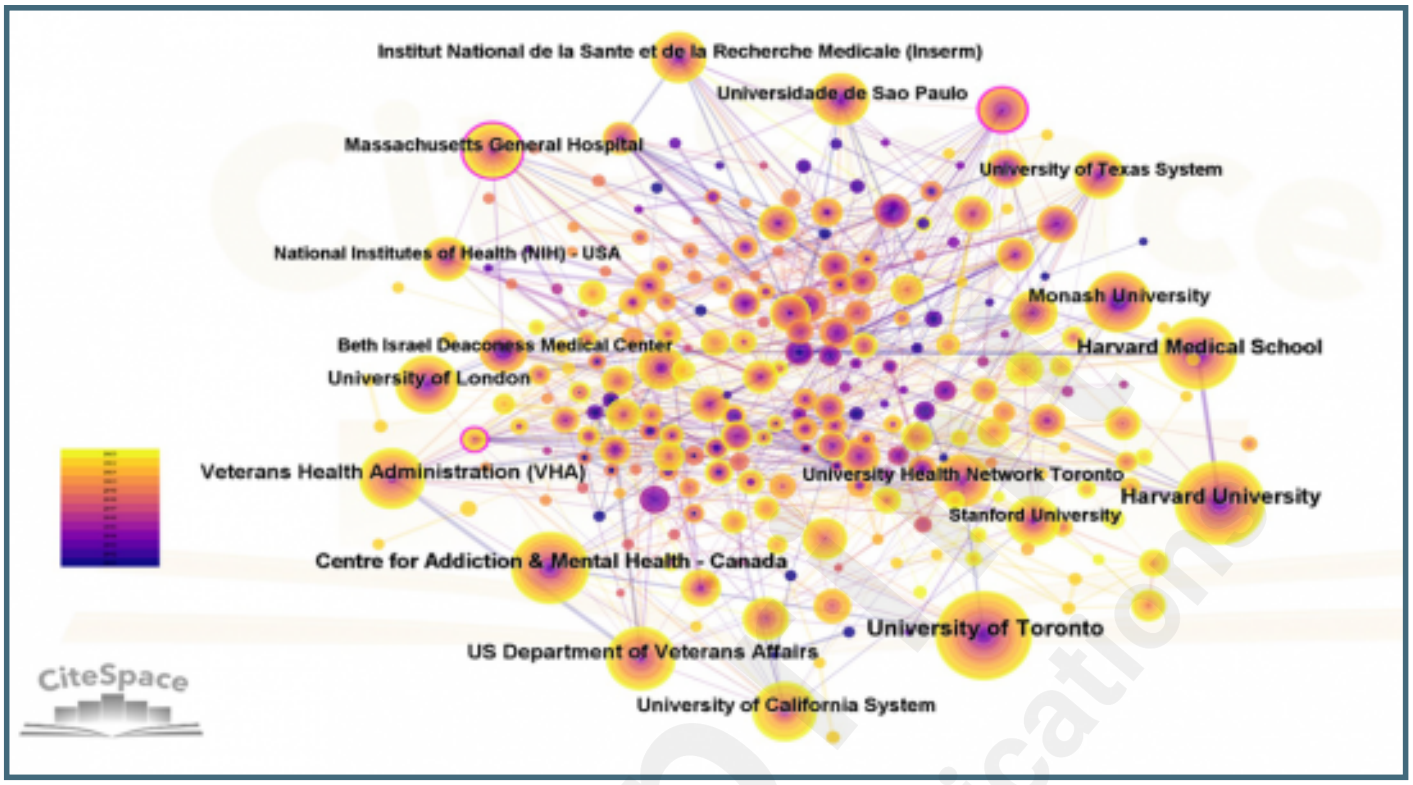
Fig 2 Trends in the number of publications in studies related to transcranial magnetic stimulation for depression from 2011 to 2023. (A) Number of publications per year. (B) Cumulative number of publications.



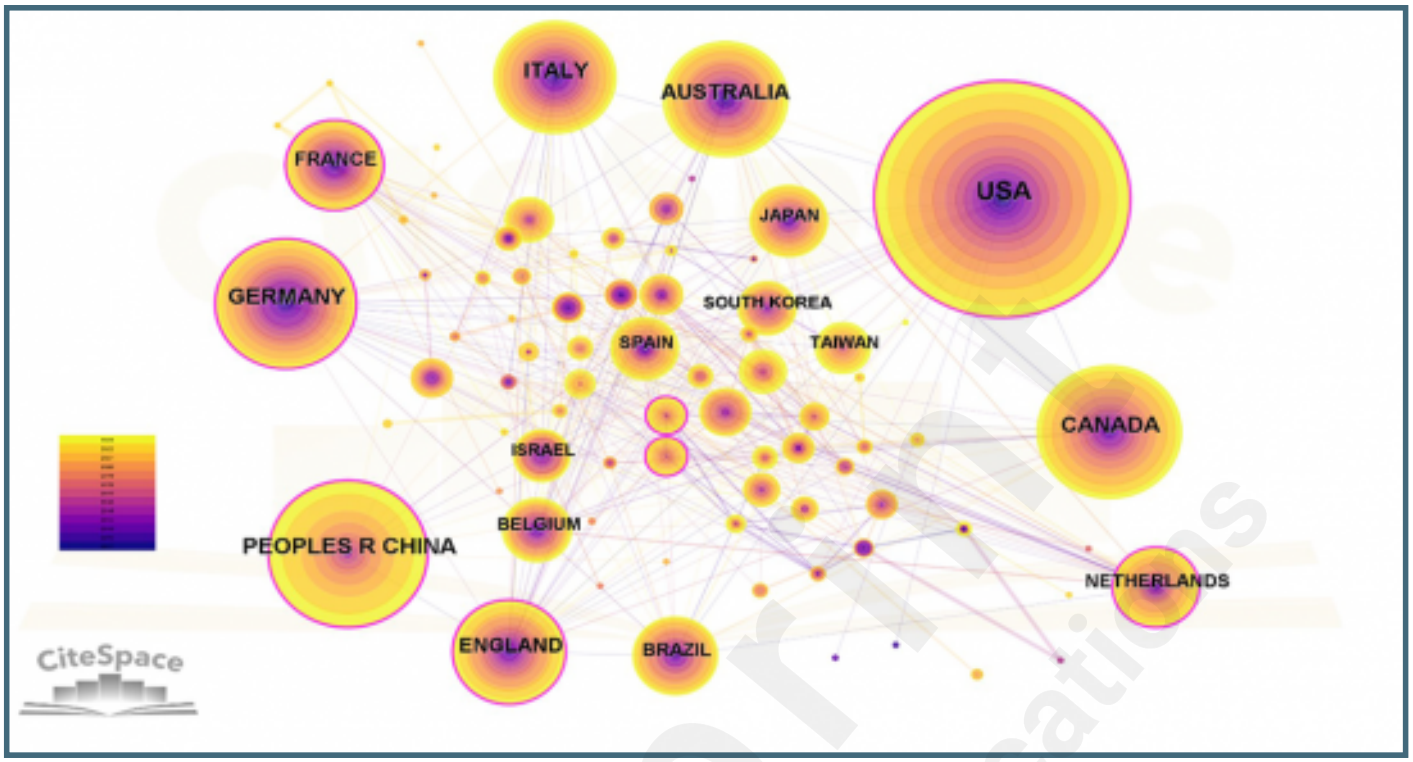
Author cooperation network (2011-2023).



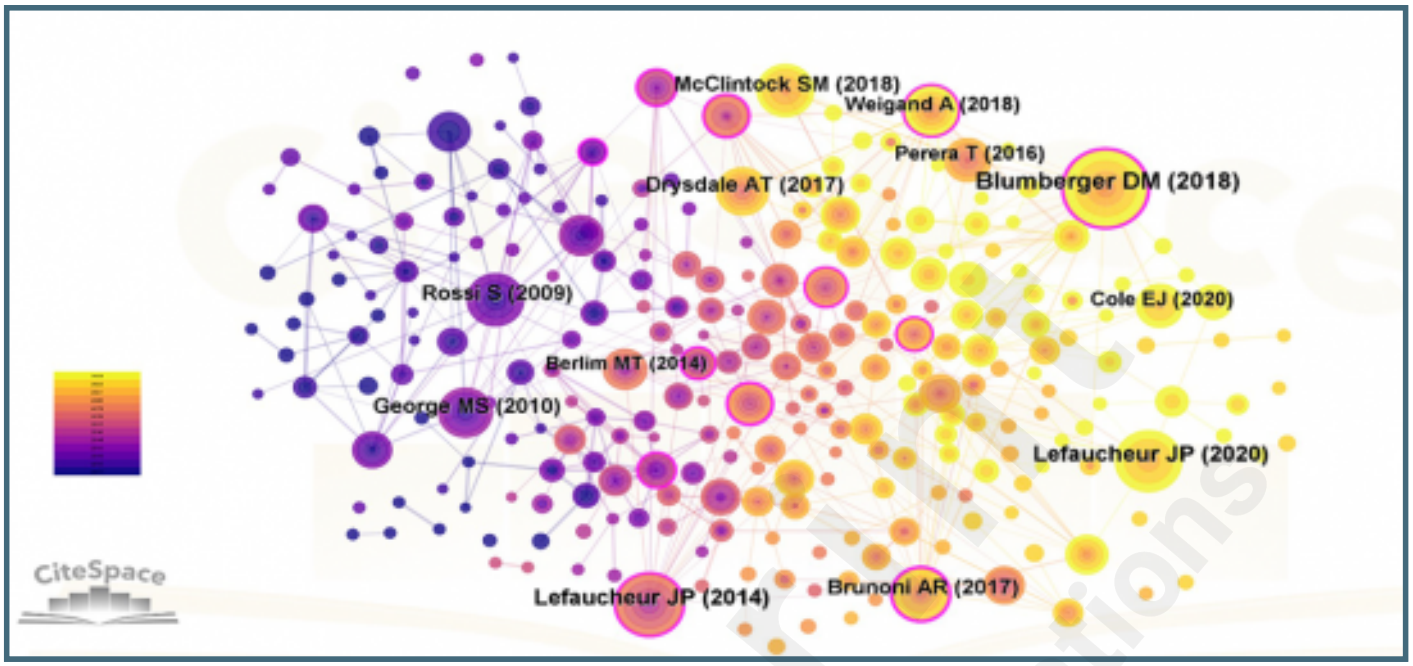
Institutional cooperation network (2011-2023).



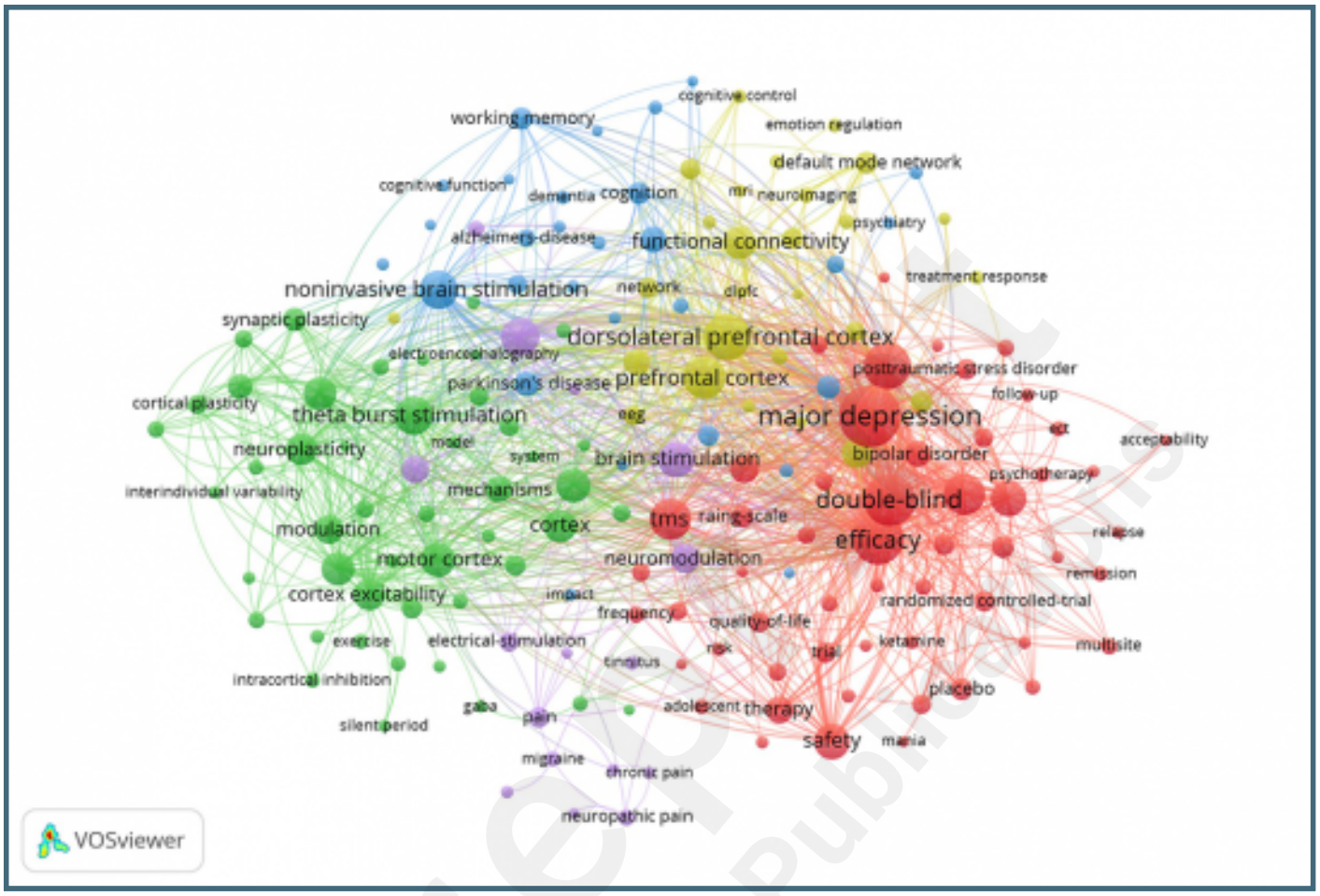
National/regional cooperation network (2011-2023).



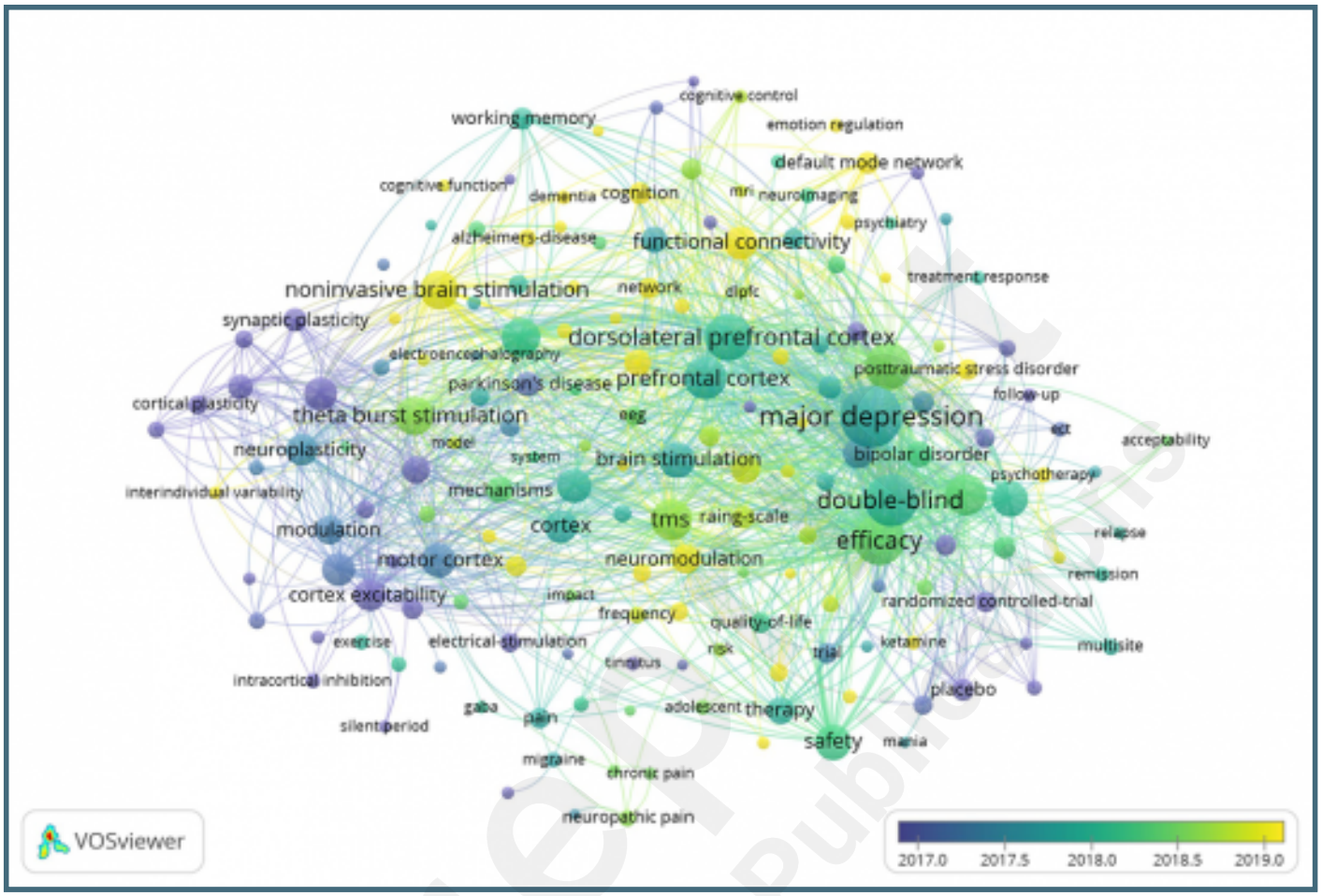
Co-citation analysis of references from 2011 to 2023. The size of the circle indicates the number of citations. The purple area of the circle indicates the centrality of the literature.



Keyword co-occurrence network. Shows the 173 items with the most occurrences out of 10,701 keywords, grouped into 5 clusters, with the color of the circle representing each cluster.



Overlay visualization of keyword co-occurrences. Shows keywords grouped by year of publication, with the color of the circle representing the average year.



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synaptic plasticity	2011	10.07	**2015**	2018	
sham controlled trial	2011	12.08	**2016**	2018	
frequency	2019	11.16	**2019**	2023	
outcm	2020	13.2	**2020**	2023	
theta burst	2020	12.45	**2020**	2023	
anxiety	2019	12.44	**2020**	2023	
reliability	2019	10.05	**2021**	2023	
stress	2021	9.52	**2021**	2023	

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