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The application of deep brain stimulation for Parkinson's disease on the motor pathway: A bibliometric analysis across 10 years

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Abstract

Parkinson's disease has been the focus of research and clinical development to date since James Parkinson reported it for the first time in 1817. The estimated prevalence of the disease is about 1% of adults over the age of 60 years. Deep brain stimulation as an alternative treatment in the end stage of the disease, has saved the lives of countless patients. The objective of this review is to examine and analyze the publications related to the influence of deep brain stimulation in the motor pathway in human Parkinson's disease in the past decade and visualize the outcomes using Citespace. Our results indicate that the United States of America (USA), United Kingdom (UK), Germany, and China are the primary contributors to this research field. University College London, Capital Medical University, and Maastricht University are the top 3 research institutions in this area. Tom Foltynie is the most published author, and the journal *Brain* and *Brain stimulation* publishes the most scholarly articles. The current research hotspots in this field that were identified by keyword burst are neuronal activity, nucleus, hyperdirect pathway, etc. In conclusion, this review has provided a new perspective through bibliometric analysis of the deep brain stimulation therapy for treating patients with Parkinson's disease, which can shed light on future research endeavors to advance our understanding of this study field.

Keywords: Deep brain stimulation, Parkinson's disease, motor pathway

Introduction

Parkinson's disease (PD, also known as paralysis agitans), is common in middle-aged and elderly people¹⁻³. As one of the common movement disorders, PD is classically characterized by static tremor, rigidity, bradykinesia, dystonia, postural instability, and other non-motor symptoms, such as hyposmia, rapid eye movement sleep behavior disorder, restless leg syndrome²⁻⁷. The Global Burden of Disease (GBD) neurological disorders collaborator group has noted that 6.2 million new individuals were distressed from 1990-2015⁸. As of now, several beneficial treatment approaches including exercise training, medication regimens (e.g., levodopa, benzhexol, amantadine), physical therapy, and surgical treatments (e.g., lesioning therapies) for PD are available, but none represent a curative approach⁹⁻¹⁷. As a slowly progressive neurodegenerative disease, PD often has a poor prognosis¹⁸⁻²¹. Most patients are competent in their job in the early stage of PD, and as the disease progresses, severe symptoms finally lead to a gradual loss of working capacity²²⁻²⁵. Patients often die from complications (e.g., pneumonia) in the end-stage of PD²⁶⁻²⁸.

The application of modern deep brain stimulation (DBS) on patients with PD was first introduced by Benabid in 1987^{29,30}. After decades of development, DBS has become an important treatment for those patients with decreased medication efficacy after long-term non-surgical treatment or intolerance of medication adverse effects³¹⁻³³. To implement DBS, one or more electrodes are implanted to specific targets in the brain. The implantable pulse generator (IPG) is connected to the other end of the electrodes³⁴. The common electrodes implanted regions of DBS are the globus pallidus interna (GPi), and subthalamic nucleus (STN)³⁵⁻³⁸. When IPG is activated, several key brain regions related to PD in the basal ganglia are affected. Therefore, the excessive inhibition induced by the degenerated basal ganglia is regulated, leading to a more activated downstream motor pathway, which can alleviate motor symptoms³⁹⁻⁴³. However, DBS is effective only in cases of rigidity and tremor and not for postural instability^{44,45}.

In the past twenty years, DBS has become an alternative treatment for end-stage PD patients, which has gained substantial progress⁴⁶⁻⁴⁸. The potential mechanisms of such a method also became the focus of much research⁴⁹⁻⁵¹. However, there are few bibliometric analysis studies in this field. This article is devoted to the DBS treatment and its influence on the motor pathway in human PD and a bibliometric analysis of publications based on Citespace to promote understanding in this area.

Materials and Methods

Data acquisition

As is described in previous studies⁵¹⁻⁵⁴, data were obtained from the Web of Science Core Collection via the library of Huazhong University of Science and Technology. The search strategy included the topics 'deep brain stimulation', 'Parkinson's disease', 'motor pathway', and 'human' from January 1, 2012, to December 1, 2022. The data was downloaded on October 24, 2022. The detailed search strategy was [TS = ['deep brain stimulation'] AND ['Parkinson's disease'] AND ['motor pathway']] AND [Articles] AND [Mesh Headings=Humans] AND [language=English].

The exclusion criteria were listed as follows: (1) Articles that were not related to the search topic, (2) Abstract, editorial material, letters, corrections, etc. The 255 validated records were then imported to Citespace 6.1 R3 for further visualization and analysis.

Data analysis

As described previously⁵⁵⁻⁵⁸, Citespace has been applied to bibliometric analysis and visualization for decades since its debut in 2004⁵⁹. After the data was imported, we conducted various analyses

of the distribution of the publications including institutions, authors, countries/ regions, and journals. The cooperation network was also constructed after the analyses. Furthermore, the analyses of keyword co-occurrence, keyword cluster, and citation burst were performed and visualized using Citespace. The Citespace parameters were set as follows: Time-slicing was chosen from 2012 to 2022, one year per slice. All the options in term slicing (including title, abstract, author keywords, and keywords plus) were selected. Pathfinder, pruning sliced networks and pruning the merged network were selected in Pruning. The node (tree ring) in the figure represents an observation (such as country, institution, author, etc.). The node size indicates the frequency of occurrence, and a larger node suggests a higher frequency of occurrence. The lines show the cooperation, co-occurring, or co-referential relationship between each observation.

Results

Analysis of the Annual Publication Outputs

From the annual trend depicted in Figure 1, it can be seen that the relative studies of motor pathway changes in DBS treatment in human PD have been an active research field with more than 10 papers published annually in the past ten years. Especially since 2016, the number of published research in this field increased significantly. We also noticed that the number of citations shows a steadily upward trend.

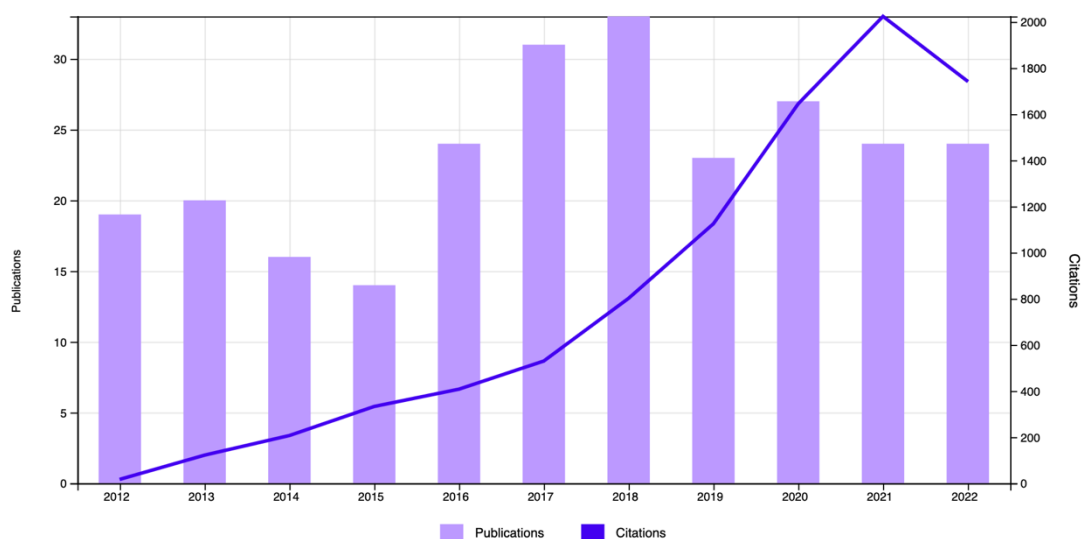


Figure 1. Annual publication and citation outputs

Analysis of articles attributed to Countries/ Regions

Citespace was used to visualize the distribution of the number of articles published in each country/ region⁶⁰. As is shown in Figure 2, there were 40 nodes on the map, suggesting that 40 countries/ regions contributed to the publication of 255 articles over the past decade. From the results displayed in Table 1, it can be seen that the top three countries in terms of publications are the United States (98 publications), Germany (43 publications), and the United Kingdom (36 publications). However, the US and the UK are ranked top 2 in the centrality rankings with 0.45 and 0.46, indicating that they are the two influential countries in research in this field. However, it is obvious that academic communication between countries is urgently needed.

Table 1. Top 10 Countries/Regions

Rank	Country/Region	Year	Publications	Centrality
1	United States	2012	98	0.45
2	Germany	2012	43	0.15
3	England	2012	36	0.46
4	People R China	2014	29	0.06
5	France	2012	23	0.03
6	Canada	2012	18	0.10
7	Netherlands	2012	16	0.13
8	Italy	2012	15	0.06
9	Spain	2012	12	0.02
10	Brazil	2016	11	0.03

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 Network: N=40, E=138 (Density=0.1769)
 Largest 5 CCs: 39 (97%)
 Nodes Labeled: 1.0%
 Pruning: None



Figure1. Distribution map of different countries

Analysis of articles published by institutions

In order to probe deeper, the co-occurrence analysis of the institution was performed (Figure 2). The map consists of 260 nodes and 356 links, suggesting that 260 institutions all over the world have made contributions to this field. The top three institutions were University College London (UCL), Capital Medical University, and Maastricht University (Table 2). The centrality of UCL was the highest, while the others were no more than 0.2.

Table 2. Top10 leading Institutions related to DBS therapy in PD patients

Rank	Institution	Year	Publications	Centrality
1	University College London	2013	17	0.23
2	Capital Medical University	2016	9	0.03
3	Maastricht University	2012	7	0.14
4	University of Minnesota	2012	6	0.02

5	Beijing Institute for Brain Disorders	2017	5	0.00
6	Johns Hopkins University	2012	5	0.00
7	Charité – Universitätsmedizin Berlin	2018	5	0.01
8	Hannover Medical School	2013	5	0.04
9	Centre National de la Recherche Scientifique	2013	5	0.06
10	University of California, San Francisco	2018	4	0.01

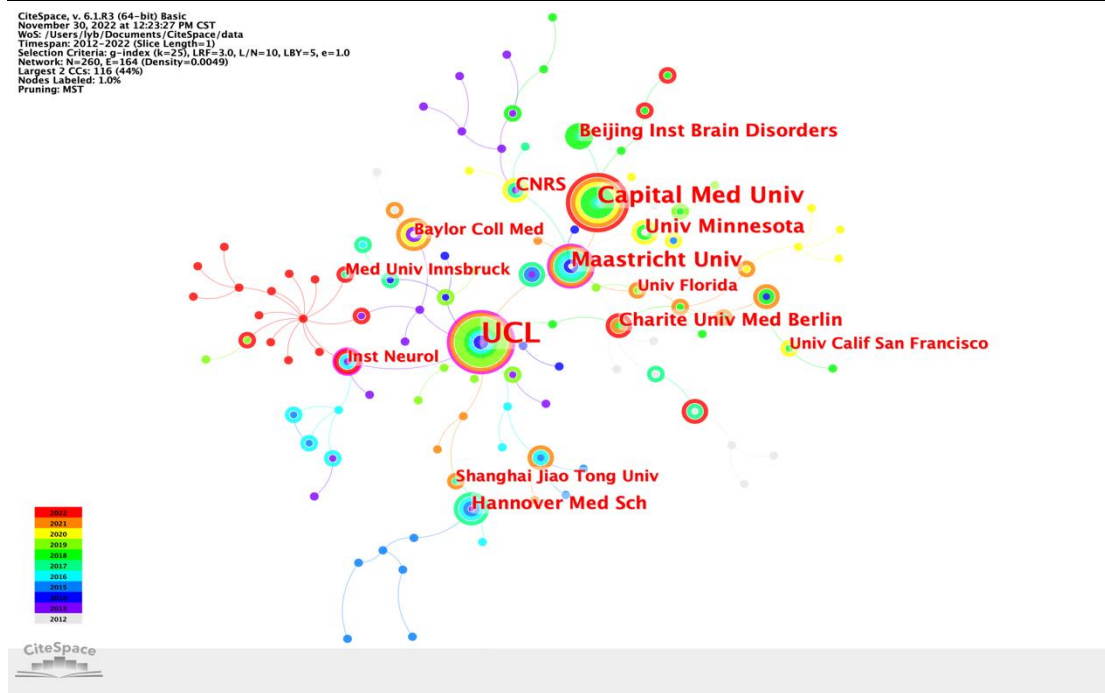


Figure 2. Network map of co-authorship from different institutions

Authors and co-cited authors

The distribution of the most active authors in this field are depicted in Figure 3. Tom Foltynie from University College London ranked first with 6 publications, followed by Harith Akram, Klaus Seppi, Patricia Limousin, and Mesbah Alam (Table 3). It is noteworthy that 6 authors of the current top 10 come from University College London. However, none of the centrality of the authors mentioned above is greater than 0.10.

Among the 438 co-cited authors shown in Figure 5, eight authors were cited more than 40 times. Atsushi Nambu from the National Institute for Physiological Science, Japan, had the highest citation (65), followed by Mahlon Delong from Emory University School of Medicine, USA (55), Roger Albin from the University of Michigan, USA (52), Alim Louis Benabid from University Grenoble Alpes, France (48), Viviana Gradinaru from California Institute of Technology (45), suggesting that these authors have the greatest influence in the field. Among the top 10 co-cited authors, there were seven with a centrality higher than 0.10.

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 Network: N=299, E=165 (Density=0.0037)
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 Nodes Labeled: 1.0%
 Pruning: MST

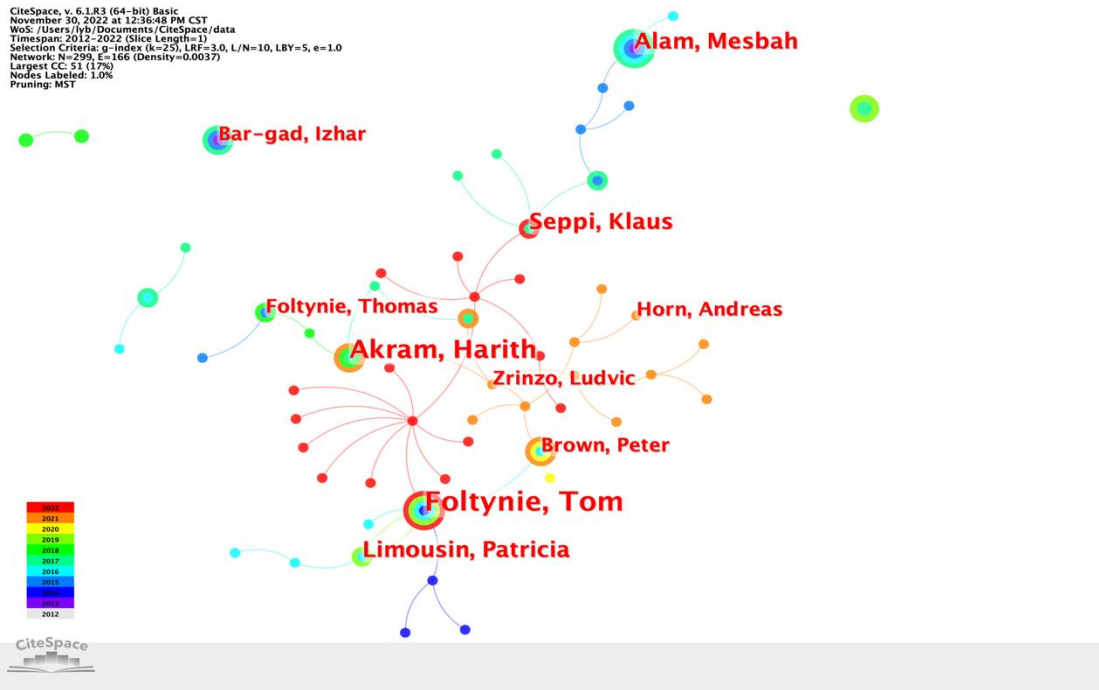


Figure 3. Map of authors related to DBS treatment in patients with PD

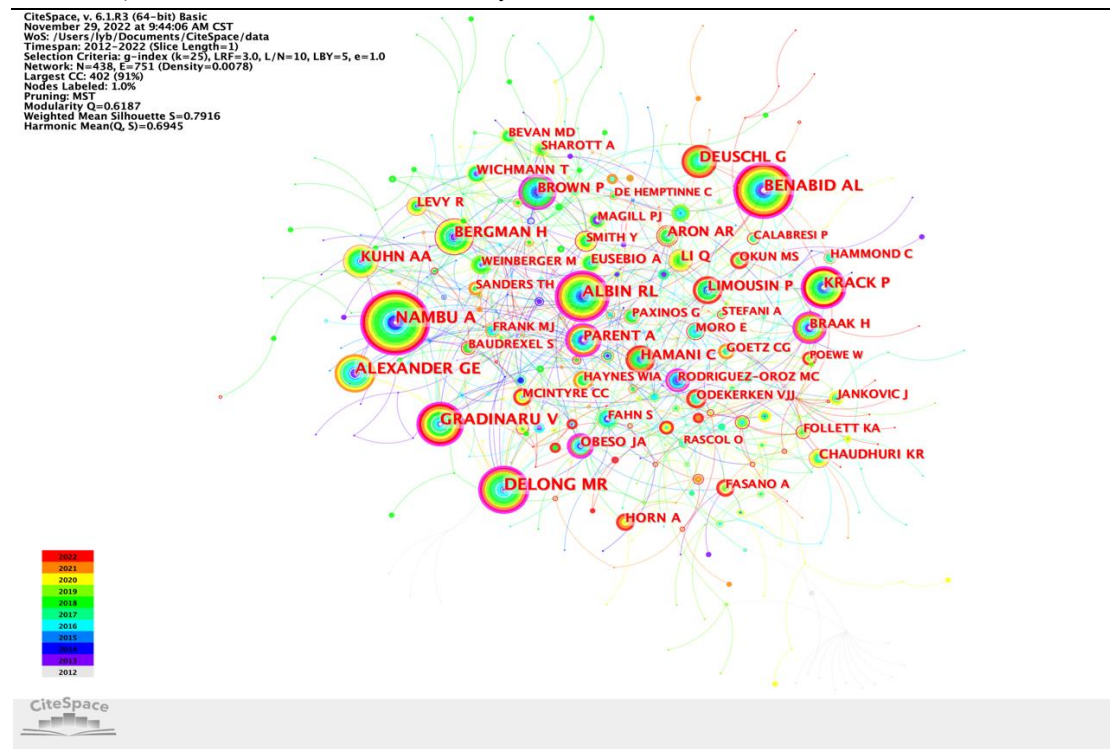
Table 3. Top 10 active authors related to DBS treatment in patients with PD

Rank	Author	Institution	Year	Count	Centrality
1	Tom Foltnie	University College London, UK	2014	6	0.03
2	Harith Akram	University College London, UK	2017	5	0.01
3	Klaus Seppi	Medical University of Innsbruck, Australia	2017	4	0.02
4	Patricia Limousin	University London College, UK	2016	4	0.00
5	Mesbah Alam	Hannover Medical School, Germany	2013	4	0.00
6	Thomas Foltnie	University London College, UK	2015	3	0.00
7	Izhar Bar-Gad	Bar Ilan University, Israel	2013	3	0.00
8	Andreas Horn	Charité – Universitätsmedizin Berlin, Germany	2021	3	0.00
9	Peter Brown	University of Oxford, UK	2016	3	0.03
10	Ludvic Zrinzo	University College London, UK	2021	3	0.02

Table 4. Top 10 co-cited authors

Rank	Co-cited Author	Institution	Year	Count	Centrality
1	NAMBU A (Atsushi Nambu)	National Institute for Physiological Science, Japan	2012	65	0.11
2	Mahlon R DeLong (DELONG MR)	Emory University School of Medicine, USA	2012	55	0.10
3	Roger L Albin (ALBIN RL)	University of Michigan, USA	2012	52	0.13
4	Alim Louis Benabid (BENABID AL)	University Grenoble Alpes, France	2012	48	0.10

5	Viviana (GRADINARU V)	Gradinaru	California Institute of Technology, USA	2012	45	0.12
6	Gene E (ALEXANDER GE)	Alexander	Johns Hopkins University School of Medicine, USA	2012	43	0.04
7	BERGMAN H		The Hebrew University-Hadassah Medical School, Israel	2012	42	0.08
8	Andrea A Kühn (KUHN AA)		Charite-Universitätsmedizin Berlin, Germany	2012	41	0.10
9	Paul Krack (KRACK P)		Joseph Fourier University, France	2012	38	0.13
10	Günther Deuschl (DEUSCHL G)		Christian-Albrechts University, Germany	2012	34	0.05



Journals and Co-cited Journals

We further analyzed the source of published articles. Two hundred and fifty-five articles related to DBS therapy in human PD were published in 141 academic journals. The journal of *Brain* (10, 3.92%) published 10 publications which was the most productive journal, followed by *Brain stimulation* (7, 2.75%), *Journal of neurophysiology* (7, 2.75%), *Movement disorders* (7, 2.75%) and *Parkinson related disorders* (7, 2.75%). The top 10 journals are presented in Table 5. The impact factor score of the *Brain* is the highest (IF: 13.501), followed by *Brain stimulation* (IF: 8.955), *Journal of neurophysiology* (IF: 2.714), *Movement disorders* (IF: 10.338), *Parkinson related disorders* (IF: 4.891). Of the top 15 journals, 40% were classified as JCR Q1, the remaining were Q2 (47%), and Q3 (13%). Table 5 also illustrates the top 15 popular co-cited journals, *Brain* (216) was the most frequently cited journal, followed by *Movement disorders* (213), *Journal of neuroscience* (196), *Neurology* (164), and *Journal of neurology and psychiatry* (160). Among the top 15 co-cited journals, 67% were classified as JCR Q1, the remaining were Q2 (20%), and Q3

(13%).

Table 5. Top 15 Journals and Co-cited Journals

Rank	Journal	Count (%)	IF (2021)	JCR (2021)	Co-cited journal	Citation	IF (2021)	JCR (2021)
1	Brain	10 (3.922%)	13.501	Q1	Brain	216	13.50	Q1
2	Brain stimulation	7 (2.745%)	8.955	Q1	Movement disorders	213	10.33	Q1
3	Journal of neurophysiology	7 (2.745%)	2.714	Q2	Journal of neuroscience	196	6.167	Q1
4	Movement disorders	7 (2.745%)	10.338	Q1	Neurology	164	9.91	Q1
5	Parkinsonism related disorders	7 (2.745%)	4.891	Q2	Journal of neurology and psychiatry	160	10.15	Q1
6	Journal of neurosurgery	6 (2.353%)	5.115	Q1	Annals of Neurology	156	10.42	Q1
7	Neuroimage clinical	6 (2.353%)	4.881	Q2	Journal of neurophysiology	146	2.714	Q2
8	Neuroscience	6 (2.353%)	3.59	Q3	Parkinsonism related disorders	139	4.891	Q2
9	Journal of neuroscience	5 (1.961%)	6.167	Q1	European Journal of neuroscience	128	3.386	Q3
10	Behavioural brain research	4 (1.596%)	3.332	Q2	Neuron	201	17.17	Q1
11	Brain research	4 (1.596%)	3.252	Q3	Experimental neurology	201	125	Q2
12	Experimental neurology	4 (1.596%)	5.33	Q2	neuroimage	201	125	Q1
13	Frontiers in neurology	4 (1.596%)	4.003	Q2	Neuroscience	201	124	Q3
14	Journal of neural engineering	4 (1.596%)	5.379	Q2	Proceedings of the national academy of sciences of the United States of	201	122	Q1

15	Neurobiology of disease	4 (1.596%)	5.996	Q1	America Science	120	47.72	Q1
							8	

Co-cited References

A total of 470 co-cited references are presented in Figure 5. We listed the top 15 most frequently co-cited references related to DBS treatment in human PD and these are listed in table 6. As shown, the most frequently cited publication was written by Ketaki Bhalsing, and published in the *Journal of neurological science* in 2013, followed by the article published in *Neurobiology of disease* in 2016, and ‘Therapeutic deep brain stimulation reduces cortical phase-amplitude coupling in Parkinson's disease’ written by Coralie de Hemptinne et al⁶¹ published in Nature neuroscience. Among the top 15 articles, ‘Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold’ written by James F Cavanagh et al. has the highest centrality of 0.18⁶².

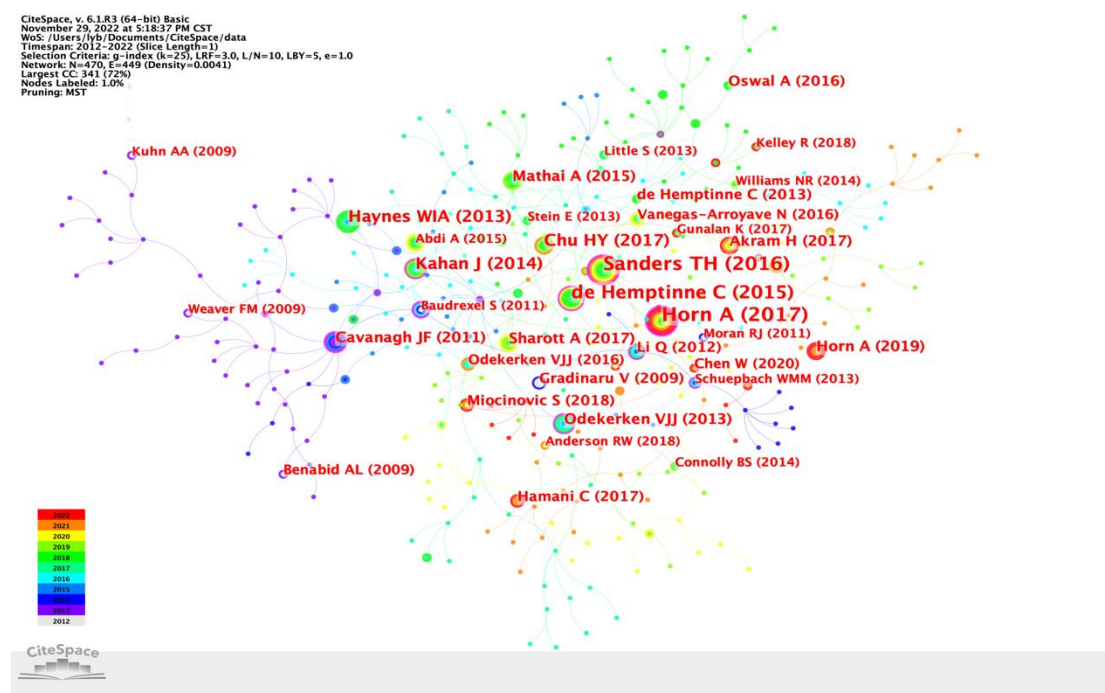


Figure 5. Map of Co-cited References

Table 6. Top 15 Co-cited References

Rank	Reference	Citation	Year	Centrality
1	Bhalsing KS, 2013, J NEUROL SCI, V335, P9, DOI 10.1016/j.jns.2013.09.003	17	2017	0.12
2	Sanders TH, 2016, NEUROBIOL DIS, V95, P225, DOI 10.1016/j.nbd.2016.07.021	16	2016	0.11
3	de Hemptinne C, 2015, NAT NEUROSCI, V18, P779, DOI 10.1038/nn.3997	14	2015	0.11
4	Kahan J, 2014, BRAIN, V137, P1377, DOI 10.1093/brain/awu001	10	2014	0.08

	P1130, DOI 10.1093/brain/awu027				
5	Chu HY, 2017, NEURON, V95, P1306, DOI 10.1016/j.neuron.2017.08.038	10		2017	0.04
6	Haynes WIA, 2013, J NEUROSCI, V33, P4804, DOI 10.1523/JNEUROSCI.4674-12.2013	10		2013	0.03
7	Cavanagh JF, 2011, NAT NEUROSCI, V14, P1462, DOI 10.1038/nn.2925	8		2011	0.18
8	Akram H, 2017, NEUROIMAGE, V158, P332, DOI 10.1016/j.neuroimage.2017.07.012	8		2017	0.13
9	Odekerken VJJ, 2013, LANCET NEUROL, V12, P37, DOI 10.1016/S1474-4422(12)70264-8	8		2013	0.11
10	Sharott A, 2017, J NEUROSCI, V37, P9977, DOI 10.1523/JNEUROSCI.0658-17.2017	8		2017	0.06
11	Mathai A, 2015, BRAIN, V138, P946, DOI 10.1093/brain/awv018	8		2015	0.01
12	Horn A, 2019, NEUROIMAGE, V184, P293, DOI 10.1016/j.neuroimage.2018.08.068	8		2019	0.00
13	Li Q, 2012, NEURON, V76, P1030, DOI 10.1016/j.neuron.2012.09.032	7		2012	0.09
14	Miocinovic S, 2018, J NEUROSCI, V38, P9129, DOI 10.1523/JNEUROSCI.1327-18.2018	7		2018	0.04
15	Miocinovic S, 2018, J NEUROSCI, V38, P9129, DOI 10.1523/JNEUROSCI.1327-18.2018	7		2013	0.02

Keyword co-occurrences and Clusters

Keyword co-occurrences and clusters reflect the research spotlight and hotspot of the research area⁶³⁻⁶⁵. The analysis of the most popular keywords is shown in Table 7. The most frequently mentioned keywords in publications of this field are basal ganglia (110), subthalamic nucleus (96), the motor cortex (31), subthalamic nucleus stimulation (27), substantia nigra (27), globus pallidus (25), high frequency stimulation (22), activation (20), transcranial magnetic stimulation (18), beta oscillation (17). However, the keyword ‘motor cortex’ has the highest centrality (0.41), followed by

‘subthalamic nucleus stimulation’ (0.35), and ‘substantia nigra’ (0.29).

We further performed a cluster analysis, which detected 15 clusters (Figure 6). We noticed that ‘reactive inhibition’ (cluster 0), ‘external globus pallidus’ (cluster 1), ‘hyperdirect pathway’ (cluster 2), ‘beta-band oscillations’ (cluster 3), ‘essential tremor’ (cluster 4), ‘locus coeruleus’ (cluster 5), ‘computational modeling’ (cluster 6), ‘pain’ (cluster 7), ‘pedunclopontine tegmental nucleus’ (cluster 8), ‘tremor’ (cluster 9), ‘guideline’ (cluster 10), ‘animal models’ (cluster 11), ‘midbrain’ (cluster 12), ‘motor function’ (cluster 13), ‘telerehabilitation’ (cluster 14), ‘subthalamic nucleus’ (cluster 15) were the spotlights in this field over the past ten years. The timeline view of the keywords is depicted in Figure 7, which presents the evolution of the keywords. The most frequently mentioned keywords from 2012 to 2022 are shown on the timeline view. The larger ring represents the frequency of occurrence.

Furthermore, citation bursts were analyzed through Citespace⁶⁶⁻⁶⁸. The top ten keywords with the strongest citation bursts are illustrated in Figure 8. Keywords that burst up to the end of 2022 are transcranial magnetic stimulation, rat model, motor, nonmotor symptom, and oscillatory activity, which indicate the frontiers of research in this area (Figure 9).

Table 7. Top 20 high-frequency keywords

Rank	Keywords	Count	Centrality	Rank	Keywords	Count	Centrality
1	basal ganglia	110	0.09	11	hyperdirect pathway	17	0.03
2	subthalamic nucleus	96	0.17	12	disease	17	0.13
3	motor cortex	31	0.41	13	cerebral cortex	14	0.01
4	subthalamic nucleus stimulation	27	0.35	14	movement	14	0.03
5	substantia nigra	27	0.29	15	model	14	0.01
6	globus pallidus	25	0.05	16	movement disorder	14	0.41
7	high frequency stimulation	22	0.02	17	functional connectivity	12	0.41
8	activation	20	0.35	18	primary motor cortex	12	0.67
9	transcranial magnetic stimulation	18	0.07	19	connectivity	12	0.55
10	beta oscillation	17	1.17	20	motor	11	0.00

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 Largest CC: 357 (96%)
 Nodes Labeled: 3.0%

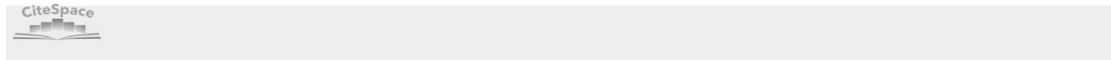
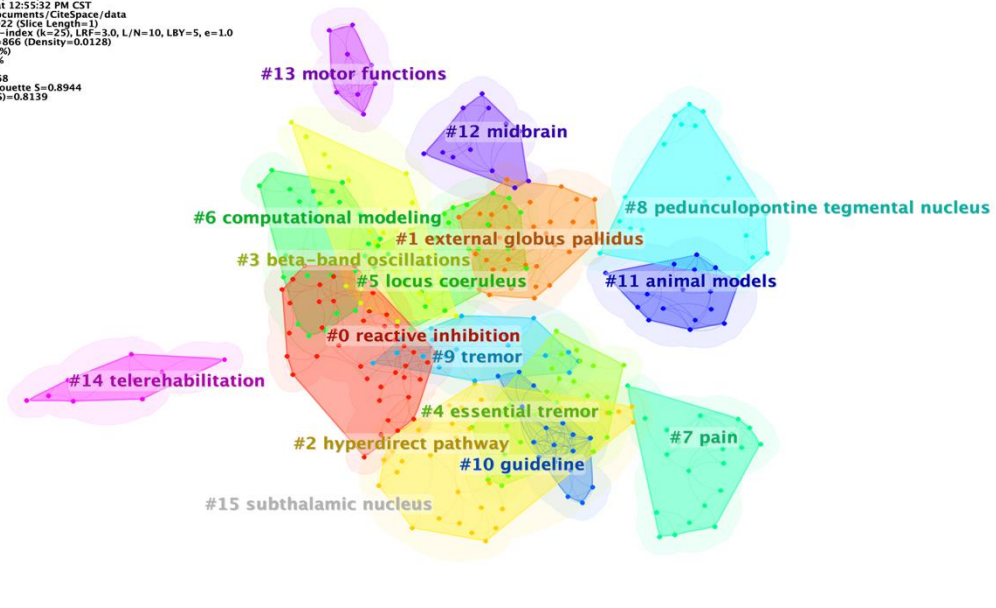


Figure 6. The map of Keyword Clustering

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 Network: N=369, E=866 (Density=0.0128)
 Largest CC: 357 (96%)
 Nodes Labeled: 3.0%

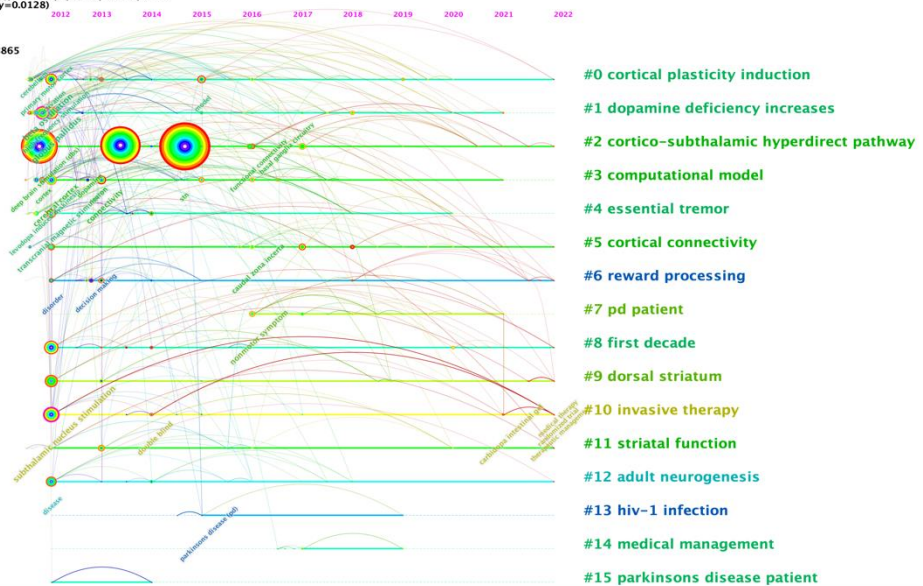


Figure 7. Timeline view of the keywords

Top 10 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2012 - 2022
neuronal activity	2012	2.48	2012	2014	
nucleus	2012	2.34	2016	2018	
hyperdirect pathway	2012	4.06	2017	2018	
external globus pallidus	2012	2.21	2017	2018	
mri	2012	2.21	2017	2018	
oscillatory activity	2012	3.08	2018	2022	
quality of life	2012	2.2	2019	2020	
rat model	2012	3	2020	2022	
motor	2012	2.72	2020	2022	
parkinson disease	2012	1.94	2020	2022	

Figure 8. The top 10 keywords with the strongest citation bursts

Keywords with the Strongest Citation Bursts in 2022

Keywords	Year	Strength	Begin	End	2012 - 2022
transcranial magnetic stimulation	2012	1.35	2020	2022	
rat model	2012	3	2020	2022	
motor	2012	2.72	2020	2022	
nonmotor symptom	2012	1.83	2019	2022	
oscillatory activity	2012	3.08	2018	2022	

Figure 9. Keywords that burst up to the end of 2022

Discussion

In this bibliometric analysis, we aimed to investigate the influence of DBS treatment in the motor pathway of PD patients based on Citespace to promote understanding in this field. The results show that developed countries including the US, UK, Japan, and Germany are the main force of related studies because most of the influential institutions and authors, such as Tom Foltynie from the UCL, Andreas Horn from Charité–Universitätsmedizin Berlin, and the University of Minnesota

come from these countries/regions. However, it is noteworthy that institutions and scientists in developing countries are also contributing to the study of DBS in PD patients. Capital Medical University and Beijing Institute for Brain Disorders from China ranked 2 and 5, respectively, in the top 10 co-occurrence analysis of the institution. The journal *Brain* published the most related studies compared with other journals, and it also has the highest centrality, suggesting that *Brain* tends to be influential in this area. The most frequently co-cited article, ‘Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold’, was written by Cavanagh et al. in 2011, and included two separate studies that elaborated the communication network between the medial prefrontal cortex and the subthalamic nucleus which is closely associated with cognitive side effects of DBS⁶².

Citespace was used to identify the frontiers and spotlights through keywords with the strongest citation bursts⁶⁹⁻⁷¹. Through this analysis, we can acknowledge the development of different hotspots. The keyword ‘hyperdirect pathway’ (4.06) had the highest burst intensity. Through the recently ended keywords with citation bursts, we observed the following two study hotspots, in which transcranial magnetic stimulation and oscillatory activity were the most popular research spotlight for DBS therapy in PD patients. Transcranial magnetic stimulation is a noninvasive brain stimulation therapy that modulates neuronal excitability in brain regions through an electromagnetic field generated by coil⁷²⁻⁷⁵. As we described above, DBS is only effective for reducing rigidity and tremor. However, DBS has little effect on nonmotor symptoms, freezing of gait, and PD-related cognitive dysfunctions. Repetitive transcranial magnetic stimulation on the motor cortex was found to be effective in PD patients with non-motor symptoms and walking speed⁷⁶⁻⁷⁸. Transcranial magnetic stimulation to the right dorsolateral prefrontal cortex (DLPFC) in PD patients also improves cognitive function⁷⁹. The therapeutic effect of combining DBS and transcranial magnetic stimulation has been confirmed in previous studies⁸⁰.

In summary, this is an important study that elaborates on the progress made on DBS treatment for PD patients. However, a major limitation is that the studies related to this field are too few compared with other bibliometric analyses. In addition, some influential publications are not well known as yet which contributed to a relatively low number of citations (obliteration by incorporation)⁸¹.

Author contributions

All authors listed made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

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