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Bibliometric analysis on global Parkinson's disease research trends during 1991–2006

Tao Li[a], Yuh-Shan Ho[b], Cheng-Yan Li[a,*]

[a] Department of Neurology, Renmin Hospital, Wuhan University, Wuhan 430060, China
[b] Bibliometric & Research Centre, I-Shou University, No. 1, Section 1, Hsueh-Cheng Road, Ta-Hsu Hsiang, Kaohsiung County 840, Taiwan

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ABSTRACT

In 10 years, we will mark the 200th anniversary of the James Parkinson's original description of the disease that now bears his name. This study was to explore an alternative statistical approach to quantitatively and qualitatively assessing current research trends on global Parkinson's disease, using the related literatures from the Institute for Scientific Information (ISI) Web of Science databases during the period of 1991–2006. Articles were concentrated on the analysis by scientific output characters, world collaboration, and the frequency of author keywords used. An exponential regression was applied to model the high correlation between cumulative number of articles and the year. International collaborative articles were more prevalent in recent years than earlier years, and increasing international collaboration would lead to more powerful articles due to the sharing of ideas and workloads, while China, Italy, Spain, and Austria are benefit a lot from the international cooperation. Finally, author keywords were analyzed contrastively, with research trends and recent hotspots provided.

In 1817, James Parkinson's Essay on Shaking Palsy published in *Neely and Jones*, provided the first clear clinical description for a progressive disorder. The disease, once called 'shaking palsy' [16], now carries the Hoxton apothecary's name, has been increasingly recognized throughout the world and his birthday 11 April, then, has become World Parkinson's Day, symbolized by the James Parkinson tulip [21]. Following cancer and cardio-cerebral-vascular diseases, Parkinson's disease (PD) has become the third most common killer for the old people in the contemporary world, affecting about 0.5% of people aged from 65 to 74 and 1–2% of people aged 75 and over [6]. Almost two centuries after Parkinson's seminal description, enormous leaps have been taken in our understanding of the pathogenesis and molecular pathology of his malady, however, rudimentary phenomenological and semantic issues remain unresolved [14]. Basic observational studies relating to quantitative and qualitative characteristics of its global research trends have not been given the sufficient attention they warrant [22].

During the past couple of decades, in the medical research fields, there has been an increasing interest in using bibliometric information for quantitative analysis and for obtaining statistics that measure the contribution of scientific publications to the advancement of knowledge within a given topic or country [15]. Mela and Cimmino [15] evaluate the distribution and scope of papers published by the European Union (EU) in rheumatological journals and the impact of rheumatological research in the EU in comparison with that produced elsewhere. Scientific publications indeed represent current research trends and can be used to identify the focus of present, past, or future research [8]. However, traditional bibliometric analysis in medical research has two inherent deficiencies: on the one hand, their original data are usually partial. Some studies only select several journals or categories to represent global research trends related to a topic [13,15]; on the other hand, the change in the citations or publication counts of countries and organizations cannot completely indicate the development trend or future orientation of the research field [3]. More information, which is closer to the research itself, such as source title, author keyword, and abstracts should be introduced in study of the research trend.

This paper presents alternative statistical methods in bibliometric analysis. Both the citation and author keywords analyses were used to describe the global trends of PD research during the period of 1991–2006. We attempt to provide all-around insights into the current state of global PD research, including annual outputs characters, international collaborations, and author keywords analyses. The results would help researchers to realize the panorama of global PD research, and point to the direction for further studies.

The documents considered in this study totally come from the Institute for Scientific Information (ISI) Web of Science in Philadel-

* Corresponding author. Tel.: +86 13 67192729; fax: +86 27 88077945.
E-mail address: fengflair@yahoo.com.cn (C.-Y. Li).

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Table 1
Articles' characteristics by year of PD scientific articles from 1991 to 2006

Year	No. A	Av. AU	No. Cr	Av. PG	Av. NR	Av. TC
1991	1,038	4.1	43	7.8	33	42
1992	1,174	4.2	46	8.0	35	41
1993	1,172	4.3	47	7.8	35	35
1994	1,327	4.7	47	8.0	36	36
1995	1,447	4.7	53	8.0	36	33
1996	1,717	4.8	54	7.6	36	31
1997	1,828	4.8	54	7.8	37	30
1998	1,931	4.8	54	7.7	37	33
1999	2,106	4.9	57	8.1	39	28
2000	2,378	4.9	60	8.1	39	27
2001	2,309	5.1	63	7.9	38	21
2002	2,453	5.2	66	8.1	40	21
2003	2,924	5.3	66	8.0	40	16
2004	2,883	5.5	67	8.3	41	12
2005	3,076	5.8	75	8.3	41	8
2006	3,452	5.8	79	8.2	40	3
Total	33,215	–	121	–	–	–
Average	2,076	5.1	–	8.0	38	22

No. A: annual number of articles; PG: page count; NR: cited reference count; Av. AU: the average number of authors; No. Cr: the number of countries participated in PD research; Av. PG: the average page count per article; Av. NR: the average cited reference count per article; Av. TC: average number of Times Cited per article.

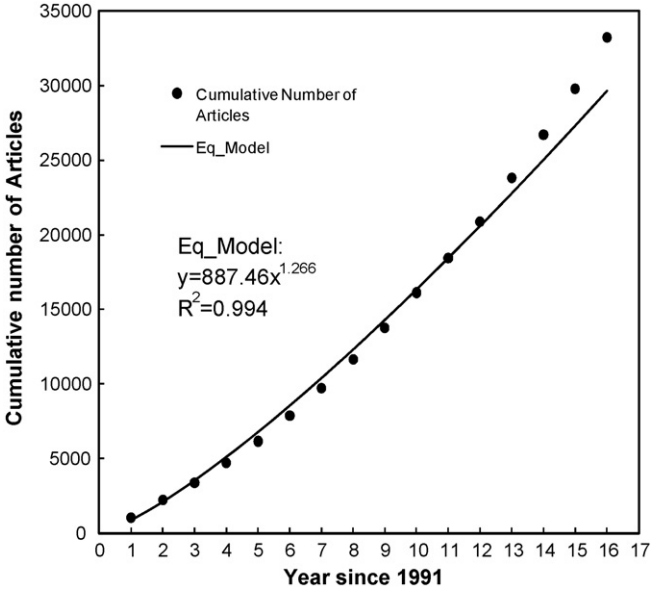

Fig. 1. Cumulative number of PD articles by year.

phia. The ISI databases provide a ready data source for bibliometric analysis. Rodrigues et al. [19] used a bibliometric indicator to map the Brazilian cancer, cardiovascular and malaria research areas from 1981 to 1995. They reported that the ISI databases can produce reliable performance indicators for the mapping of scientific capabilities and for monitoring scientific capabilities and activity in Brazil in health-related areas. We do not use the Medline database, because it does not record all the address listed on a paper, but only that of the first author. Therefore some authors are not always found and the articles retrieved are limited to those where country appears in at least one of the Medline search fields (address, title, abstract, etc.). Moreover, Medline does not provide information concerning citations of publications, while the performance of the articles can hardly be exhibited.

The keywords "parkinson" or "shaking palsy" were used to search titles, abstracts, and other keywords, from 1991, when ISI abstract search was initiated, through 2006, the last year for which complete data was available at the time of search, which indexes 6164 major journals with citation references across 172 scientific disciplines. Articles originating from England, Scotland, Northern Ireland, and Wales were re-categorized as being from the United Kingdom. The collaboration type was determined based on the address of each author, with the term 'independent article' being assigned if the addresses of the researchers were only in one country. The term 'international collaborative article' was assigned to articles co-signed by researchers from multiple countries.

There were 49,012 publications that met the selection criteria mentioned above, including 16 document types. As journal articles represented the majority of document types that were also peer-reviewed within this field, 33,215 articles (68%) were identified and further analyzed in this study.

Several publication outputs characters of current PD research during the time span of 1991 through 2006 was summarized in Table 1. The annual number of articles, the average number of authors, and the annual number of countries and journals published PD-related literature increased significantly. 1038 articles were published in 1991, while the number of publications rose to 3076 in 2005 and 3452 in 2006. There is an average of 4.1 authors per PD article in the year 1991, while the number steadily increasing to 5.8 in 2006. The annual number of countries participated in PD research increased fast during the past 16 years, from a minimum of 43 countries in 1991 to a maximum of 79 in 2006. The average article lengths fluctuated slightly, with an overall average of 8 pages. Thirty-three references were cited per article in 1991, compared to 40 references per article in 2006, with the number slightly increased through the 16 years. As Times Cited (TC) for an article is highly correlated with the length of time since its publication [10], it can be seen in Table 1 that average TC of individual PD article distinctly reduced in our study period.

For further study, a significant correlation was found between the yearly cumulative number of publications and the year from 1991 to 2006 (Fig. 1). In this study period, the cumulative progression was simulated by an exponential model, which can be expressed as follows:

$$P = 887.46Y^{1.266} \quad (1)$$

Due to the high coefficients of determination ($r^2 = 0.994$) of Eq. (1), the world publications related to PD research could be estimated using this model. It can be predicted that the number of scientific articles on the topic of PD is still growing at a high rate in the future. Moreover, it can be calculated that, in 2018, the number of scientific articles on the topic of PD will be twice of the number of publications in 2006.

Besides PD, Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Huntington's disease (HD) and Friedreich's ataxia (FRDA) are all neurodegenerative diseases, associating with the presence of abnormal proteins. Although similar publication search results indicate obviously increasing activities among all these disease above during the period of 1991–2006, it can be seen as a trend that neurological researchers focus more attention on AD (86,232 ISI publications including all document types), MS (57,879), and PD (49,012), with less concern on HD (13,636) and FRDA (995).

Author address information was not available for 178 (5‰) articles in the ISI. Thus, 33,037 articles were included in this part of analysis. Analyzing all the countries producing PD papers, the mainstream of participation and collaboration on PD research was obtained. Among the total 121 countries/territories over the investigation period, 46 countries/territories had no publication output during 1991–1996, and 11 countries/territories just began to publish papers in the year 2006. Top 15 most productive countries

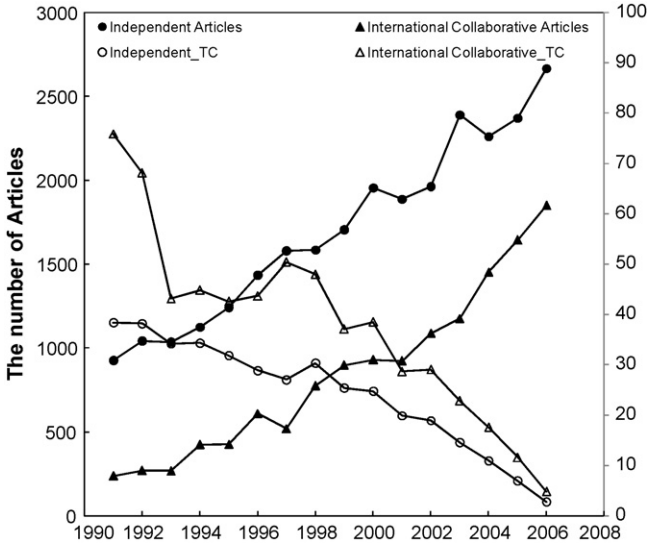

Fig. 2. Comparison the growth trends of international collaborative and independent PD articles in the world in number and Times Cited during the last 16 years.

participated in more than 90% of all world PD articles from ISI database, while thirty countries (25%) published only one article. Domination and imbalance in publication from mainstream countries was not surprising since this pattern occurred in most scientific fields [4].

Collaboration among countries, playing an ever-growing role in contemporary scientific research, can usually manifest itself in internationally co-authored papers tracked by bibliometric tools [20]. Among the 33,037 articles with address information, 82% were publications from single country, and others were international collaborative work. In Fig. 2, international collaborative articles were more prevalent in recent years than earlier years, from a 20% percentage of world ISI articles in 1991 to 41% in 2006. In general, the ascending trend of collaborative article proportion to world publication was somewhat owing to the rising number of institutes and countries that engaged in the research, and the increased ease of communication in a technologically connected world. Moreover, TC indicators of international collaborative articles are much higher than that of independent publications all through the study period (Fig. 2), which indicates that international collaborative articles have higher visibility than others. Of all the 33,215 PD articles during our investigation period, 30,055 (90%) papers had a TC value. Among them, 5556 articles are international collaborative publications. These articles had an average TC of 30, while the others by single countries had a lower average TC of 23. Therefore, it would be reasonable to assume that more international collaboration would lead to more powerful articles due to the sharing of ideas and workloads. However, the total papers from 32 developing countries were signed by at least one foreign author, which may also reveal the incapability in independent conducting research. They probably still need more help from the developed nations to do more research in this field.

The top 15 countries/territories were ranked by number of publications, including the number and TC of single country articles and international collaborated articles (Table 2). Two North American countries, ten European countries, two Asian countries, and Australia were ranked in the top 15 of publications. There are still no African or Latin American countries getting into the top 20 productive countries. These 15 productive countries occupied 99% of international collaborated articles, which indicated their great ability in the PD research fields. The countries or regions with the highest average TC scores for both independent and international collaborative papers were USA and UK. China has the lowest average TC per article among all the top 15 countries. As has been stated above, the average TC indicators of all the 15 countries' international collaborative articles are markedly higher than their national independent articles. Large increases in average TC can be easily found between the independent and international collaborative articles of China, Italy, Spain, and Austria, which indicates that these countries benefit a lot in the international cooperation.

Author keywords, by supplying 'reasonably' details of the articles' subject, could offer the information of research trend which is most concerned by researchers. Bibliometric method concerning author keywords analysis can only be found in recently years, whereas using the author keywords to analyze the trend of research is much more infrequent [3]. The technique of statistical analysis of keywords might be aimed at discovering directions of science, and prove important for monitoring development of science and programs [9]. Author keywords appeared in the articles refer to on PD from 1991 to 2006 were calculated and ranked by total 16-year study and 8-year-time periods. Those appeared more than 400 times in last 16 years are displayed in Table 3, and research changes can be roughly found occurred. 'Parkinson's disease', 'Parkinsons disease', 'Parkinsonism', and 'Parkinson disease' are four common

Table 2
Most productive countries or regions (total, single and cooperation) in Parkinson's disease research from 1991 to 2006

Country/region	TP	Independent			International collaborative			CP/TP (%)
		IP	TC	Av. TC	CP	TC	Av. TC	
USA	12,775	9725	278,885	29	3050	103,141	34	24
UK	3,637	2275	65,729	29	1362	46,871	34	37
Germany	3,225	1999	28,538	14	1226	34,907	28	38
Japan	3,058	2445	36,109	15	613	18,758	31	20
France	2,221	1409	29,818	21	812	27,904	34	37
Italy	2,159	1416	17,644	12	743	25,004	34	34
Canada	1,947	1156	27,581	24	791	29,561	37	41
Spain	1,262	872	10,617	12	390	10,957	28	31
Sweden	942	459	10,800	24	483	15,906	33	51
Netherlands	903	503	9,546	19	400	12,355	31	44
Australia	863	566	8,882	16	297	7,122	24	34
Israel	629	407	7,379	18	222	7,473	34	35
Switzerland	602	233	5,281	23	369	10,020	27	61
Austria	593	264	3,665	14	329	10,456	32	55
China	459	245	1,363	5.6	214	3,703	17	47

IP: the number of independent articles; CP: the number of international collaborative articles; TP, total articles; CP/TP, the percentage of international collaborative publications in total publications.

Table 3
Frequency of author keywords used more than 400 times in world PD research articles

Author keywords	1991–2006		1991–1998		1999–2006	
	P	*R* (%)	*P*	*R* (%)	*P*	*R* (%)
Parkinson's disease	7543	1(33)	1458	1(13)	6085	1(28)
Dopamine	2022	2(9)	742	3(6.4)	1280	2(5.9)
Parkinsons disease ↓	1183	3(5.2)	1169	2(10)	14	621(0.065)
Basal ganglia	890	4(3.9)	245	7(2.1)	645	3(3)
Parkinsonism	885	5(3.9)	323	5(2.8)	562	5(2.6)
Striatum	867	6(3.8)	333	4(2.9)	534	6(2.5)
Alzheimer's disease	772	7(3.4)	178	14(1.5)	594	4(2.8)
Substantia nigra	741	8(3.3)	241	8(2.1)	500	9(2.3)
MPTP ↓	680	9(3.0)	248	6(2.1)	432	14(2)
Oxidative stress ↑	639	10(2.8)	117	21(1)	522	7(2.4)
Neurodegeneration ↑	593	11(2.6)	82	33(0.7)	511	8(2.4)
Apoptosis ↑	566	12(2.5)	96	26(0.83)	470	12(2.2)
Levodopa ↓	553	13(2.4)	189	9(1.6)	364	17(1.7)
Neuroprotection ↑	532	14(2.4)	83	32(0.71)	449	13(2.1)
Dementia	522	15(2.3)	179	12(1.5)	343	19(1.6)
6-Hydroxydopamine	521	16(2.3)	177	15(1.5)	344	18(1.6)
Alpha-synuclein ↑	504	17(2.2)	12	350(0.1)	492	10(2.3)
Deep brain stimulation ↑	497	18(2.2)	12	350(0.1)	485	11(2.2)
Parkinson disease	492	19(2.2)	89	29(0.76)	403	15(1.9)
Rat	450	20(2.0)	182	11(1.6)	268	22(1.2)
Subthalamic nucleus	447	21(2.0)	48	74(0.41)	399	16(1.8)
Tyrosine hydroxylase	435	22(1.9)	133	18(1.1)	302	20(1.4)
L-DOPA ↓	421	23(1.9)	167	16(1.4)	254	24(1.2)
Aging	410	24(1.8)	179	12(1.5)	231	26(1.1)

P: publications in the study period; *R* (%): the rank and percentage of the author keyword; ↓ percentage went down significantly over time; ↑ percentage went down significantly over time.

author keywords to name this shaking palsy disease, while 'Parkinsons disease' was gradually abandoned in the period of 1999–2006. Apart from 'Parkinson's disease' and 'Parkinsons disease', the other two most frequently searching keywords were 'dopamine' (2022, 9%) and 'basal ganglia' (890, 3.9%) in this study. One believes that the cause of PD is a 'dopamine' deficiency in the 'basal ganglia' of the brain [12]. Dopamine is a neurotransmitter, a chemical messenger in the nervous system. It is discovered that when dopamine supply is abnormally low, Parkinson's symptoms start to appear [7]. Bernheim et al. [1] reasoned that it would possibly help Parkinson patients if the level of dopamine was restored to normal levels, therefore primal treatments in PD research would tend to boost the dopamine production up to higher levels. Besides, researchers expressed sustaining concern on 'striatum' (867, 3.8%) and 'substantia nigra' (741, 3.3%) during the past 16 years. It was discovered that the 'substantia nigra' had lost its pigment in Parkinson patients [2]. As has been mentioned above, subsequent studies showed that dopamine levels in the 'striatum' were drastically reduced. These observations suggests that the dopaminergic pathway between the striatum and substantia nigra are degenerated in PD patients, while the frontal cortex is less activated which would account for most of the Parkinsonian symptoms [11].

The cause of PD is still disputed, so large amount of studies are focus on its pathogenesis. When in the early 1980s, several users of an illegal drug developed Parkinsonian symptoms. It was discovered that this was caused by a toxic contamination called 'MPTP', which damaged the extra pyramidal nervous system, and resulted to PD [11]. So MPTP was once frequently used in animal models to understand how it causes Parkinsonian symptoms. But it can be seen in Table 3 that the percentage of 'MPTP' significantly decreased in the period of 1999–2006, which indicates the less use about this toxin in recent years. Similar decrease in rank and percentage can be found in 'levodopa' and 'L-DOPA'. 'Levodopa', also called 'L-DOPA', is a precursor in the biosynthesis of dopamine in nerve cells, and causes the remaining dopaminergic cells to increase the production of dopamine [5]. Therefore it was commonly used to treat PD as a medicine in the past. However, long-term use of L-DOPA frequently results in fading of the therapeutic effect and the development of serious side effects, which lead researchers to find some alternative therapy methods and accordingly the proportions of these author keywords reduced during the recent years (Table 3). We may make a conjecture that these gradually declining trends will be continue in the future PD research field due to some alternative therapy methods appear in 21st century. By contraries, 'alpha-synuclein' and 'deep brain stimulation' had extremely high increasing rate in ranking and percentage of all the author keywords in the study period. The number and proportion of articles including 'alpha-synuclein' boomed, from '49, 0.4%' in 1991–1998 to '674, 3.1%' in 1999–2006, which indicated apparently that 'alpha-synuclein' had attracted extensive attention during the latest 8 years. The cause research of PD concentrated on the effects of the alpha-synuclein accumulation, which represent the human understanding of PD pathology entering a new epoch [18]. Similarly, there are 533 articles referring to 'deep brain stimulation' in their author keywords, comprising 'deep brain stimulation' (497), 'deep brain stimulation (DBS)' (11), 'subthalamic nucleus deep brain stimulation' (3), 'high-frequency deep brain stimulation' (3), deep brain stimulation surgery (2), and other keywords including the same phrases, while only 13 articles used 'deep brain stimulation' before 1998. Deep brain stimulation (DBS) is a latest surgical procedure used to treat for PD, especially used for PD patients whose symptoms cannot be adequately controlled with medications. It uses a surgically implanted, battery-operated medical device called a neurostimulator – similar to a heart pacemaker and approximately the size of a stopwatch – to deliver electrical stimulation to targeted areas in the brain that control movement, and block the abnormal nerve signals that cause tremor and PD symptoms [17]. Without destroying brain tissue, DBS effectively relieve tremor and many other PD symptoms. It can be concluded that, research in the topic related on 'deep brain stimulation' application to PD therapy will undoubtedly maintain the hotspots of PD research in 21st century. In conclusion, Author key-

words analysis serves as an innovative approach for mapping global PD research.

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