



Review

Psychogenic nonepileptic seizures publications in PubMed: Geographical distribution of the publications

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ABSTRACT

Purpose: The aim of the current study was to depict a comprehensive geographical picture of the existing literature on psychogenic nonepileptic seizures (PNES) and to highlight the needs for future works.

Methods: We searched the electronic database PubMed on June 8, 2019 for articles that included any of the related key words to analyze all the relevant literature. We applied the advance search; field was adjusted to the title and dates were adjusted to 01/01/2000 until 06/08/2019. We selected the relevant articles. Location of the study was determined according to the affiliation(s) of the authors.

Results: 1017 papers were included. Interest in research and publication on PNES has risen over the past two decades. Six hundred and nine full length research original papers and 199 review articles were published on PubMed from 2000 until 2019. Continent-wise, most articles were from North America and Europe (41.1% of the whole publications from Europe and 40.8% from North America; 833 papers totally), followed by Asia (92 papers), Oceania (36 papers) and South America (31 publications), while only 0.9% of the papers (9 papers) were from Africa.

Conclusion: A global campaign is necessary to inform and educate the world on the issue of PNES and its significance. While PNES merit further epidemiological investigations, there is a significant disparity with regard to the location of the studies. There is a huge need to invest more on studies on various aspects of PNES in many places in the world, including African nations, India, and China.

1. Introduction

Psychogenic nonepileptic seizures (PNES) are common occurrences in epilepsy centers [1]. Currently, the diagnosis is often made by neurologists/epileptologists and the treatment is usually offered by psychologists/psychiatrists. But, misdiagnosis and delay in making a definite diagnosis and consequently maltreatment practices are common in these patients [2]. In addition, there is no universally accepted terminology, definition and classification system for this common condition [3,4]. Similarly, pathophysiology and neurobiological underpinnings of PNES are still poorly understood [5,6]. Finally, the current best practice in the treatment of PNES [combined cognitive behavioral therapy (CBT) with drug therapy for psychiatric problems] offers about 60% seizure reduction [7], while a follow-up study of untreated patients showed that more than half of the patients may become free of seizures after they received a definite diagnosis and with the passage of time (while receiving neither psychological nor psychiatric treatments) [8].

All the above mentioned challenges highlight the need for more

investment and research in this field. In a recent study of bibliometric analysis and visualization of the scientific landscape of the condition [9], automated textual analysis of all titles and abstracts revealed research clusters around three major topics: differential diagnosis, management and treatment, and psychopathology [9]; areas such as epidemiology, neurobiology, and outcome were scarcely investigated. This previous study did not investigate the geographical distribution of the studies on PNES.

In an international survey by the ILAE PNES Task Force [10], PNES were acknowledged as a diagnostic and therapeutic challenge in all nations. However, it is clear that what we do not know about this common condition dominates what we know and there is a great need for the scientific community to invest in this field. A primary prerequisite for any plausible and wise investment is having a good knowledge of the current situation, the pitfalls, and the opportunities ahead for meaningful advancements. The aim of the current study is to depict a picture of the geographical distribution of the existing literature in this field (based on their citations in PubMed) and to highlight

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the shortcomings and the needs for future works.

2. Materials and methods

We started our search in the electronic database PubMed on May 10, 2019 for articles that included any of the search terms that are mentioned in Table 1 to analyze all the relevant scientific literature on the topic (any publication pertaining to any aspect of PNES). We updated our search on all key-words on June 8, 2019 to have consistency for all searches. We applied the advance search; field was adjusted to the title and dates were adjusted to 01/01/2000 until 06/08/2019. We selected the relevant articles (even if they also included other patients such as those with epilepsy) after reviewing their titles, abstracts, and full texts. Duplicate articles were excluded. The search results were screened by the two first authors independently and in cases of uncertainty or dispute they were reviewed by the senior author (AAP). The following data were collected: year of publication, type of the article [full length research (original) vs. review (all kinds of review articles) vs. case reports vs. others (letters, comments, editorials)], and place of the study (i.e., country and continent). Location of the study was determined according to the affiliation(s) of all authors of the study. If they had multiple affiliations from different countries and the study was original (full length research), the nature (i.e., being multicenter or single country) was determined according to the data collection strategy in the methods section of the article. To provide the trend of the number of publications during the study period, we arbitrarily compared the two time periods: (from 2000 until 2004; the first five years) and (from 2014 until 2018; the last five years). We defined and calculated the publication per population index (PPPI) by dividing the number of the original research publications from each country during the study period by 10 million of population [number of original articles / (population/10⁷)] [11]. We used this index as an indication of the number of works that has been done per population in each country to provide a fair comparison of the geographical distribution of the publications.

3. Results

Table 1 shows the search results that were yielded from each keyword (1169 primary hints and 1099 relevant articles). After dropping duplicate articles (82 articles), 1017 papers were included in the analyses. Number of the publications on PNES has risen over the past two decades (Fig. 1); from 2000 until 2004, 171 papers were published and from 2014 until 2018, 390 papers were published in PubMed; a 128 percent increase in publications. Six hundred and nine original full length research papers (60% of the total publications) and 199 review articles (20% of the total publications) were published in PubMed from 2000 until 2019 (Fig. 2). From 2000 until 2004, 103 original full length research papers were published in PubMed and from 2014 until 2018, 223 original papers were published in PubMed; a 117 percent increase in the number of original research publications. Continent-wise, most of the articles were from Europe and North America (41.1% of the whole publications were from Europe and 40.8% were from North America; 833 papers totally), followed by Asia (92 papers; 9%) (East Asia 28 papers, South Asia 34, and West Asia 30 papers), Oceania (Australia and New Zealand) (36 papers; 3.5%) and South America (31 publications; 3%), while only 0.9% of the papers (9 papers) were from Africa (Fig. 3). Country-wise, most of the articles were from the USA (393 papers; 38.6%) and the UK (173 papers; 17%), followed by Italy (40 papers; 3.9%), India (31 papers; 3%), Australia (29 papers; 2.9%), the Netherlands (29 papers; 2.9%), Iran (28 papers; 2.8%), and Germany (28 papers; 2.8%) (Fig. 4). The UK and the Netherlands had the highest PPPI (Table 2). Only 11 original research papers (1.1%) were multicenter and international in nature in the past 20 years. Epilepsy & Behavior (302 papers; 29.7%) and Seizure - European Journal of Epilepsy (100 papers; 9.8%) published most of the articles. Epilepsia (80 papers; 7.9%), Neurology (44 papers; 4.3%), Journal of Neurology,

Table 1

Search results that were yielded from each keyword.

Keyword	Primary yield	Relevant articles
Non-epileptic seizure	7	7
Non-epileptic seizures	241	241
Nonepileptic seizure	22	22
Nonepileptic seizures	497	497
Pseudoseizure	12	12
Pseudoseizures	55	55
Pseudo-seizure	1	1
Pseudo-seizures	2	2
Nonepileptic events	35	30
Nonepileptic event	6	0
Non-epileptic event	4	0
Non-epileptic events	16	9
Pseudoepileptic seizure	2	0
Pseudoepileptic seizures	6	6
Pseudo-epileptic seizures	6	6
Pseudo-epileptic seizure	0	0
Psychogenic Seizure	4	4
Psychogenic Seizures	39	39
Psychogenic event	8	0
Psychogenic events	2	2
Psychogenic Seizure-like event	0	0
Psychogenic Seizure-like events	1	1
Seizure-like episode	1	0
Seizure -like episodes	6	1
Hysteroepilepsy	0	0
Hystero-epilepsy	0	0
Psychogenic nonepileptic attack	4	4
Nonepileptic attack	11	11
Psychogenic nonepileptic attacks	6	6
Nonepileptic attacks	10	10
Psychogenic non-epileptic attacks	3	3
Non-epileptic attacks	6	6
Psychogenic non-epileptic attack	4	4
Non-epileptic attack	15	13
Psychogenic attack	15	8
Psychogenic attacks	3	3
Psychogenic event	8	3
Psychogenic events	2	2
Psychogenic episode	4	0
Psychogenic episodes	0	0
Nonepileptic episode	1	0
Nonepileptic episodes	5	2
Non-epileptic episodes	0	0
Non-epileptic episode	1	0
Psychogenic nonepileptic episode	0	0
Psychogenic nonepileptic episodes	3	3
Psychogenic non-epileptic episodes	0	0
Psychogenic non-epileptic episode	1	0
Dissociative seizure	12	8
Dissociative seizures	18	18
PNES (Psychogenic non-epileptic seizures)	50	48
PNESD (Psychogenic non-epileptic seizures disorder)	0	0
PWNES (Patient with nonepileptic seizure)	0	0
Functional non epileptic attack	0	0
Functional non epileptic attacks	3	3
FNEA (Functional non epileptic attack)	0	0
Hysterical seizures	1	1
Hysterical seizure	0	0
Non epileptic spell	0	0
Non epileptic spells	2	0
Functional non epileptic attack	0	0
Functional non epileptic attacks	3	3
Dissociative convulsion	2	2
Dissociative convulsions	3	3
Total	1169	1099

*82 relevant papers were duplicates and were dropped.

Neurosurgery and Psychiatry (26 papers; 2.6%), and Psychosomatics (19 papers; 1.9%) also published a large number of the articles. Only 22 authors published five or more papers (as the first author) during the study period (Fig. 5). Twenty-one of these authors were from the North America, Europe, and Oceania.

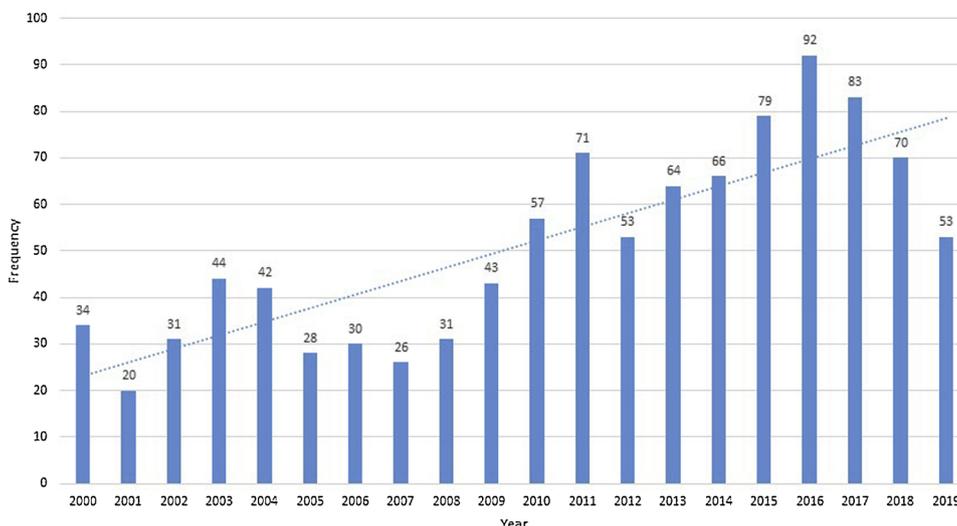


Fig. 1. Interest in publication on psychogenic nonepileptic seizures has risen over the past two decades. Data on publications during 2019 includes: 1/1/2019 to 06/08/2019.

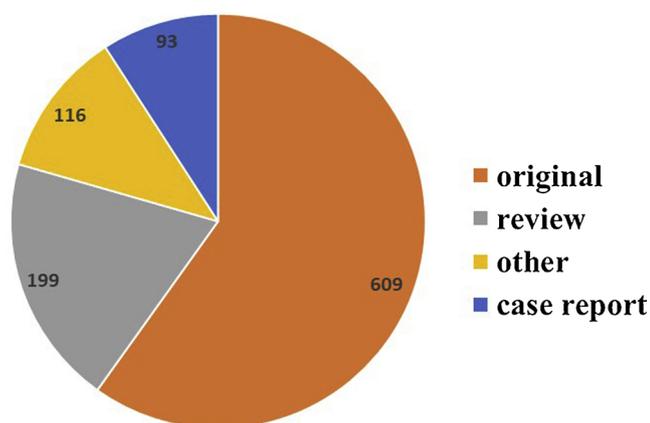


Fig. 2. 60% of total publications were original research articles and 20% of total publications were reviews.

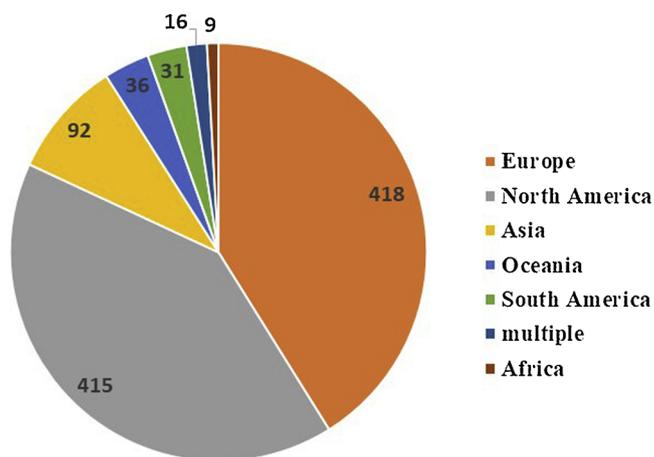


Fig. 3. Continent-wise most of the articles were from Europe and North America (81%), while only 0.9% of the papers were from Africa.

4. Discussion

We analyzed 1017 articles, which were published in PubMed since January 2000, on PNES. We did not investigate other databases and sources. However, considering the size of the study and the good reputation of the journals that are indexed in PubMed, we believe that this has not affected our results and conclusions significantly. While we tried to include all publications with citations in PubMed, we may have missed some information, because for example, some co-authors' affiliations may not have been indexed in PubMed before 2013 [12].

We observed that the number of the publications on PNES has risen over the past two decades; this is consistent with the general trend for all publications in the literature (in PubMed) [12]. While the number of published articles superficially looks impressive, our analyses showed many shortcomings in the field. Firstly, just 30 original research articles per year were published in the past two decades, which is a very disappointing number considering the fact that PNES is relatively a common condition; incidence of PNES was estimated to be 1.4–4.9/

100,000 population/year and the prevalence was calculated to be up to 33 per 100,000 population, making it a significant neuropsychiatric condition [1]. While interest in research and publication on PNES shows a steady increase (Fig. 1), it is yet not enough to tackle all the issues and challenges around this relatively common condition (some of which were listed in the introduction). However, we are not sure that simply pumping out a greater number of publications would do that much for patients with PNES. Rather, we believe it is more likely that in-depth research in certain key areas (e.g., epidemiology, neurobiology, treatment, long-term outcome) result in significant changes/improvements for these patients. Therefore, it seems that a global campaign is necessary to inform and educate the world (lay people, authorities, industry and professionals) on the issue of PNES and its significance. This may attract attentions and seek and convince sponsors and researchers to invest more in the field. For example, everybody should know that PNES is a common occurrence [1] and compared to epilepsy, people with PNES have consistently reported worse health-related quality of life [13]. Secondly, while most of the effort by the

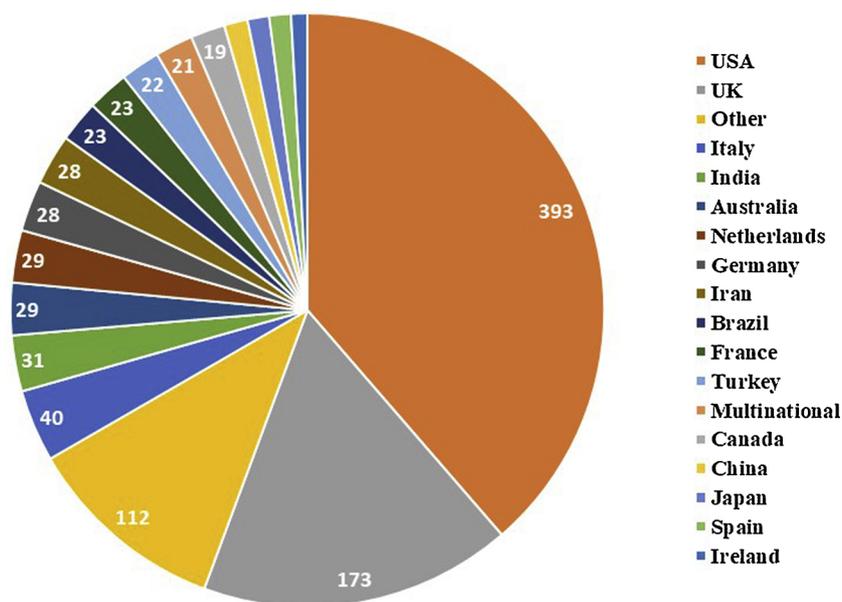


Fig. 4. Most of the published articles were from the USA and the UK.

Table 2

Paper per population index for countries with more than 10 original research publications.

Country	Population /10 million	Original papers	Paper per population index
UK	6.69	108	16.14
Netherlands	1.71	20	11.70
Australia	2.50	20	8
USA	32.90	218	6.63
Italy	5.92	19	3.21
Canada	3.72	10	2.69
Iran	8.28	20	2.42
Turkey	8.29	20	2.41
Germany	8.24	18	2.18
France	6.54	10	1.53
Brazil	21.23	17	0.80
India	136.87	19	0.14
China	142.00	10	0.07

scientific community has been devoted to the research on the differential diagnosis, management, and psychopathology [9], there are scarcity of studies on neurobiology and the outcome of PNES; the scenario on the epidemiological studies is even worse [1,9]. Obviously, any plausible clinical study on any medical condition depends on many layers of the background knowledge including (but, not limited to) the epidemiology of the condition and its biological underpinnings. Clearly, an international consensus about PNES terminology, definition and classification is very helpful and is very much needed if we are to standardize measures that can be used in future research in this area [4]; by looking at the Table 1, we can observe the chaotic situation in the fundamentals of this condition (i.e., terminology) that exists among the scientific community!

Finally and probably more importantly, by looking at the numbers of the publications on PNES in different geographical areas of the world, we can notice that there is a significant disparity with regards to the distribution and location of the studies. While PNES represent a universal human condition and are recognized as a worldwide phenomenon [10], more than 80% of all publications have come from North America and Europe (with 1.3 billion population together) and less than 1% are from Africa with 1.2 billion population or only 1.3% of

the publications are from China with 1.4 billion population (Fig. 3). Therefore and obviously, we lack enough information on all aspects of PNES (including its semiology) in places like Africa, India, and China. Interestingly, in two recent multicenter international studies we observed that there were significant semiological differences between the countries, both in adults and in children with PNES [14,15]. Therefore, in order to have a clear worldwide picture of the semiology of PNES there is a huge and significant need to invest more on research in PNES in many places in the world including African nations, India and China, among other developing countries [e.g., paper per population index was very low for India and China, the two most populated countries in the world (Table 2)]. A potentially smart strategy is to have a geographically focused transition of the research priorities. While, the Western countries (e.g., North America and Europe) may focus on the largely unresolved issues such as epidemiology, neurobiology and treatment strategies in PNES, developing nations may focus on the semiology and psychopathology of PNES in their regions (since even data on well-published topics is still needed for these latter regions).Of course, the geographical disparity in the scientific productions is not limited to the field of PNES, rather it is widely observed in other fields as well [16,17]; findings for PNES research have followed the general trends and are not unusual in any ways. We should keep in mind that international cross-cultural studies can make important contributions to our understanding of PNES across cultures and borders [14,15,18,19]. Unfortunately, so far very little attempt has been made to carry out such studies.

Contributions

Ali A. Asadi-Pooya, M.D.: Idea development, study design, statistical analysis, manuscript preparation. Others: Data collection, statistical analysis, manuscript preparation.

Disclosures

Dr. Ali A. Asadi-Pooya, M.D., consultant: UCB Pharma; Honorarium: Cobel Daruo, Sanofi, and RaymandRad; Royalty: Oxford University Press (Book publication). Others report no disclosures.

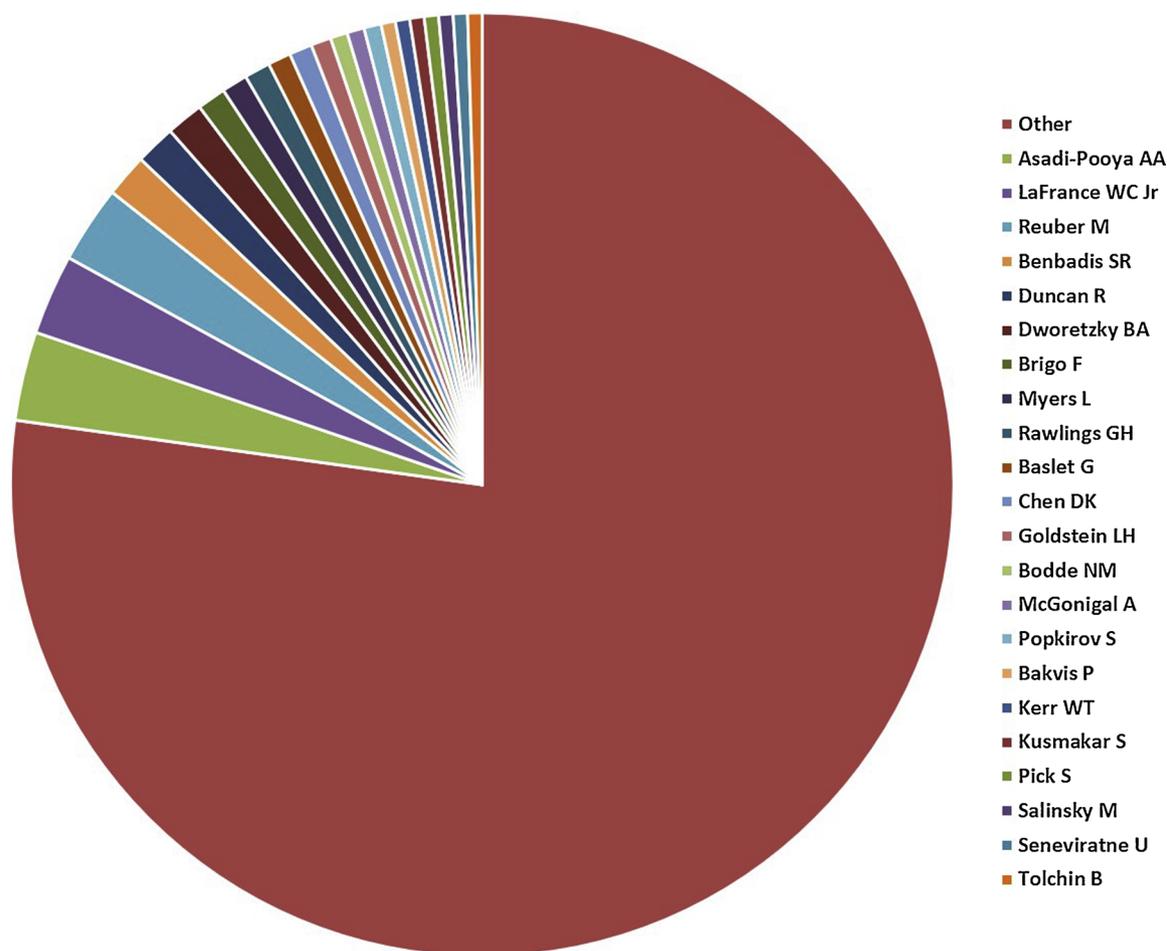


Fig. 5. Only 22 authors published five or more papers (as the first author) during the study period.

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This was an unfunded study.

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