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Review Article

Parkinson's genetics research on underrepresented AfrAbia populations: current state and future prospects

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Abstract: Parkinson's disease (PD), the most common motoric neurodegenerative illness, has been extensively researched to better understand its complex pathophysiology. Nearly 80% of genome-wide association studies have been conducted on persons of European ancestry, indicating a lack of diversity in human genetics. Disparate representation may result in disparities that impede the equitable adoption of personalized medicine and may also limit our knowledge of illness etiology. Even though Parkinson's disease (PD) is a global affliction, the AfrAbia population remains understudied. We conducted a dynamic and longitudinal bibliometric analysis to investigate existing studies on Parkinson's disease genetics in the AfrAbia area and identify data gaps and possible new research avenues. All PD papers concentrating on PD genetics were found using the search terms "Parkinson's Disease", "Genetics", and "Africa" in the PubMed/MEDLINE database. Only English publications published between 1992 and 2023 were chosen using filters. Original English-language research publications disclosing genetic results on Parkinson's disease in non-European Africans were examined for inclusion. Two sets of independent reviewers discovered and extracted pertinent data. The bibliometric study was carried out using the R software packages Bibliometrix and Biblioshiny. The narrowed search yielded 43 publications, all published between 2006 and 2022. Yet, after applying filters and considering the inclusion requirements, the search results comprise just 16 original articles out of 43 articles. There were 27 articles eliminated. This study puts emphasis on the critical need for more diverse participant demographics in Parkinson's disease investigations. AfrAbia-PD-Genetic Consortium (AAPDGC) is GP2 initiative that helps to represent AfrAbia PD genetics.

Keywords: AfrAbia, Parkinson's disease, genome wide association study, genetic, challenges, bibliometric analysis, AfrAbia-PD-Genetic Consortium (AAPDGC)

Introduction

Parkinson's disease (PD) affects 1% of the global population. It disproportionately affects the elderly and has major effects for their quality of life [1, 2]. Neuron loss in sensitive brain regions (particularly, but not solely, the substantia nigra) and the formation of Lewy bodies in the few neurons that survive are assumed to be the result of a complex interplay between genetic and environmental factors [3]. According to an assessment of the indexed literature, African scholars have published relatively little about Parkinson's disease. AfrAbia is experiencing a demographic change that will result in an older population (an increase in the percentage of people aged 65 and over) by 2050, as well as a rise in the prevalence of diseases that mostly affect the elderly, such as Parkinson's disease [4].

The loss of substantia nigra pars compacta (SNpc) mesodiencephalic dopaminergic (mdDA) neurons is a hallmark of Parkinson's disease (PD) [5, 6]. Lewy bodies, which are seen in some of PD's surviving neurons, are another diagnostic feature of the disorder. Motor, sensorymotor, and motivational actions are all under tight regulation by mdDA neurons [7, 8]. Several motor and non-motor PD symptoms may be traced back to the degeneration of these cells [6]. Resting tremor, bradykinesia, stiffness, postural instability, and many more are all examples of such symptoms. Since symptoms often don't appear until a person has lost 50-60% of their DA neurons [6], more frequent

examinations are required. Most instances of PD have no identifiable cause. Single-gene mutations (SNCA, LRRK2, and VPS35) and double-gene mutations (PARK2, PINK1, and DJ1) account for 5% to 10% of PD patients, respectively [9, 10]. While the molecular function of the newly discovered loci associated with PD remains unclear, many more have been discovered in recent years [9]. The various uncommon mutations found only in one family or in small groups contribute to the high genetic heterogeneity that underlies PD [9]. After years of research, the pathogenic mechanisms that lead to PD remain mostly unknown [10]. Next Generation Sequencing (NGS) methods are widely used in the diagnostic field, but their application to PD is still limited to a small number of patients with a clear family history and to a small number of causative mutations due to the high genetic heterogeneity of the disease and the difficulty in interpreting test results.

Africa is defined by a higher incidence of diseases, trauma, and violence, as well as more exposure to harmful chemicals and starvation, against a background of significantly greater genetic variability. Many of these factors point to the potential for the African neuroscience community to make fundamental discoveries and create personalized medicines to improve brain health and well-being throughout the continent. Although the high prevalence of mental, neurological, and substance-use disorders provides unique difficulties to the African neuroscience community [11, 12], the opportunities are also vast. Low physician-to-patient ratios, for example, expose the typical clinician to a large number of patients, increasing opportunities for field-specific competence growth. This enhanced clinical exposure provides research ideas that are directly relevant to the local population and increases the feasibility of clinical investigations, benefiting not only the African community but also the Global North. In Africa, for example, recruiting patients for clinical trials on traumatic brain damage takes less time than in Europe. Finally, there is a lot of room for clinically focused neuroscience research to improve healthcare in Africa, especially for young people. Particular goals include improving developmental potential and mental health, as well as reducing mortality and neurological disability. AfrAbia includes both Arab League and African Union countries. Historical and geographical factors link the two overlapping areas of Africa and the Arab world [13].

It is well-known that researchers have a tendency to favor European people while doing genetic research. Despite efforts from major research funders, we still have a ways to go before we attain the necessary fairness [14]. A lack of diversity remains a fundamental impediment to understanding the molecular basis of the condition across all groups, despite the fact that research on PD genetics has advanced over the previous two decades. Researchers are aware of the problem posed by the lack of URPs in PD genetic studies, as well as the hazards associated with avoiding or failing to establish diversity. Yet, only a small number of these pieces rely on hard scientific evidence; the rest are mostly editorials, letters, and commentary. Despite the fact that these articles helped shed light on the issue, a thorough understanding of the geographical and ethnic extent of PD genetic research is necessary for developing a realistic road map for increasing diversity. The present investigation focused on PD genetic studies undertaken in non-European populations, namely the AfrAbia population, to better comprehend the magnitude of this bias.

Genetic and molecular diversity in PD

For a number of reasons, most genetic investigations, especially those related to Parkinson's disease (PD), are undertaken primarily with people of European descent [15]. Insufficient representation of AfrAbian communities in these studies may lead to missed opportunities for novel gene discoveries, pharmaceutical development, and advances in care for multiethnic AfrAbian people. Various population-specific variations in Parkinson's disease have been observed [16, 17], revealing a male predominance in the disease. Similarly, genetic studies have shown demographic differences in both monogenic and complex Parkinson's disease. The LRRK2 G2019S variant is more frequent in Ashkenazi Jewish, North African, and European people and very rare in East Asian people, while the G2385R variant is only seen in East Asian people [18, 19]. These two LRRK2 protein variants correspond to separate functional domains [20]. Although kinase activity may not be linked to PD pathogenicity, East

Asians (with a carrier incidence of 6-11%) are likely to need a different PD medication that targets LRRK2 than other ethnicities [19]. Because of the discrepancy in occurrence between communities, it is vital to gather information concerning variation affects from local populations [21-23]. Similar issues are caused by the GBA gene. If mutations are limited to one ethnic group [24], the carrier frequency of GBA gene mutation varies significantly (3-31%) across populations [25]. The R163Q variant, for example, is deemed "harmless" yet is predominantly observed among East Asians. In this case, research confirming the role of pathogenicity should be conducted only in East Asia.

Demographic differences may have a role in sporadic Parkinson's disease. Foo et al. (2020) replicated the findings of some European-ancestry studies in one of the biggest East Asian Genome-Wide Association Studies (GWAS) on Parkinson's disease (PD). Notably, the researchers uncovered two previously unknown loci in European-ancestry genome-wide association studies [26]. The functional relevance of these discoveries is unknown, but they underline the need for more research to solve the puzzle of PD pathogenicity. Atypical Parkinson's disease and other neurological diseases are affected by the same variables. The polygenic risk score, when combined with regional data, might be one of these strategies [27].

East Asians, particularly Han Chinese, tend to have the LRRK2 G2385R and R1628P variants. It has been shown that Japanese and Koreans are more likely to have the G2385R variety than the R1628P version [28], whereas Thais are the other way around. High rates of PD were associated with the G2385R and R1628P polymorphisms in both the Malay and Chinese populations in Malaysia [29]. The N551K variant has been shown to prevent Malay individuals from developing Parkinson's disease [30], but these results need to be replicated in Malay communities from other Southeast Asian countries including Indonesia and the Philippines. In Malaysia, where several races coexist, researchers looked at how GBA differs between the Malay, Chinese, and Indian populations. The most common mutation was L483P, although researchers also found P71L, L411P, and L15S. Common European risk variants E365K, T408M, and N409S were not found [31]. In a study limited to the Malay community, Mohamad Pakarulrazy et al. [32] discovered that GBA polymorphisms were associated with PD and might change the age of onset; a similar finding was made in Thai populations [33].

It is possible that ethnic differences have a role in recessive variants of genetic PD. The PINK1 L347P variation, which has not been seen in other groups, was more prevalent among Filipinos [34]. Recent reports in Malay ethnic groups [35] and in two individuals of Indian heritage in Malaysia [36] corroborate the pathogenicity of the L347P mutation. Another example of population differences is the PINK1 variation reported in Vietnamese people with PD, where the A340T variant was more prevalent in early-onset PD (EOPD, OR = 5,704) [37]; the reverse connection was seen in Han Chinese populations [38]. Although these results emphasize genetic variety, the sample sizes of the majority of research were tiny. Similarly, in order to clarify the genetic architecture of PD in AfrAbia communities, bigger research are required.

Several consortiums were formed in Africa [39], Central Asia, East Asia [40], Latin America [41], and South Asia to address this dearth of diversity [42]. Their major goal is to investigate the genetic basis of Parkinson's disease in several populations [43]. Importantly, these consortiums have started transitioning from a largely genetic relationship to a platform for researchers to join new partnerships and solve critical clinical issues. The more our understanding of PD, the more efficiently we can manage our patients. We should encourage more diversity in the research of PD and actively promote this among the larger community in order to gather more support.

Genome wide association (GWA) for AfrAbia PD: challenges and hopes

Since the Human Genome Project, new large-scale, high-throughput sequencing tools have emerged for genotyping and DNA sequencing, making it possible to conduct a huge number of genome-wide association studies (GWASs). Yet, as prior analyses of GWAS datasets have demonstrated, these studies have failed in a critical respect: they do not effectively represent genetic variation on a worldwide scale. These

methods and their supporting analyses have transformed disease genetics research. Whether of sample availability, financial restrictions, recruitment obstacles, or statistical power, populations of European ancestry continue to make up the bulk of included individuals [44, 45]. This similarity has stifled research into potentially fruitful fresh directions, such as the discovery of novel genetic links for complex features or the discovery of novel genetic origins of monogenic forms of sickness. Hence, it may impede the progress of precision medicine and endanger the health of at-risk people [45-47].

Parkinson's disease (PD) is classified as a multifactorial disorder due to the complex interaction of inherited and environmental factors. Considering the absence of a cure or prophylactic treatment, studying the disease's origin is critical for developing medical improvements. Over 20 genes have been related to familial or monogenic variants of Parkinson's disease, which are more frequent in persons of European heritage [48]. In a recent GWAS meta-analysis, ninety risk alleles were postulated, accounting for about a quarter of the illness's heritability. Since only persons of European ancestry were included in this study, there are limits to the replicability of these results to populations that were not included in this study [49]. East Asians were recently discovered to have the highest PD GWAS outside of Europe [26]. The research included over 7,000 persons with Parkinson's disease, and two additional risk loci were found. Although the number of PD genetics research has increased over the past two decades, a lack of diversity between study groups remains a key impediment to development in this field.

Like the rest of genetics, GWASs are plagued by a bias towards European groups. Progress toward the essential equity is gradual and insufficient [50], despite the fact that key research funders have started striving to overcome this problem. To further explain this prejudice, Schumacher-Schuh et al. [15] looked into PD genetic studies in non-European groups, which include people of many different races. Almost half of the research is devoted to the people of Greater China, with the rest split between the people of the Middle East and North Africa, East Asia (other than Chinese people), and Latin America and the Caribbean. Also, they discovered that increasing the number of publications in Greater China each year was the most effective technique for bringing more people from underrepresented groups into genetics research [44]. Yet just five books were released that dealt with Central Asia specifically, and all of them were authored by authors outside the area. Black Americans made up just 4% of study participants, and there was no growth in the number of studies focusing on this population over time. The bulk of the world's Black population resides in low- and middle-income countries in sub-Saharan Africa and South America. Hence, financial restrictions promote a lack of investment and progress toward research and innovation, particularly for noncommunicable disorders like PD. As a corollary, many areas in the AfrAbia region lack fast access to neurologists and other sorts of expert medical personnel who may aid in the identification of sickness. Last but not least, historical bias and misconceptions regarding the purpose of research are associated to lower participation rates among this demographic. Nevertheless, PD is a logistical and financial burden because of the necessity to recruit massive samples in order to have adequate power to identify minor effects and correct for confounders. It is more feasible to study monogenic forms in countries with lower per capita GDP due to the reduced sample size needed for such studies. Genetic analysis for rare forms may be expensive, but it may be viable to do so through international partnerships with research facilities in nations with higher per capita revenues. The largest sample sizes were found in studies of Asian populations, especially in Greater China, suggesting that this may be a proxy for the study's reliability.

A high sample size is essential for genetic research, making joint studies crucial. A research network may also benefit developing countries by increasing their authority, facilitating data interchange, and extending their research capacity. According to the research, the United States, Germany, and Canada play an important role in increasing variety by collaborating with countries that have a high prevalence of URPs. South Asian and Greater China population PD genetic study relies mostly on samples from a single institution, with little international collaborations. South and Southeast Asia saw an increase in the number of local multicenter studies, although overseas

collaborations remained limited. Collaboration indicators such as the number of authors per publication and the percentage of articles published by authors from a single country both indicate a lower rate of cooperation among Asians, adding validity to these results. This tendency might be explained in part by Asia's expanded research capacity, notably in East and Southeast Asia.

There are several countries where significant international collaborations might be hindered by strong local restrictions on data and biospecimen sharing, which are meant to prioritize and improve local skills. Some barriers to widespread collaboration include a lack of trust between therapists and researchers from diverse socioeconomic backgrounds and academic evaluation systems. If the authorship of the study is unclear, a researcher from a poor nation may be unwilling to devote significant time and effort to it. Scientists in nations with limited resources for exploration may be reluctant to share their findings for concern that their "competitors" may acquire an edge. There are a number of additional factors that may contribute to the limited partnerships, such as language barriers and cultural issues that prevent people from working together. Indications of increased collaboration in research on the Middle East and North Africa include the prevalence of transnational multicenter studies and an increase in the number of authors from many countries. While the LRRK2 p.G2019S mutation is more common in North African and Ashkenazi Jewish groups, it has garnered global interest and paved the way for international collaboration [51, 52]. There is a possibility that the high upfront expenditures of developing breakthrough technologies may stimulate collaboration with more developed countries.

The lack of URPs in PD genetic studies poses a concern to researchers, as do the hazards associated with avoiding or failing to attain diversity. Yet, rather than concrete evidence, most academic publications that have addressed this topic have relied on reader comments, editorials, and letters [53]. Regardless of how valuable these articles are in bringing insight, a complete understanding of the geographical and ethnic breadth of PD genetic research is required for developing a solid road map for increasing diversity. This review aims to provide an overview of the current status in PD genetics in URPs (individuals of non-European ancestry), particularly the AfrAbian population, in order to clarify the main gaps, identify opportunities to ensure more diversity, and establish a baseline to measure the impact of future global efforts.

To summarize, AfrAbia has various challenges when it comes to GWAS and other forms of genetic research, including: 1) a dearth of high-quality and numerous prevalence and incidence studies; and 2) a lack of appropriately powered clinical trials. 3) underrepresentation in global studies, with PD not being prioritized as a public health problem, and 4) an inadequate neurological and neuroscience workforce for research, as well as an immature research infrastructure. AfrAbia, on the other hand, offers a number of promising research and development avenues, including (1) genetic uniqueness and diversity, (2) geographical and environmental influences on disease, (3) demographic shift and economic muscle, (4) investigation of health disparities and their impact on disease outcome, (5) ethical imperative and virtual learning, and (6) diversity and inclusiveness discussion with WHO PD technical brief.

AfrAbia-PD-Genetic Consortium (AAPDGC): what gives us hope?

Nearly all research that have resulted in novel approaches of detecting or treating Parkinson's disease have used White people. These results might be extended to a larger population by using genetic data from ethnically diverse African tribes, which have been shown to contain at least 10% more DNA than current human reference genomes and around 3 million extra variants [27, 54]. Just a few genetic studies on Parkinson's disease have been completed in Africa, and they have all been conducted in North Africa. They (Gouider-Khouja and colleagues) investigated the inheritance patterns of familial PD in 21 Tunisian homes [55]. They found that the onset of symptoms in familial Parkinson's disease patients happened at a younger age (as compared to reports of sporadic PD). We now know that at least two separate inheritance types exist (autosomal recessive and autosomal dominant with decreased penetrance) [55]. Tassin and colleagues [56,

57] linked autosomal recessive juvenile-onset Parkinsonism to the PARK2 gene on chromosome 6 in one Algerian family (along with 10 European families). There were clinical similarities to juvenile idiopathic Parkinson's disease. Gouider-Khouja and colleagues [58] recently presented the clinical, pathologic, and genetic findings of a Tunisian family with autosomal recessive juvenile-onset Parkinsonism caused by a mutation in the parkin gene.

Shifting gears to concentrate on Sub-Saharan Africa (SSA). Just nine studies that we are aware of have looked at the genetic origins of Parkinson's disease in SSA communities. The great majority of these case studies are about people in South Africa [59-62]. Thus far, all parkin gene mutations reported have been the result of screening for PD-causing genes, with only three patients with compound heterozygous parkin mutations identified [62, 63], two of whom are Black South Africans and one of whom is Zambian. Both the South African patient and his sister (AAO b 50 years) showed characteristic tremor-predominant Parkinson's disease. The second South African patient had tremor-predominant Parkinson's disease (PD) and was 56 years old at the time of onset. This single incident occurred in Zambia and was seen in a young individual (AAO = 16 years). Despite the considerable genetic heterogeneity throughout Africa, the pathogenic G2019S mutation in the LRRK2 gene, which is common (30-40%) in North African Arab groups [64], has yet to be discovered in a Black SSA PD patient. Since just a few mutations have been detected in SSA PD patients, it is probable that the known PD genes have a little role in the development of the illness in this population. Difficulties with diagnosis and low referral rates may contribute for the relatively low number of Black people evaluated in published research (the largest study had just 57 participants, with less than 200 patients overall across all studies) [65].

The Global Parkinson's Genetics Program (GP2) has an AfrAbian initiative named the AfrAbia-PD-Genomic Consortium to better investigate Parkinson's disease and other neurodegenerative disorders in AfrAbian population (AAPDGC). This Consortium is a collaboration between GP2 and academic institutions in five African countries: Ghana, Egypt, Ethiopia, Tunisia, Algeria, and the Democratic Republic of the Congo. The long-term objective of the AfrAbia consortium is to build an intracontinental network that will allow the recruitment and registration of 3,000 patients with Parkinson's disease and 3,000 healthy controls throughout AfrAbia, as well as the construction of a registry for future cooperative research. The emphasis will be on identifying genetic factors to Parkinson's disease and exploring the relationship between risk genes and disease parameters (such as disease subtypes, age of onset, and motor and nonmotor symptoms). The ultimate objective of the AfrAbia collaboration is to investigate innovative techniques to diagnosis and therapy, including as GWAS and precision medicine, for the AfrAbian Parkinson's disease population.

The partnership will assist its AfrAbia outposts in increasing their skills via training and education. Moreover, the research network is partnering with regional communities and patient advocacy groups to improve awareness of Parkinson's disease. Our initial aim is to develop culturally relevant educational materials in commonly spoken AfrAbia languages for both patients and caregivers, with the goal of eliminating stigma and improving health outcomes. We hope that the formation of the AfrAbia consortium will improve the efficiency of medical research and boost patients' health. Our basic philosophy is one of close collaboration, and we will aim to ensure that all AfrAbian researchers have equal chances and access to resources, as well as patient and public engagement.

Methods

All PD publications focusing on PD genetics were retrieved from the PubMed/MEDLINE database using the search strings "Parkinson's disease", "Genetics" and "Africa". Using filters and the following inclusion criteria: 1) only English articles published between 1992 and 2023 were selected, 2) documents type include case report and journal article revealing genetics findings on PD in non-European African groups only, 3) core source of Bradford's law zone. There were two rounds of independent reviewers that found and retrieved relevant data. The Bibliometrix and Biblioshiny packages from R software were used to conduct the bibliometric analysis. Bradford's Law

Table 1. Main information about collected data

Description	Results
MAIN INFORMATION ABOUT DATA	
Timespan	2006:2022
Sources (Journals, Books, etc.)	5
Documents	16
Annual Growth Rate %	7.11
Document Average Age	8.44
Average citations per doc	0
References	1
DOCUMENT CONTENTS	
Keywords Plus (ID)	70
Author's Keywords (DE)	30
AUTHORS	
Authors	122
Authors of single-authored docs	1
AUTHORS COLLABORATION	
Single-authored docs	1
Co-Authors per Doc	8.81
International co-authorships %	0
DOCUMENT TYPES	
journal article	16

of Scattering is a law pertaining to declining returns and dispersion. For each single topic or subject area, the top third (Zone 1 or core) reflects the journals that are most often referenced in the relevant literature and are hence most likely to be of interest to researchers in that field. The middle third (Zone 2) consists of journals with an average number of citations, and the bottom third (Zone 3 or tail) consists of publications that are seldom referenced and considered to be of minimal significance to the topic. Thus, we used core source of Bradford's law zone in our search criteria to focus on the most cited articles that are of great interest to researchers.

Results

There is no available paper that focus on PD genetics on AfrAbia patients. The initial search identified 43 articles, all of which were published between 2004 and 2022. However, after filter application and considering the inclusions criteria, the search results include only 16 original articles out of 43 articles. Twenty-Seven articles were omitted. The primary grounds for elimination were as follows: the studies were not published in English and based on their titles and abstracts, none of these studies were original article with original data. In addition, people from URPs and those with PD were not included, no genetic study was conducted, and the initial findings were not publicized.

The first paper was published in 2006. It was a thorough evaluation of research on the epidemiology and genetics of PD patients. This review summarizes PD research conducted in Africa during the last six decades (1944 to 2004). Clearly, there are still many potentials for study; nevertheless, major methodological concerns must be addressed. Typically, the clinical series published to far have been small, and many hospital-based series have been obtained from admission data. Nonetheless, PD is largely addressed in outpatient settings, and hospitalization data likely underreport illness incidence. There was an increased trend in the number of articles published since then. The annual scientific production was highest in 2022 with 3 articles compared with 1 article in 2006, with an annual growth rate of 7.11% and 0.0% international co-authorship (**Tables 1**, **2**; **Figure 1**). The most important study was published in August 2022 to examine the methylation of alpha-synuclein in a Sudanese cohort of 172 PD patients. They detected a unique pattern of DNA methylation in a young Sudanese population with familial PD, confirming the significance of SNCAintron1 methylation for PD. This phenomenon seems to be independent of ethnicity, environmental variables, drug use, and family clustering. In terms of cumulative source dynamics, Parkinsonism and related disorders journal was the most mentioned journal with 6 articles compared with 2 articles in Frontiers in neurology (**Figure 2**). Country wise, Sudan was the most contributing country (16 articles), followed by Senegal (7 articles), then Morocco (6 articles).

Regarding word dynamics and cloud, humans was mentioned in 13 articles (11%), PD in 10 articles (9%), mutations in 5 articles (4%) and genetics only in 2 articles (2%) (**Figure 3**). Furthermore, according to the thematic evolution analysis, between 2006-2016, black people, humans and prevalence were used simultaneously, however, since 2017, PD has frequently been discussed within the same cluster (**Figure 4**). As shown in **Figure 4**, each node

Table 2. Characteristics of the studies according to main inclusion criteria

No	Authors	Title	Journal	Year	DI
1	Schumacher-Schuh AF; Bieger A; Okunoye O; Mok Ky; Lim Sy; Bardien S; Ahmad-Annuar A; Santos-Lobato Bl; Strelow Mz; Salama M; Rao Sc; Zewde Yz; Dindayal S; Azar J; Prashanth Lk; Rajan R; Noyce Aj; Okubadejo N; Rizig M; Lesage S; Mata IF	Underrepresented Populations in Parkinson's Genetics Research: Current Landscape and Future Directions.	Movement Disorders: Official Journal of The Movement Disorder Society	2022	10.1002/mds.29126
2	Bakhit Y; Schmitt I; Hamed A; Ibrahim Eaa; Mohamed In; El-Sadig Sm; Elseed Ma; Alebeed Ma; Shaheen Mt; Ibrahim Mo; Elhassan Aa; Eltom K; Ali Ha; Ibrahim Ya; Almak Me; Abubaker R; Ahmed Ma; Abugrain Aa; Elrasheed Sm; Omar Ma; Almahal Ma; Mohamedsharif Aa; Tahir My; Malik Sm; Eldirdiri Hs; Khidir Rj; Mohamed Mt; Abdalla A; Omer Fy; Elsayed Leo; Babikir Heh; Bukhari Ea; Seidi O; Wüllner U	Methylation of Alpha-Synuclein in A Sudanese Cohort.	Parkinsonism & Related Disorders	2022	10.1016/j.parkreldis.2022.05.009
3	Müller-Nedebock AC; Meldau S; Lombard C; Abrahams S; Van Der Westhuizen Fh; Bardien S	Increased Blood-Derived Mitochondrial DNA Copy Number in African Ancestry Individuals with Parkinson's Disease.	Parkinsonism & Related Disorders	2022	10.1016/j.parkreldis.2022.06.003
4	Fall M; Dardare Im; Diop Am; Pelagie Ma; Kahwagi J; Dechacus Gc; Gaye Nm; Rizig M; Diagne Ns; Ndiaye M; Diop Ag	Spectrum of Movement Disorders: Experience of A one and Half Year of Existence of The First Specialized Centre in Senegal.	Parkinsonism & Related Disorders	2021	10.1016/j.parkreldis.2022.03.015
5	Du Plessis S; Bekker M; Buckle C; Vink M; Seedat S; Bardien S; Carr J; Abrahams S	Association Between a Variable Number Tandem Repeat Polymorphism within the Dat1 Gene and The Mesolimbic Pathway In Parkinson's Disease.	Frontiers In Neurology	2020	10.3389/fneur.2020.00982
6	Dekker MCJ; Coulibaly T; Bardien S; Ross OA; Carr J; Komolafe M	Parkinson's Disease Research on The African Continent: Obstacles and Opportunities.	Frontiers In Neurology	2020	10.3389/fneur.2020.00512
7	Oluwole Og; Kuivaniemi H; Carr Ja; Ross Oa; Olaogun Mob; Bardien S; Komolafe Ma	Parkinson's Disease in Nigeria: A Review of Published Studies and Recommendations for Future Research.	Parkinsonism & Related Disorders	2018	10.1016/j.parkreldis.2018.12.004
8	Mahne AC; Carr JA; Bardien S; Schutte CM	Clinical Findings and Genetic Screening for Copy Number Variation Mutations in A Cohort of South African Patients With Parkinson's Disease.	South African Medical Journal	2015	10.7196/SAMJ.2016.v106i6.10340
9	Geldenhuys G; Glanzmann B; Lombard D; Boolay S; Carr J; Bardien S	Identification Of a Common Founder Couple For 40 South African Afrikaner Families with Parkinson's Disease.	South African Medical Journal	2013	10.7196/samj.7747
10	Van Der Merwe C; Haylett W; Harvey J; Lombard D; Bardien S; Carr J	Factors Influencing the Development of Early- or Late-Onset Parkinson's Disease in A Cohort of South African Patients.	South African Medical Journal	2012	10.7196/samj.5879
11	Jasinska-Myga B; Kachergus J; Vilariño-Güell C; Wider C; Soto-Ortolaza Al; Kefi M; Middleton LT; Ishihara-Paul L; Gibson RA; Amouri R; Yahmed SB; Sassi SB; Zouari M; El Euch G; Ross OA; Hentati F; Farrer MJ	Comprehensive Sequencing of The Lrrk2 Gene in Patients With Familial Parkinson's Disease From North Africa.	Movement Disorders: Official Journal of The Movement Disorder Society	2010	10.1002/mds.23283
12	Haugarvoll K; Wszolek Zk	Clinical Features of Lrrk2 Parkinsonism.	Parkinsonism & Related Disorders	2010	10.1016/S1353-8020(09)70815-6
13	Change N; Mercier G; Lucotte G	Genetic Screening of The G2019s Mutation of The Lrrk2 Gene in Southwest European, North African, And Sephardic Jewish Subjects.	Genetic Testing	2008	10.1089/gte.2007.0098
14	Okubadejo Nu	An Analysis of Genetic Studies of Parkinson's Disease in Africa.	Parkinsonism & Related Disorders	2007	10.1016/j.parkreldis.2007.08.006
15	Funalot B; Nichols Wc; Pérez-Tur J; Mercier G; Lucotte G	Genetic Screening for Two Lrrk2 Mutations in French Patients with Idiopathic Parkinson's Disease.	Genetic Testing	2007	10.1089/gte.2006.10.290
16	Okubadejo NU; Bower JH; Rocca WA; Maraganore DM	Parkinson's Disease in Africa: A Systematic Review of Epidemiologic and Genetic Studies.	Movement Disorders: Official Journal of The Movement Disorder Society	2006	10.1002/mds.21153

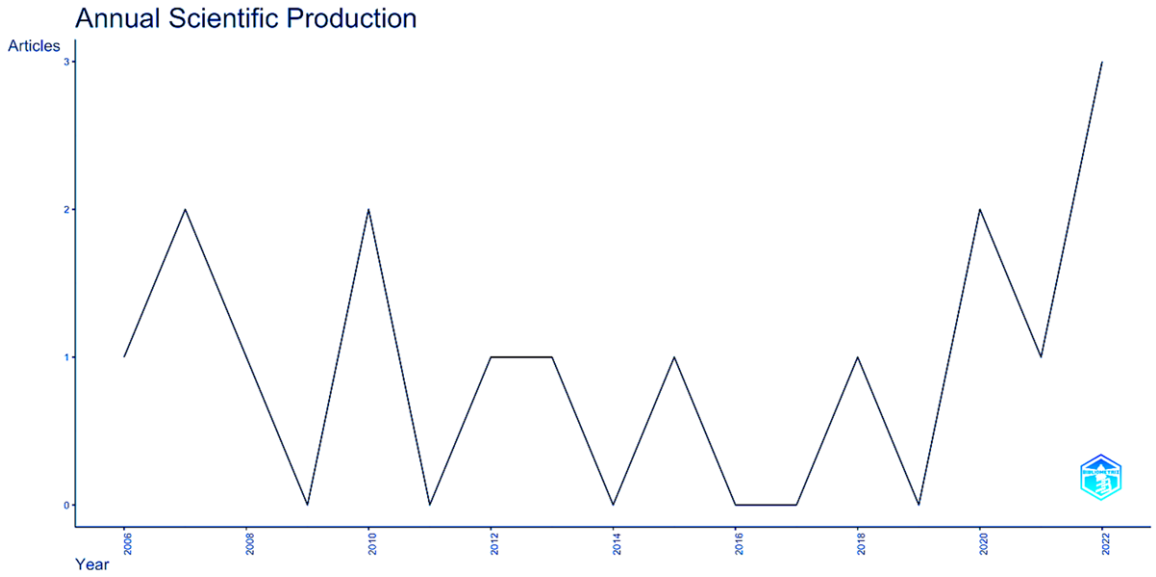

Figure 1. Annual scientific production regarding PD genetic studies in Africa from 2006-2022.

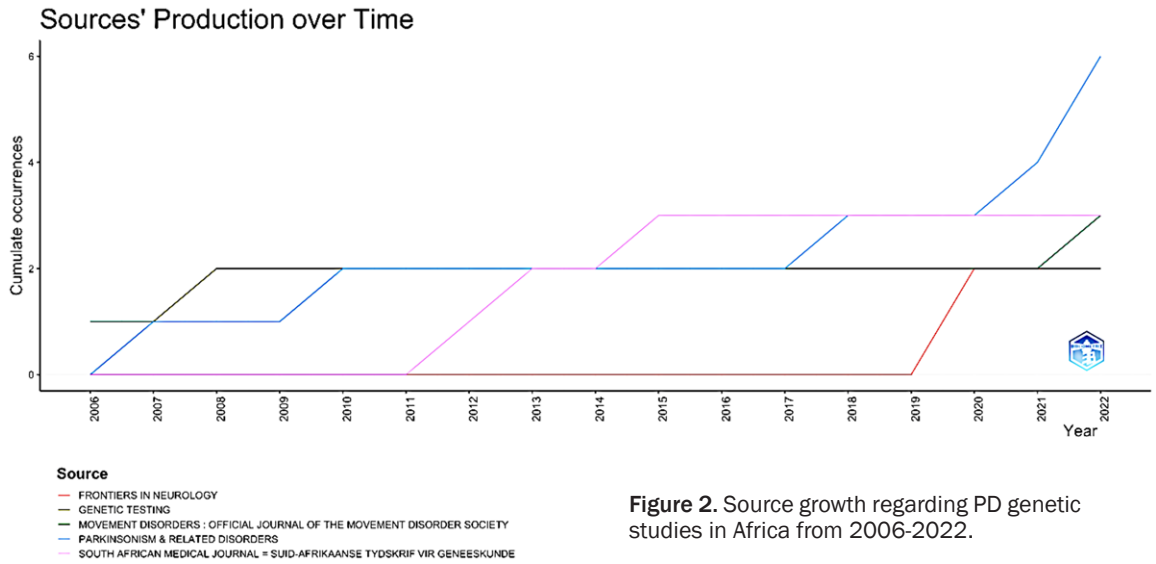

Figure 2. Source growth regarding PD genetic studies in Africa from 2006-2022.

inside a network represents a keyword object. wherein: (1) the size of the node indicates the occurrence of the keyword (i.e., the number of times that the keyword occurs), (2) the link between the nodes represents the co-occurrence between keywords (i.e., keywords that co-occur or occur together), (3) the thickness of the link indicates the occurrence of co-occurrences between keywords (i.e., the number of times that the keywords co-occur or occur together), and (4) the larger the node, the greater the Each color indicates a thematic cluster whose nodes and connections may be used to demonstrate the theme's (cluster's) coverage of subjects (nodes) and the linkages (links) between topics (nodes) falling under that theme (cluster).

In terms of research and scientific collaboration in this field, most of collaboration were South-North teams with the United States is in the lead. South-South collaborations were mainly between Nigeria and South Africa, Mali, and Tanzania. Also, there was a collaboration between Sudan and Saudi Arabia (1 article); and between South Africa and Mali (1 article), and Tanzania (1 article) (**Figure 5**). Co-authorship analysis investigates the interconnections

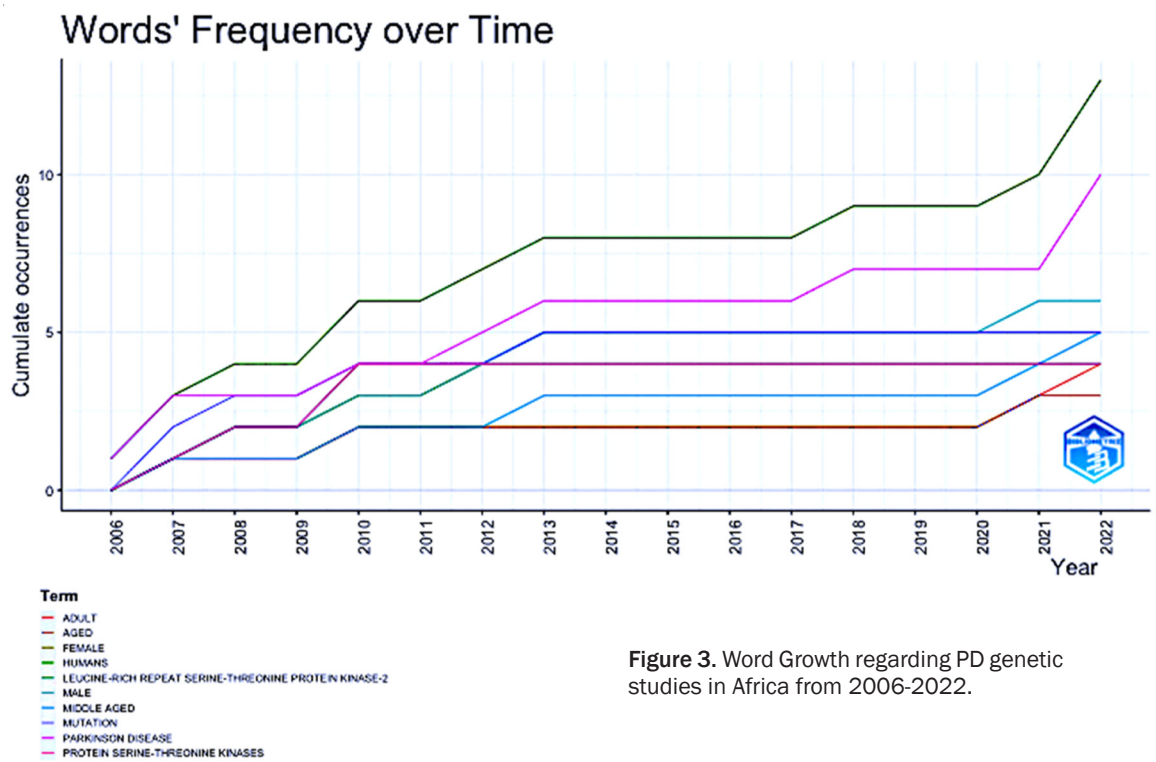

Figure 3. Word Growth regarding PD genetic studies in Africa from 2006-2022.

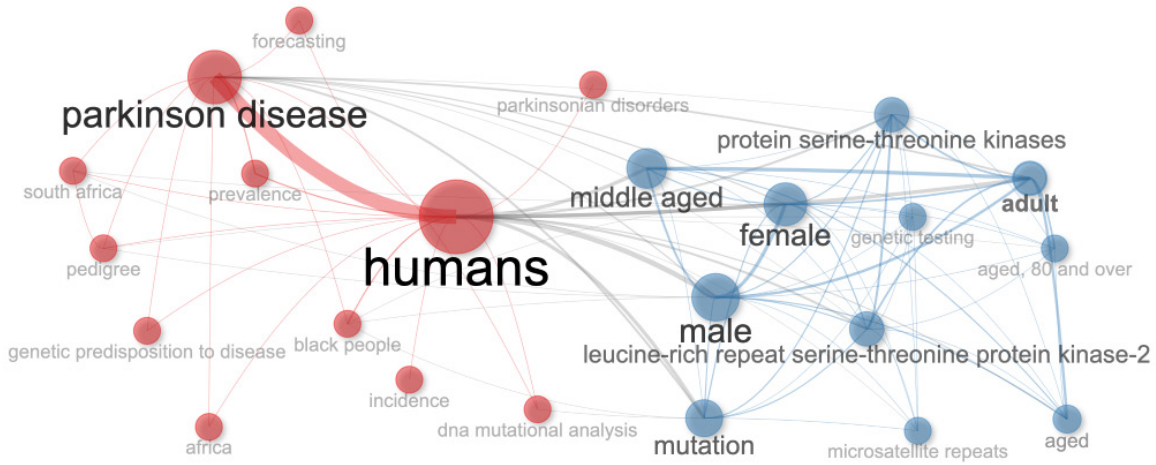

Figure 4. Keyword co-occurrence regarding PD genetic studies in Africa from 2006-2022.

between researchers in a AfrAbia. As co-authorship is a formal method of intellectual cooperation amongst academics, it is essential to comprehend how scholars communicate with one another (including author qualities such as connected institutions and nations). In truth, scholarly partnerships may result in advancements in research; for instance, inputs from many academics might contribute to better clarity and deeper insights. The analysis allows collaborations to be mapped across different time periods, allowing scholars to review the trajectory of intellectual development in relation to collaboration networks and equipping aspiring scholars with valuable information to reach out to established and trending scholars in the research field.

Discussion and insights

In this work, a bibliometric analysis of PD genetic studies on the AfrAbia group was employed.

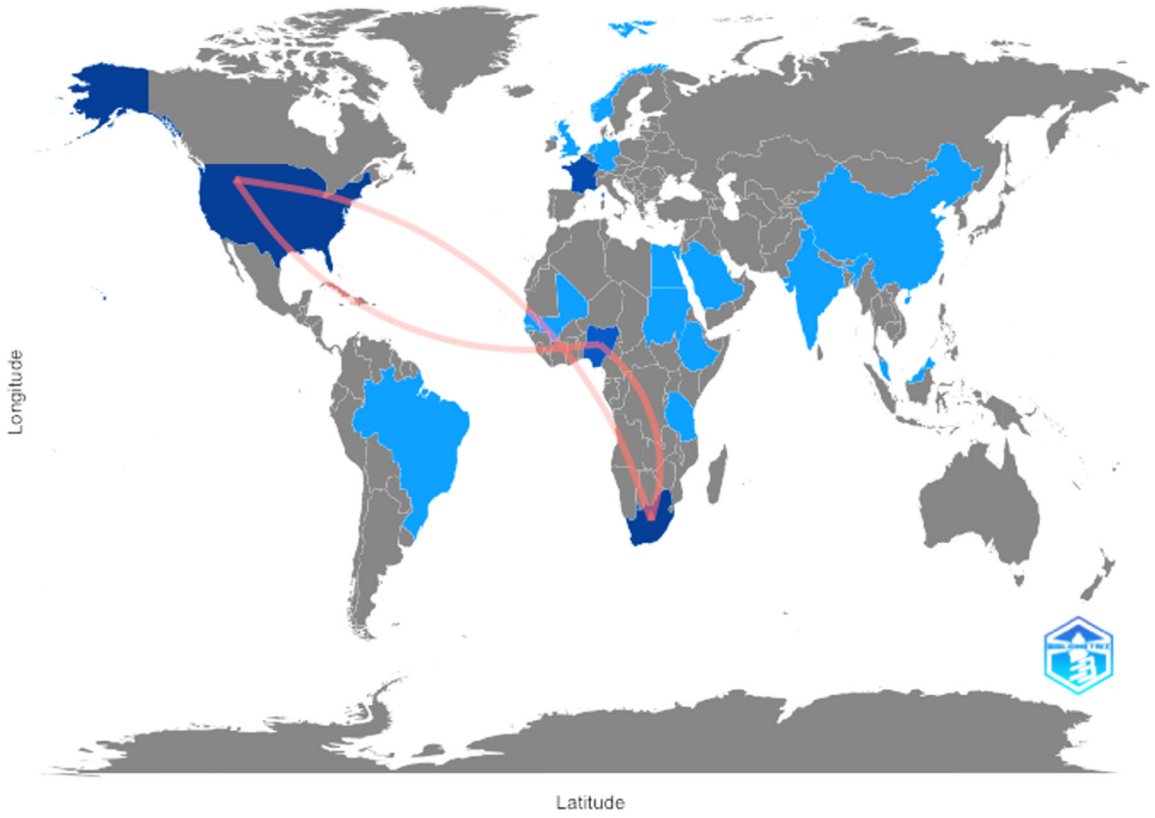

Figure 5. Country collaboration regarding PD genetic studies in Africa from 2006-2022.

The goals were to discover emerging article trends, patterns of collaboration, and research components, as well as to explore the intellectual structure of a certain field in existing literatures. Bibliometric analysis is a useful technique to find out what scientists have learnt and how their disciplines have evolved over time by making sense of a large amount of unstructured data in a systematic fashion. As a result, the present bibliometric research may set the framework for furthering a discipline in novel and significant ways. This is because it permits and empowers academics to (1) acquire a comprehensive picture in one location, (2) identify knowledge gaps, (3) generate new research ideas, and (4) position their intended contributions to the subject.

The present findings are consistent with those of Schumacher-Schuh and colleagues [15], who highlight the urgent need for more varied sample sizes in PD investigations by underscoring the existing paucity of demographic variety, particularly among African populations. Genetics, archaeology, and anthropology all point to AfrAbia as the location where modern humans first appeared 200,000 years ago [66]. Based on linguistic, genomic, and archaeological evidence, the majority of the AfrAbia population has been shown to have a high degree of genetic variation, with more private alleles than in any other region [67]. As a result, there are significant genetic differences between AfrAbia and European tribes. Moreover, as a result of significant environmental variability, AfrAbia groups have a wide range of cultural and phenotypic variances, making these populations intriguing for studying gene-environment interactions. This has the potential to advance biological research by revealing novel gene-gene and gene-environment interactions. This is consistent with the retrieved article number 6 (Dekker et al., 2020), which highlighted the substantial variation in neurological and genetic research capacities throughout the African continent, as well as various undiscovered areas for Parkinson's disease research in Africa. Few countries have the requisite infrastructure and people, whereas the majority have yet to develop these skills. Local research is severely constrained by budget constraints, and unidirectional export of biological samples

and genetic data remains a barrier. Local-regional partnerships, in collaboration with global PD consortia, should offer an ethical method for reducing inequality and promoting capacity development on the African continent.

It is worth noting that there is a scarcity of high-quality research on the prevalence of Parkinson's disease in Africa, both in terms of the quantity of studies and their geographic scope. To ensure that enough AfrAbia patients are recruited for genetic studies, collaboration across AfrAbia countries is essential to pool resources and patient samples. The development of a mutation screening core laboratory for AfrAbia Parkinson's disease patients would significantly enhance genetic research on the African continent. Moreover, identifying AfrAbia PD families amenable to whole exome sequencing research might aid in the discovery of additional PD genes. Additional neurologists and movement problem specialists must be trained in AfrAbia, but this will need both long-term, persistent labor and a large financial commitment.

We agree with Popejoy and Fullerton [44] that future efforts to increase genetic variety should use both bottom-up and top-down methods. While formulating research aims and proposing robust study designs, researchers should consider genetic diversity and its relationship to socioeconomic and environmental factors. Community involvement and the presenting of solutions to health care issues are two techniques that have been shown to be effective in enrolling individuals from underrepresented groups in scientific investigations. Because of the variety of Parkinson's disease, full clinical characterization of people from many ethnic origins is critical in genetic research. To maximize the study's etiological implications, efforts to increase genetic diversity must be combined with efforts to standardize phenotypic descriptions and inclusion criteria. Trans-ethnic fine-mapping and other analytical tools provide ever-increasing depths of understanding. Moreover, funding organizations must promote involvement by granting special monies, improving chances for underrepresented groups to participate in research, and translating results to health-care delivery systems [50]. This is consistent with the retrieved article number 8 (Mahne et al., 2015), which revealed clinical and genetic results in a group of black South African Parkinson's disease patients. The patients studied had the same characteristics as those in Western studies, with maybe a higher proportion of tremor-dominant sickness. One mutation in the parkin gene was discovered via genetic study. Further sequencing-based research is needed to improve our knowledge of PD-causing genes and mutations in African black individuals.

When engaging with potentially vulnerable populations, ethical supervision by culturally competent agents, a fully informed consent procedure, respect for local regulations, data protection, and the return of value are all required [70, 71]. A code of ethics by the San people of southern Africa [72], recommendations issued by the Human Heredity and Health (H3Africa) Guidelines for Community Engagement [73], and a policy for genetic research and data sharing being developed by the Navajo Nation in the United States [74] are among the new sets of rules emerging to protect indigenous people from being exploited and abused in genetic research. When partners are able to freely communicate their thoughts and concerns via established channels of communication, trust difficulties may be minimized. Additionally, extreme transparency should be implemented throughout the research process, from its goals to its funding to its administration to its publication standards. Capacity building in countries with a high prevalence of URPs is another key step toward ensuring long-term studies, independence, and a diverse pool of genetics researchers [39, 75, 76]. Having the names of younger researchers appear as co-authors in multi-authored papers isn't adequate; a clear career development strategy should be implemented, with a plan for them to produce first-author or senior-author publications in the future. Our results underline the need of enabling local researchers and authorities in order to foster long-term variety in genomics research. Working with countries with higher per capita incomes or developing regional development plans with centralized hubs would achieve this aim. International organizations play an important role in organizing disadvantaged nations for regional companies or forming relationships with countries that have more to offer economically. Greater diversity on editorial boards would be a good first step in this direction, and journals and editors should be

conscious of the need of correctly reflecting society. URP-centric versions with tight inclusion criteria may also be offered. Lastly, if peer review is to be a pleasant, constructive process that supports inclusion for all participants, it must be conducted with care. Similarly, article 16 (Okubadejo et al., 2006) discovered that the prevalence and incidence rates of Parkinson's disease in Africa were lower than those reported for populations in Europe and North America. Just a few genetic studies on Parkinson's disease have been published from Africa, and none of them have involved persons of African heritage. There have been no reported PD case-control or cohort studies in Africa. The analysis in that report evaluated the preceding 60 years of PD research in Africa and highlighted knowledge gaps and future research possibilities.

To this end, the Global Parkinson's Genetics Program (GP2, http://gp2.org/) is gathering massive amounts of data from URPs all around the globe and empowering researchers from those communities to move this study forward (GP2, 2021). To achieve this lofty objective, GP2 formed a specialized working group (the Underrepresented Populations Working Group, https://www.gp2.org/working-groups/underrepresented-populations-working-group/) made up of scholars from a variety of nations and ethnicities. The Black and African American Connections to Parkinson's disease study, which is part of GP2, is a consortium and set of programs to recruit people from URPs inside the United States. The program provides substantial funding for ongoing activities in East Asia (IPDGC-Asia), India (LUX-Giant), Latin America (LARGE-PD), and Africa (IPDGC-Africa). In addition to data collecting, GP2 is able to carry out initiatives like a trans-ethnic meta-analysis and fine-mapping thanks to tactics for collaborative data upload, access, and analysis. Online courses, master's and doctoral degree programs, and short-term training sessions on genetics and bioinformatics are just some of the options GP2 offers to researchers throughout the world to help them learn to work together and pool their resources.

According to the present study, despite worldwide attempts to diversify PD genetic research, there is still a disturbing imbalance in the number of research programs dedicated to each URP. According to our findings, as economies rose, so did the number of publications produced in those countries; however, the pace was slower in those with lower per capita incomes. Understanding diversity's ability to promote both equality and scientific development would need concerted effort. Researchers, institutions, and funders (both public and private) may work together to encourage sustainable diversity via cooperative initiatives, capacity development, training, data sharing, and strategic resource diversification. GP2 is actively recruiting leaders, researchers, and study volunteers from all URPs in more developed countries throughout Africa, Asia, the Middle East, and South America to help accomplish this aim. Provided that the present research climate improves in the next years, we may see an increase in high-quality publications from URPs, which might ultimately lead to larger improvements in health care for all populations.

Surely, the tremendous genetic heterogeneity reported in Parkinson's disease patients, who are all genetically and physiologically distinct and carry diverse genetic combinations of uncommon variations not shared by the majority of PD patients, may make interpretation of the genetic data difficult. Therefore, future genetic research should use a novel technique in a bigger cohort of Parkinson's disease patients and controls. This method should allow us to quantify the amount of rare variations in the panel of candidate genes for each individual in order to identify individuals at high risk of acquiring Parkinson's disease. This will be a complement to GWAS and standard co-segregation studies of NGS data for finding variants associated in sporadic Parkinson's disease, with the emphasis on the importance of rare variants in the genetics of Parkinson's disease.

Conclusions and study limitations

Bibliometric analysis is a common and thorough technique for examining and interpreting vast quantities of scientific data. It helps us to dissect the evolutionary subtleties of a certain topic and offer light on its developing areas. Notwithstanding its virtues, bibliometric analysis is still relatively new in business research, and in many situations it is not used to its full potential. This happens when bibliometric research depend on a narrow collection of biblio-

metric data and procedures, resulting in a fragmented knowledge of the studied topic. It is important to note that there is no authoritative guide to bibliometric analysis in business research, which poses a significant challenge for business scholars who wish to learn more about the bibliometric methodology and its application to business research in a comprehensive, easily-digestible format.

Although while bibliometric analysis is a valuable technique for summarizing and synthesizing literature, its limitations must be acknowledged. Furthermore, since bibliometric data from scientific databases such as Scopus and Web of Science are not designed specifically for bibliometric analysis, they may include mistakes that may affect any research done using such data. To limit the chance of errors, we rigorously remove duplicates and inaccurate entries from the bibliometric data we've acquired. The second limitation is intrinsic to the bibliometric method. Due to the quantitative nature of bibliometric study, in which the relationship between quantitative and qualitative conclusions may be vague, the qualitative claims of bibliometrics can be particularly subjective. In this setting, we exercise extra care when making qualitative assertions based on bibliometric data, and where appropriate, we back these assertions with content analysis. In conclusion, the current bibliometric study can only give a short-term forecast of the PD genetic studies in AfrAbia; hence, academics should refrain from making too ambitious assertions about the research field and its long-term significance. Notwithstanding these limitations, the bibliometric method may help AfrAbian neurologists to overcome their fear of dealing with large bibliometric datasets and perform ambitious big genetic data research retrospectives. In reality, bibliometric analysis may facilitate the creation of data in genetic field. In this strategy, a quick but vital step is taken towards understanding the genetic variability among AfrAbian PD patients.

Perspectives

Researching the underlying genetics of PD in AfrAbian populations is an once-in-a-lifetime chance. The number of alleles that affect illness susceptibility or response to therapy may vary between populations, according to some evidence. Furthermore, it has been proposed that groups (like the Yorubans in Nigeria) with shorter-range linkage disequilibrium and higher haplotype diversity may provide benefits for fine-structure mapping to pinpoint the exact nucleotide alteration responsible for a trait [77, 78]. All of these things make it imperative to investigate the molecular epidemiology of PD in AfrAbia. Furthermore, more research has to be done on the genetics of PD among African-Americans [79, 80].

There is a lack of knowledge on environmental and genetic risk factors for PD in AfrAbia, and there have been no case-control or cohort studies of PD in AfrAbia to far. Despite the fact that people with PD and other movement disorders in AfrAbia have similar healthcare requirements to those in industrialized nations, this was shown to be the case [81]. As a result, there is a paucity of information on the social and economic impacts of PD in AfrAbia, such as drug responsiveness, quality of life, survival, and other related topics. Research into these questions would help people all across the globe, not only in AfrAbia, by shedding light on the causes of Parkinson's disease (PD) and improving health care planning for the continent's residents. Researchers in AfrAbia face significant obstacles due to a lack of resources (including money, human resources, and materials), which might be mitigated by international cooperation.

Disclosure of conflict of interest

None.

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