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EDITORIAL

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African neuroscience on the global stage: Nigeria as a model

1 | INTRODUCTION

Neuroscience is a multidisciplinary endeavour that broadly connects across STEM disciplines as well as economics, marketing and law. This breadth has led to a global brain research race exemplified by several large-scale government-funded projects in recent years launched in Europe, the United States, Japan and China, to unravel the complexity of the nervous system in health and disease, and the application of this data to accelerate technological development (Poo et al., 2016).

In contrast, most African governments do not give neuroscience the same level of attention. Indeed, Africa has a rich medicinal plant resource, placing the continent in a strong position in the area of drug discovery (Abegaz, 2016). Most of our today's understanding of the brain comes from research performed in 'The Global North', with only minor contributions from Africa (Abd-Allah et al., 2016), where access to quality science education and infrastructure remains difficult (Okeke, Babalola, Byarugaba, Djimde, & Osoniyi, 2017). Research infrastructure is generally weak, funding levels minimal and teaching load on scientists enormous. Furthermore, suitable research equipment is typically lacking, in disrepair, or disused due to a lack of local expertise or surrounding basic infrastructure (Yusuf, Baden, & Prieto-Godino, 2014). For example, the lack of reliable power across large stretches of the continent continues to make it difficult to acquire, use or store common tools and consumables used in bioscience, thus hampering African-led scientific innovation. Likely as one result, Africa generated only 0.1% of the world's patents in 2013 (Baskaran, 2017).

Some of these challenges have been targeted by local and international programmes focused on training African scientists and to set-up laboratories for cutting-edge research within Africa. In neuroscience, organisations like The International Brain Research Organisation (IBRO) or The International Society for Neurochemistry (ISN), among others, have focussed on supporting mostly young African neuroscientists to acquire further training within and outside Africa. Organisations like Teaching and Research in Natural Sciences for Development in Africa (TReND) (www.trendinafrica.org) or Seeding labs (https://seedinglabs.org) in addition facilitate equipment donations to boost laboratory infrastructure within Africa, or lead scientist-volunteer exchange programmes (for a detailed review see Karikari, Cobham, & Ndams, 2016). Together, these types of efforts have likely contributed to an increased interest in neuroscience among African scientists in the recent past.

In Nigeria, Africa's most populous nation, neuroscience is now a popular career option for many aspiring scientists, as perhaps best exemplified by the high number of Nigerians attending African neuroscience summer schools and meetings (typically, about half of all African applications come from Nigeria). Indeed, a recent estimate placed Nigeria as the third hotspot for neuroscience research in Africa, following South Africa and Egypt (Abd-Allah et al., 2016). Database mining efforts estimated a total of 1,079 neuroscience publications affiliated with Nigeria between 2003 and 2013 (Abd-Allah et al., 2016) and 1,774 between 1997 and 2017 (Balogun, Cobham, & Amin, 2017). However, from here it is difficult to quantify the specific contribution of Nigerian laboratories to these publications. Common search strategies rarely differentiate between studies that were truly driven from within Africa and studies driven by Africans abroad, foreign laboratories merely affiliated with African institutions or even non-African led research conducted on African populations. For example, 68.7% of publications from Sub-Saharan Africa in 2014 had non-African co-authors (Baskaran, 2017), which leaves unclear as to what extent the experimental work

Abbreviations: ABUAD, Afe Babalola University; ABU, Ahmadu Bello University; ELISA, Enzyme-linked immunosorbent assay; FUTA, Federal University of Technology Akure; H & E, Haematoxylin and eosin staining; HPLC, High-performance liquid chromatography; IBRO, International Brain Research Organisation; IF, Impact factor; ISN, The International Society for Neurochemistry; LSU, Lagos State University; NIPRD, National Institute for Pharmaceutical Research and Development Abuja; NUC, Nigerian National University Commission; OAU, Obafemi Awolowo University; OOU, Olabisi Onabanjo University; PCR, Polymerase chain reaction; qPCR, quantitative polymerase chain reaction; STEM, Science, technology, engineering, and mathematics; TETFund, Tertiary Education Trust Fund; TReND, Teaching and Research in Natural Sciences for Development in Africa; UDUS, Usman Danfodiyo University; UniAbuja, University of Abuja; UNICAL, University of Calabar; Unimad, University of Maiduguri; UNN, University of Nigeria, Nsukka.

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presented in these publications has been conducted within the continent.

To source reliable data about Africa's true scientific output, we therefore present here a strategy to extract and analyse publications specifically driven by researchers within Africa and trial our approach on Nigerian neuroscience output over the past two decades. We hope that the resultant data set will enable existing African research institutions to assess their strategies and scientists to evaluate the impact of their work, and inform governments and funders on the strengths and weakness of neuroscience research in different regions of the continent and thus enable the development of programmes focussed on the specific need of neuroscience researchers in the region. For instance, it is not clear to what extent powerful and more affordable research models such as fruit flies, zebrafish, *C. elegans* or genetically modified cell cultures have been adopted in African research. To therefore establish and test a framework for evaluating neuroscience output from the continent as a whole, we here extracted PubMed-indexed Nigerian neuroscience publications from 1996 to 2017 and manually extracted articles following stringent criteria that specifically identify articles from Nigerian laboratories (Table 1). From here, we categorised them into either basic or clinical and epidemiological research, and analysed each for overall direction, research models and techniques used and citation metrics.

TABLE 1 Article selection criteria

Exclusion
Articles with external collaboration where only a minor fraction of the work was conducted within Nigeria, such as plant extract collection. Articles with external collaborators in which study location was unclear. Research conducted by Nigerians (or on Nigerians) outside Nigeria
Inclusion
Studies conducted in Nigeria and articles that investigate aspects of the nervous system, even if the focus was not neuroscience
Advanced Techniques (for Africa)
Electron microscopy, western blotting, immunohistochemistry, cell culture techniques, cloning, flow cytometry, fluorescence (confocal) microscopy, whole brain imaging, sequencing and identifying genes of interest, molecular cloning and recombinant DNA technology, gene delivery strategies, making and using transgenic organisms, manipulating endogenous genes etc. (Strickland, 2014)
Standard Techniques
Histology, Biochemical Assays, e.g. Enzyme-linked immunosorbent assay (ELISA), extract preparation, High-performance liquid chromatography (HPLC), behavioural analysis, blood analysis, craniometric analysis etc.

2 | THE STRATEGY USED TO ASSESS THE NEUROSCIENCE RESEARCH OUTPUT FROM NIGERIA

Using PubMed search, we retrieved 1,247 neuroscience publications from Nigeria between 1996 and 2017. In contrast, the same search terms entered into Dimensions (https://www.dimensions.ai/) returned 340,338 publications, while 693 articles were retrieved for 1996–2017 according to Scimago (https://www.scimagojr.com/). In view of this striking variability between search engines, it is difficult to assess the ‘true’ number of Nigerian-led neuroscience publications. However, in view of PubMed's leading role in indexing scientific publications, we think that most internationally important Nigerian led-studies would be captured in our sample. Therefore, the articles retrieved from PubMed were further reviewed for duplicates and unrelated articles, reducing them down to 990 articles. Next, to specifically identify Nigerian-led articles, we retrieved full texts of all articles for further analysis according to defined inclusion and exclusion criteria (Table 1). Application of these criteria reduced articles down to a final set 572. For the compilation of techniques in studies conducted in collaboration with a centre outside Nigeria, only the techniques used in Nigeria were collected.

Next, manual scoring (Figure 1a, Methods) revealed that only about half of the PubMed identified publications ($n = 572$, 54%) were primarily driven by Nigerian laboratories. From here, we categorised each remaining article as either basic research (‘Basic’, $n = 255\%$, 45.5%) or ‘clinical and epidemiological’ research (‘Clinical’, $n = 318\%$, 55.5%) based on the criteria for types of studies in medical research (Röhrig, du Prel, Wachtlin, & Blettner, 2009). This numerical dominance of clinical over basic research output is consistent with previous studies (Abd-Allah et al., 2016). However, as discussed below, basic research on average scored significantly higher than clinical and epidemiological work when comparing citations and journal impact factors.

3 | NEUROSCIENCE PUBLICATION TREND IN NIGERIA

Between 1996 and 2017, annual numbers of publications gradually increased, with initially a larger number of clinical papers published each year (Figure 1b). However, since 2012/13, the number of basic and clinical studies was on par, with both showing a striking increase after ~2013 that was particularly pronounced for basic research. Together with the recent and ongoing increase in the number of neuroscientists in Nigeria, trained locally and abroad, this suggests that the annual number of Nigeria's neuroscience publications may

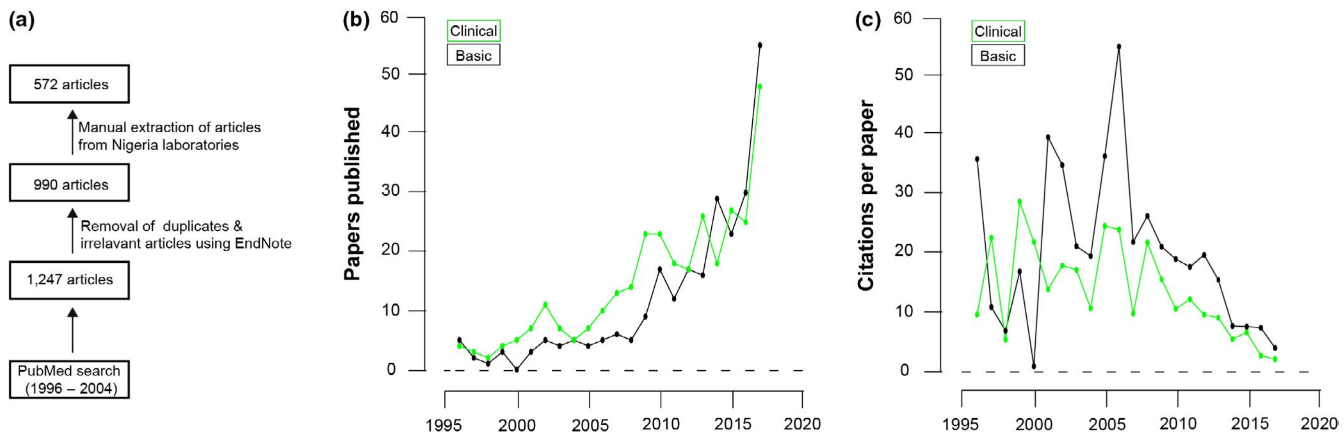

FIGURE 1 Study design and publication trends. (a) Workflow of publication retrieval and sorting strategy. (b) Total publication per year for clinical (green) and basic research (black). (c) Mean citations per annum

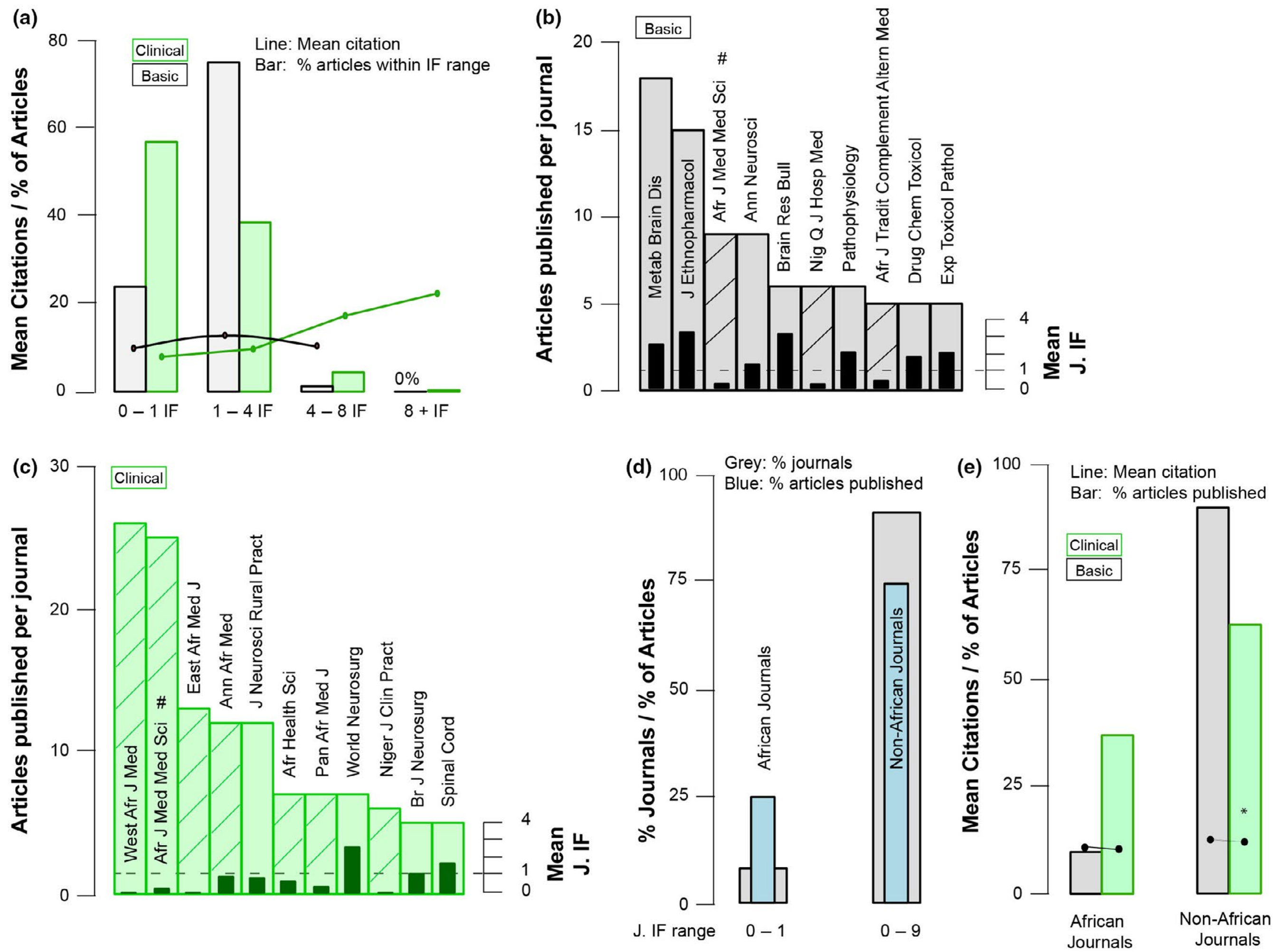

FIGURE 2 Citations and journal metrics for Nigerian neuroscience publications. (a) Journal impact factor (IF) parallels paper citations over the period studied. (b, c) Journals publishing basic (b) and clinical neuroscience articles (c). # indicates journals in which both basic and clinical papers were published. (d) Percentage of African and non-African journals (grey) and percentage articles they published (blue). (e) Percentage and mean citation of basic and clinical papers in African and non-African journals. African journals: $p > 0.05$; Non-African journals: $p = 0.\ 0.04$. Mann–Whitney U test. Errorbars in SEM

continue to exponentially rise in the near future. Since 2000, basic neuroscience studies were consistently more cited than clinical studies (Figure 1c).

4 | POPULAR JOURNALS FOR NEUROSCIENCE PUBLICATION IN NIGERIA

Next, we evaluated the types of journals used and their impact factors (IF, Figure 2). There are many shortfalls in focusing on journal IF to evaluate research influence. However, Nigeria's science generally lacks visibility. Most local journals, including The journal of the Nigerian Society of Neuroscience itself (http://www.neurosciencenigeria.org/journal-articles/), are not yet indexed in online databases. We find that across both basic and clinical neuroscience, most articles were published in either 'low' (IF 0-1, 42%) or 'mid-tier' (IF 1-4, 55%) journals, with only 18 papers (3%) ranking higher. The highest IF publication appeared in 'Movement Disorders' (IF 8.324). Accordingly, while there is clear evidence of steady publication output in reputable international journals, across the more than two decades investigated, only one Nigerian-led neuroscience papers was published in a journal with IF above 8.

Next, basic research scored consistently higher on both citations per paper and journal IF (Figure 2a–c). For example, while most clinical studies were published in journals with IF below 1 (57%), most basic studies fell into the IF 1-4 bracket (75%). Overall, 142 papers (25%) were published in 21 different African journals which all had an IF below 1 (Figure 2d). These 142 articles were mostly clinical articles (82%), with comparatively few basic research articles (18%). Instead, most basic research articles (90%) were published in 243 (92%) different non-African journals (Figure 2d,e). Even though by numbers applied neuroscience research dominates in Africa (Abd-Allah et al., 2016), these publication and citation trends indicate an overall strength in basic rather than applied neuroscience research in the region. To improve the research visibility of Nigerian science, the Nigerian National University Commission (NUC) which is responsible for regulating universities in Nigeria has in recent times organised

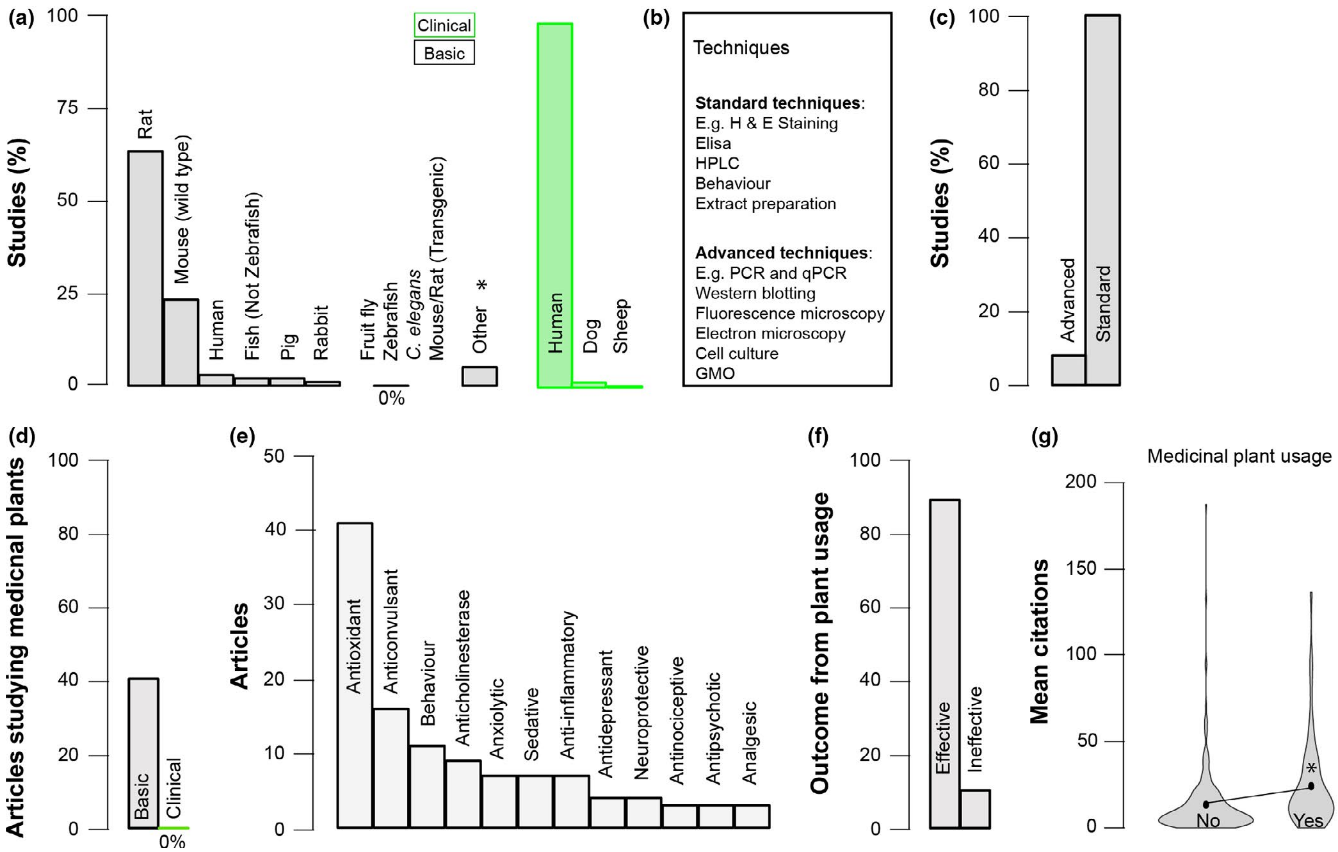

FIGURE 3 Model systems, techniques and medicinal plants. (a) Model systems used in basic and clinical research. (b) Standard and advanced techniques used in Nigerian neuroscience. (c) Techniques used in basic neuroscience. (d) Articles studying medicinal plants. (e) Research questions of studying medicinal plants. (f) Outcome from studies conducted to evaluate the effectiveness of medicinal plants. (g) Violin plot of mean citations depending on medicinal plant usage (Mann–Whitney U test p = 0.0001, Error bars in SEM). *other models include cat, cattle, cell culture (not genetically modified), Egg yolk, goat, pangolin and guinea pig

workshops for academics to encourage publishing in high impact journals worldwide.

5 | MODEL SYSTEMS, TECHNIQUES AND RESEARCH ON MEDICINAL PLANTS

Fruit flies, zebrafish and *C. elegans* are powerful model organisms in biological and biomedical research used in the West due to their many advantages such as relatively short generation time, genetic tractability and affordability (Clovis, 2017). In contrast, these model organisms were wholly absent in Nigerian neuroscience publications over the 21-year period, nor was there any use of genetically modified mammalian systems (Figure 3a). Instead, wild-type rat (64%) and mouse models (23%) dominated basic research, followed mainly by other non-genetically modified mammals (Figure 3a). In other words, research using genetically modified models appears to be completely absent from the Nigerian neuroscience research output over the two decades surveyed.

Apart from model systems, a further striking problem concerned the types of research techniques employed in Nigerian neuroscience laboratories. Many key 'advanced' methods available to researchers outside Africa, such as cell culture, PCR and qPCR, western blotting, fluorescence and electron microscopy, among others, are rarely available in African laboratories. In Nigeria, researchers commonly use histological techniques such as 'standard' haematoxylin and eosin staining (H&E) for microscopic examination, enzyme-linked immunosorbent assay (ELISA) and high-performance liquid chromatography (HPLC) for enzymatic/hormonal analysis and morphological examinations to assess gross abnormalities or rodent behavioural analysis to investigate changes to learning and memory (Figure 3b). We accordingly categorised the methods reported in the Nigerian basic neuroscience publications into 'standard' and 'advanced' (Figure 3b, Table 1). This revealed that only 8% of basic neuroscience studies used any 'advanced' methods (Figure 3c).

Next, across Africa medicinal plants have been used for centuries to treat disease. As a consequence, much local research has been devoted to understanding their effectiveness, mechanisms of action, isolation of components adaptable for drug production or eventual use in clinical trials (Ntie-Kang et al., 2014; Shang, Huwiler, Nartey, Jüni, & Egger, 2007; Tang, Tang, & Leonard, 2017). In agreement, 41% of all basic neuroscience publications examined set-out to test the utility of medicinal plants for future medical application (Figure 3d). In particular, most studies assessed the antioxidant and anticonvulsant activity of candidate plant extracts (Figure 3e, Supporting Information Data S1). Out of these studies, 89% reported that the medicinal plant extracts were effective, while the remaining 11% were reported to be either ineffective or toxic (Figure 3e). Based on these reults, it might be expected that this would at times translate into clinical research. However, strikingly, zero clinical studies or case report involved the use of medicinal plants, suggesting that the results from basic science were not taken towards eventual patient care. This disconnect between basic and clinical research may have many causes. Perhaps most importantly, while many studies explored the effects of plant extracts on rodent behaviour and induced pathology, these studies rarely went on to actually isolate potential active compounds for further study. This issue is likely linked to the near complete absence of research infrastructure and expertise in 'advanced' research methods. Nonetheless, basic neuroscience studies that used medicinal plants were significantly more cited and were on average published in higher IF journals compared to other basic neuroscience publications at the same time (Figure 3f).

6 | NEUROSCIENCE HOTSPOTS IN NIGERIA

Nigeria is host to more than 100 universities and polytechiques, with many harbouring the active research departments. To identify neuroscience hotspots in the country, we further analysed all institutions with at least ten neuroscience publications (basic and clinical summed) over the analysed 21-year period. We compared mean publication numbers and citations (Figure 4). This revealed that the University of Ibadan, the oldest in the country, produced the largest number of neuroscience publications (165). However, publications from other universities were more cited. For example, the 'only' 10 publications from the National Institute for Pharmaceutical Research and Development Abuja (NIPRD) were on average cited three times more frequently (Figure 4b). Notably, all publications from NIPRD were basic research, in comparison to only 37% of articles from the University of Ibadan (cf. Figure 2), which may be linked to some of this difference. Interestingly, all these institutions have at least one publication in which an advanced technique was used locally, except NIPRD and University of Nigeria, Nsukka (UNN), implying that most Nigerian research institutions have at least partial access to more modern research infrastructure, if only sporadically so. Overall, this highlights some of the top institutions engaged in neuroscience research in Nigeria. However, it is possible that other institutions in the country did not make it to the list because they published in journals that were not indexed or their articles failed the criteria used in this study. All data that contributed to this study are available in the Supporting Information Data S1.

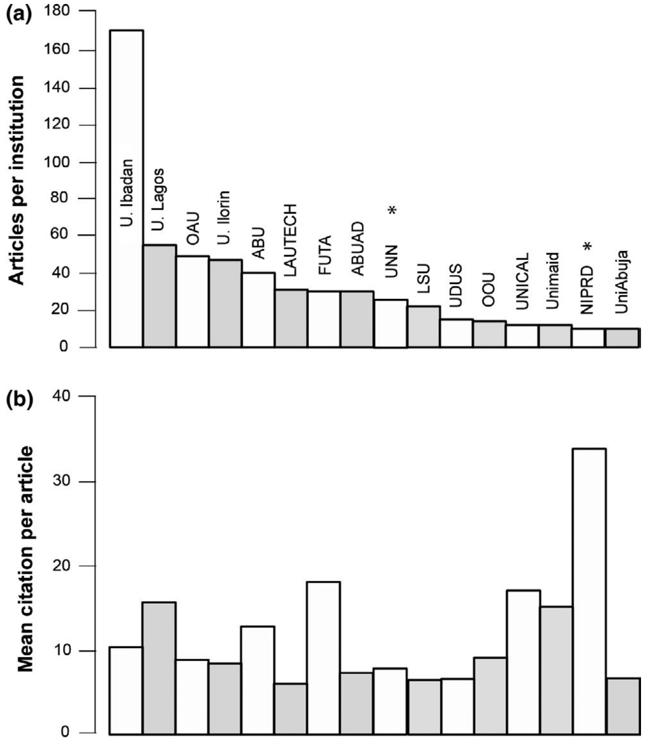

FIGURE 4 Neuroscience hotspots in Nigeria. (a) Top institutions engaged in neuroscience research based on total publications over the whole period surveyed. * Indicates institutions whose publications has no evidence of local use of advanced technique. (b) Top institutions based on average article citation over the period surveyed. OAU: Obafemi Awolowo University; ABU: Ahmadu Bello University; UDUS: Usman Danfodiyo University; FUTA: Federal University of Technology Akure; ABUAD: Afe Babalola University; LSU: Lagos State University; OOU: Olabisi Onabanjo University; UNICAL: University of Calabar; Unimad: University of Maiduguri; NIPRD: National Institute for Pharmaceutical Research and Development Abuja; UNN: University of Nigeria, Nsukka; UniAbuja: University of Abuja

7 | DISCUSSION

The number of Nigeria's neuroscience publications has seen a speedy increase since 2000. This could be attributed to increased support from international organisation towards education in the country that peaked in the early 2000s (Ogunyinka, 2013), the political will to invest in education that started with the return of democracy (Chinyere & Goodluck, 2015), or the slow implementation of Education Tax Act since the 1990s and the re-introduction of new acts, such as the Tertiary Education Trust Fund (TETFund) Act in 2011 that is currently the main source of research fund in the country (http://www.tetfund.gov.ng/index.php/about-us/history). The neuroscience society of Nigeria (http://www.neurosciencenigeria.org/) currently has over 200 members, some of whom are currently pursuing higher degrees in neuroscience-related disciplines within and outside Nigeria, suggesting that the annual number of Nigeria's neuroscience publications may continue to exponentially rise in the near future.

Although there is a clear evidence of a solid neuroscience research base and steady publication output in reputable international journals, across the nearly two decades investigated, only one Nigerian-led neuroscience paper was published in a 'top-tier' journal. Moreover, clinical papers tend to be mostly published in African journals, which typically have poor international visibility and a correspondingly low IF. Indeed, most African journals are not PubMed indexed which again likely results in poor access and visibility of African research on the global stage (Goehl & Flanagin, 2008). This is also worrying because it limits the extent to which African-specific clinical problems can be identified and addressed in the global research community. It also limits the extent to which local basic research questions can be sparked by clinical findings. Overall and under the explicit caveat of using IF and citations as problem-ridden impact metrics (Aragón, 2013, Hutchins, Yuan, Anderson, & Santangelo, 2016), Nigeria's neuroscience publication and citation trends indicate an overall strength in basic rather than applied neuroscience research in the region.

Another striking finding is the complete absence of popular model systems like zebrafish, fruit flies or *C. elegans*, which are cheaper and genetically tractable compared to many mammalian models. Indeed, of Nobel Prizes in Physiology and Medicine awarded between 1996 and 2017, one-third relied heavily on non-mammalian yet genetically accessible model species. Many of the specific challenges facing African researchers (e.g. low research funding, unreliable power) would make the oftentimes 'more hardy' and low-cost models such as *Drosophila* ideal for research on the continent. In fact, like humans, evolutionary history places the origins of Drosophilids on the African continent (Keller, 2007). Encouragingly, 2018 actually did see the possibly first *Drosophila* neuroscience paper published by an all-Nigerian laboratory (Akinyemi, Oboh, Ogunsuyi, Abolaji, & Udofia, 2018), perhaps hinting at a future turn of the tide in the use of model species in the region. Taken together, this in particular calls for increased investment to facilitate the use of small, genetically amenable and affordable model species in African laboratories, as championed by a number of international organisations (e.g. TReND in Africa www.TReNDinAfrica.org or DrosAfrica http://drosafrica.org/).

Another striking problem concerned the types of research techniques employed in Nigerian neuroscience laboratories. Out of the 8% of basic neuroscience studies in which advanced techniques were used, none included techniques like western blotting, PCR, or advanced microscopic approaches. Indeed, to the authors' knowledge there is currently no functional transmission electron microscope or confocal microscope in Nigeria (although there are a handful of operational confocal microscopes on the continent, including to the author's knowledge ones in research institutions in

Ghana, Kenya, Tanzania and South Africa). Furthermore, laboratory consumables such as antibodies are difficult to procure and when available, difficult to store due to unreliable power. Moreover, many scientists lack technical training or experience in the use of key modern neuroscience methods. As a result, Nigerian scientists often fly to non-African laboratories, for example with paraffin blocks to conduct their work in better-equipped conditions abroad, and many talented scientists end up staying. Publication in the world's 'top' journals typically requires interdisciplinary approaches and state-of-the-art techniques. Here, Nigerian neuroscience studies are likely not making it into these journals in part due to the general absence of advanced neuroscience techniques in Nigerian laboratories, and in part due to poor international visibility of their preceding work. Our findings demonstrate an urgent need for an increase in local research funding and training in state-of-the-art techniques to modernise Nigerian research infrastructure. In addition, only few local or international training schemes in the region have focussed on the introduction of more modern neuroscience research techniques, with many instead bolstering competence in existing research technique (e.g. behaviour, histology etc.). Although recent funding initiatives by local (e.g. TETFund) and international (e.g. ISN, IBRO, The World Academy of Sciences) sources have led dozens of Nigerians to acquire modern neuroscience skills in foreign laboratories, the absence of biomedical research infrastructure locally in Nigeria further restrict to which extent trained scientists put their skills into practice.

Next, Nigeria has a rich pool of medicinal plants which if utilised could make the country a global hub for drug discovery. However, currently the complete absence of clinical studies using medicinal plants investigated in basic research towards eventual patient care is striking. In addition to the need for improved research infrastructure, this indicates a need for increased local collaboration between basic and clinical scientists to increase translational research opportunities. All research models used to study the medicinal plants were all wild-type mammalian species; this reiterates the need for Nigerian laboratories to consider genetically accessible models in their research, which include numerous established disease models. For example, using *Drosophila* models for Epilepsy or Alzheimer's Disease, researchers could screen for the ameliorative effects of medicinal plants against such diseases.

In summary, even though Nigeria is among the hotspots of neuroscience on the African continent, here we argue that for Nigerian neuroscience to reach a global impact, several core issues must be addressed. In particular, two clear access points for the support of Nigerian neuroscience in the future stand out: Investment in the sustained training and infrastructure in the use of more modern research techniques, and the widespread promotion of genetically amenable model species. Moreover, any such effort might consider specifically targeting existing basic over clinical or epidemiological research efforts. Clearly, Nigerian laboratories must be improved through the funding for equipment, equipment donations and, critically, extensive and sustained training of local scientists in the use and management of these equipments. Otherwise, Nigeria will continue to lose its talent to developed nations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

The study was conceived, organised and analysed by MBM. Data curation was done by YMG, BAM, AU, SAT, IHA, MA, HSK, YAU, AMA and managed by MBM. The paper was written by MBM and TB.

ORCID

Mahmoud Bukar Maina https://orcid.org/0000-0002-7421-3813

Mahmoud Bukar Maina[1,2,†]
Yunusa Garba Mohammed[2,3,†]
Ali Maina Bukar[4]
Umar Ahmad[5,6]
Abubakar Tijjani Salihu[7]
Harun A. Ibrahim[8]
Muhammad Abdurrazak[9]
Suleiman Kwairanga Hamidu[2,†]
Aisha Umar Yaro[10]
Mosab Ali Awadelkareem[11,†]
Fayza Eid Nasr[12,†]
Tom Baden[1,†]

[1]*School of Life Sciences, University of Sussex, Brighton, UK*
[2]*College of Medical Sciences, Gombe State University, Gombe, Nigeria*
[3]*International Max Planck Research School, University of Konstanz, Konstanz, Germany*
[4]*Centre for Visual Computing, University of Bradford, Bradford, UK*

[5]*Medical Genetics Laboratory, Genetics and Regenerative Medicine Research Centre, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, Malaysia*
[6]*Department of Anatomy, Faculty of Basic Medical Sciences, Bauchi State University, Bauchi, Nigeria*
[7]*Hasiya Bayero Paediatric Hospital, Kano, Nigeria*
[8]*Misr University for Science and Technology, Cairo, Egypt*
[9]*Department of Biochemistry, Bayero University, Bayero, Nigeria*
[10]*College of Medical Sciences, University of Maiduguri, Maiduguri, Nigeria*
[11]*Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan*
[12]*Faculty of Science, Alexandria University, Alexandria, Egypt*

Correspondence
Mahmoud Bukar Maina, School of Life Sciences, University of Sussex, Brighton, UK.
Email: m.bukar-maina@sussex.ac.uk
[†]TReND in Africa gUG (www.TReNDinAfrica.org)

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.