Neuroimaging Research on Dementia in Brazil in the Last Decade: Scientometric Analysis, Challenges, and Peculiarities

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The last years have evinced a remarkable growth in neuroimaging studies around the world. All these studies have contributed to a better understanding of the cerebral outcomes of dementia, even in the earliest phases. In low- and middle-income countries, studies involving structural and functional neuroimaging are challenging due to low investments and heterogeneous populations. Outstading the importance of diagnosing mild cognitive impairment and dementia, the purpose of this paper is to offer an overview of neuroimaging dementia research in Brazil. The review includes a brief scientometric analysis of quantitative information about the development of this field over the past 10 years. Besides, discusses some peculiarities and challenges that have limited neuroimaging dementia research in this big and heterogeneous country of Latin America. We systematically reviewed existing neuroimaging literature with Brazilian authors that presented outcomes related to a dementia syndrome, published from 2010 to 2020. Briefly, the main neuroimaging methods used were morphometrics, followed by fMRI, and DTI. The major diseases analyzed were Alzheimer’s disease, mild cognitive impairment, and vascular dementia, respectively. Moreover, research activity in Brazil has been restricted almost entirely to a few centers in the Southeast region, and funding could be the main driver for publications. There was relative stability concerning the number of publications per year, the citation impact has historically been below the world average, and the author’s gender inequalities are not relevant in this specific field. Neuroimaging research in Brazil is far from being developed and widespread across the country. Fortunately, increasingly collaborations with foreign partnerships contribute to the impact of Brazil’s domestic research. Although the challenges, neuroimaging researches performed in the native population regarding regional peculiarities and adversities are of pivotal importance.

Keywords: Alzheimer’s disease, Brazil, dementia, mild cognitive impairment, MRI, neuroimaging, scientometric analysis
INTRODUCTION

The majority of people with dementia live in low- and middle-income nations, as is the case of Brazil, the largest and the most populated country in Latin America (LA). LA is experiencing an unprecedented and fast demographic change in the last decades, with the increasing aging of the population (1). As well, Brazil has experienced significant changes in the population age pyramid. Nowadays, the country counts more than 30 million people over 60 years old (14% of the population), and by 2060 this number is projected to increase to 73 million (2). Such a consequence is the increase in the prevalence of dementia cases. In LA is expected a four-fold rise in subjects with dementia by 2050 (3). In Brazil, a recent meta-analysis, which included seven Brazilian studies, found a pooled dementia prevalence of 14.3% (6.8–23.9), but with substantial heterogeneity (4).

Neuroimaging research can provide useful diagnostic images and experimental outcomes that report and support evidence-based clinical practice (5). Moreover, is an essential part of dementia workup to exclude non-neurodegenerative causes of cognitive impairment, as well as to evaluate possible patterns of brain atrophy and cerebrovascular disease (6).

Since the creation of the multicentric study Alzheimer’s disease Neuroimaging Initiative (ADNI) in the United States in 2004, there was a significant increase both in the number of studies and Magnetic Resonance Imaging (MRI) techniques that have contributed to better understand the cerebral repercussions of the disease, even in the earliest phases (7). After then, different techniques have been improved, like brain volumetry (automated, manual, semi-automated), voxel-based morphometry (VBM), cortical thickness analyses, diffusion tensor imaging (DTI), and functional MRI (fMRI), especially functional connectivity, among others (8).

Outstanding the importance of neuroimaging examinations in dementia, especially in Alzheimer’s disease (AD) and mild cognitive impairment (MCI), we aimed to evaluate the scientometric characteristics of Brazilian research in this field in the native population. We analyzed studies published on structural and functional neuroimaging in the last decade in a manner to assess the Brazilian scientific work dedicated to research projects in diagnostic, therapeutic, and experimental outcomes that report and support evidence-based clinical practice (5).

RESULTS

Article Selection

Figure 1 shows schematically the article selection process. The PubMed search resulted in 300 matches from which 135 met the aforementioned criteria. Thirty-two reviews or perspective articles were selected for a separate analysis. From the remaining 103 original research papers, 74 studied Brazilian subjects, among them: 9 case reports, 55 transversal studies, 8 longitudinal studies, and 2 controlled trials. Case reports were excluded from the main analyses. Selected articles are listed in Table 1 with the main findings, and in Supplementary Material 2 with all findings.

Reviews

Review papers found covered a wide range of topics. Nineteen out of 32 papers were published in non-Brazilian journals and 16/32 were coauthored by non-Brazilians. Concerning gender, males were the first authors in 20/32 papers, the median number of male and female authors was 5 and 2, respectively. Publication in international journals was correlated with international coauthorship ($\chi^2 = 4.66, p = 0.031$) and marginally correlated with a female first author ($\chi^2 = 3.12, p = 0.077$). The number of publications per year is presented in Figure 2. Time was not associated with an increasing number of publications during these years (Spearman $p = 0.42, p = 0.19$).

The median number of citations per article was 7 (IQR 2.75–23.75). A multivariate linear model showed a negative correlation of citation number with the Publication Year ($p = 0.045$). International Coauthorship, Journal Nationality, and First Author Gender showed no correlation. Due to the latency expected for an article to be cited, we repeated this analysis with papers published up to 2015, resulting in a median of 7 (IQR 6–33) citations. Regression results were non-significant. The journal’s impact factor (JIF) was available for 21/32 papers, with

METHODS

PubMed (https://pubmed.ncbi.nlm.nih.gov/) was queried using the search strategy described in Supplementary Material 1. The results were inspected by IKA to select relevant matches. In brief, research papers were selected if they: (a) had a Brazilian author; (b) presented some kind of neuroimaging result, either quantitative or qualitative; (c) either concerned a primary or secondary neurological disease presenting with a dementia syndrome or represented cognitive aspects of the aging process; and (d) were published during or after the year of 2010 until the date of access in the year of 2020.

Papers were classified according to their nature and design (e.g., review, longitudinal design, controlled trial), international participation in authorship, and journal nationality (Brazilian or international), first author gender, and the number of male and female authors. Web of Science (webofknowledge.com) was consulted for the number of citations received by each paper and the journal’s impact factor (Journal Citation ReportsTM-JCR). Original research papers were further inspected and tabulated as to their MRI and other imaging methods (e.g.,18-FDG-PET), number of participants in each group (e.g., AD, MCI, controls), AD biomarker reporting, the Brazilian state where the study was performed, and funding agencies (the latter two were only accessed if the study concerned Brazilian participants).

Statistical analyses were performed using SciPy 1.5.3 (9), pandas 1.1.4 (10), and statsmodels 0.12.1 (11).
a median of 4.35 (IQR 3.093–8.329). The multivariate regression showed no correlation with other variables.

**Original Research**

Figure 3 shows the characteristics of the selected papers. Concerning the number of publications per year, there was no trend toward increasing or decreasing the number of publications (Spearman ρ = 0.13, p = 0.70) (Figure 3A). The most studied pathologies were AD (54%, n = 35) and MCI (48%, n = 31), followed by vascular dementia (4.6%, n = 3) (Figure 3B). Most studies used morphometric methods (58%, n = 38) followed by fMRI (23%, n = 15) and closely by DTI (18%, n = 12) (Figure 3C). Some methods addressed by only a single study nonetheless worth mentioning included spectroscopy (40), texture analysis (21), magnetization transfer ratio, and relaxometry (39).

Regarding gender analyses of original research papers, we found that females are more frequently first-authors (60%). 26/65 of the first authors are male, with a significant time effect for female authorship (Wilcoxon rank-sum test, p = 0.022). However, when considering all co-authors, males are more frequent (5/4 ratio). The median number of male and female authors was 5 and 4, respectively, with significantly more male authors per paper (Wilcoxon sign-rank test, p = 0.001). These findings might indicate that gender inequalities are less relevant in this specific field. Nineteen-out-of-sixty-five articles were co-authored by non-Brazilians. The most common nationalities among those were North-Americans (n = 14), British (n = 3), German (n = 2), Chilean (n = 2) and Swiss (n = 2).

There is great heterogeneity in the distribution of the research centers in the country. Research activity in Brazil has been restricted almost entirely to a few centers in the Southeast of Brazil. The vast majority of studies were set in the state of São Paulo (65%, n = 43), with studies also from Rio de Janeiro (20%, n = 13), Minas Gerais (7.6%, n = 5), Rio Grande do Sul (4.5%, n = 3), Pernambuco and Goiás (each with 1.5%, n = 1) (Figure 3D). Funding could be the main driver for publications. The São Paulo Research Foundation (FAPESP) was the most common funding agency, supporting 33 studies, followed by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), responsible for the funding of 28 studies, and Coordenação de Aperfeiçoamento de Pessoal do Ensino Superior (CAPES), with 14 studies being supported. Other agencies worth mentioning include Fundação de Apoio a Pesquisa do Rio de Janeiro (FAPERJ, 3 studies), Fundação de Apoio a Pesquisa do Estado de Minas Gerais (FAPEMIG, 4 studies), and the Welcome Trust (3 studies). Seventeen studies did not report the source of resources.

The median number of citations received by original research papers was 5 (IQR 2–18). Considering only articles published up to 2015, the median was 17 (IQR 5–28). We produced three multivariate linear models to better understand what drives citation: (a) a regression for author and journal variables; (b) a regression for imaging technique; and (c) a model for the disease studied. All models were repeated restricting the sample to papers published up to 2015. The first model included Publication Year, International Coauthorship, First Author Gender, and Journal Nationality, showing a significant effect for publication in an international journal (p = 0.001) and the publication year (p < 0.001). Repeating the analysis with the papers up to 2015, only the effect of publication in an international journal remained significant (p = 0.037). None of the imaging techniques were associated with citation numbers either with the full or restricted sample (all ps non-significant). AD studies were associated with a higher number of citations (p = 0.003) and MCI studies showed a correlation with fewer citations (p = 0.04). In the restricted sample, only AD studies remained significant (p = 0.017).

JIF was available for 55/65 papers, with a median of 2.94 (IQR 1.90–4.35). The same models described for citations were used to predict JIF. In the first model, omitting Journal Nationality as a regressor, International Coauthorship was marginally associated with a higher JIF (p = 0.055). For imaging technique, Amyloid PET (p = 0.077) and fMRI (p = 0.061) showed a marginal positive correlation with JIF. None of the specific pathologies were associated with JIF.

**PECULIARITIES AND CHALLENGES THAT HINDER NEUROIMAGING DEMENTIA RESEARCH IN BRAZIL**

Dementia research in low- and middle-income regions is challenging. Like other countries in LA, due to different historical processes that have occurred since the end of the fifteenth century, Brazil has its own social, cultural, racial, and regional peculiarities (147). The heterogeneity makes the diagnosis of dementia and mild cognitive
### TABLE 1 | Main findings of articles included in the present review.

| Author                        | Journal                      | Year | Type | Methods     | Pathology | Reference |
|-------------------------------|------------------------------|------|------|-------------|-----------|-----------|
| Balthazar et al.              | J Int Neuropsych Soc         | 2010 | T    | Morph       | AD, MCI   | (12)      |
| Balthazar et al.              | J Int Neuropsych Soc         | 2010 | T    | Morph       | AD, MCI   | (13)      |
| Porto et al.                  | Dement Neuropsychol          | 2010 | CR   | Quali       | PCA       | (14)      |
| Chaves et al.                 | J Neuroinflamm              | 2010 | T    | Morph       | AD        | (15)      |
| Oliveira et al.               | J Alzheimers Dis             | 2010 | T    | Morph       | AD        | (16)      |
| de Toledo Ferraz Alves et al. | Curr Opin Psychiatr         | 2010 | R    |             |           | (17)      |
| Baldaçara et al.              | Rev Bras Psiquiatr          | 2011 | L    | Morph       | AD, MCI   | (18)      |
| Caramelli et al.              | Dement Neuropsychol          | 2011 | P    |             |           | (19)      |
| Avila et al.                  | Neurobiol Aging              | 2011 | T    | Morph       | Depressed Eld. | (20)     |
| de Oliveira et al.            | Am J Neuroradiol             | 2011 | T    | Morph, Other| AD, MCI   | (21)      |
| Balthazar et al.              | Dement Neuropsychol          | 2011 | T    | Morph       | AD, MCI   | (22)      |
| Ferreira et al.               | Clinics                      | 2011 | R    |             |           | (23)      |
| Ferreira et al.               | Neurobiol Aging              | 2011 | R    |             |           | (24)      |
| de Souza et al.               | Lancet                       | 2011 | CR   | Quali       | HAND      | (25)      |
| Caixeta et al.                | Clinics                      | 2011 | CR   | Quali, SPECT| PPA       | (26)      |
| Oliveira et al.               | Arq Neuro-Psiqiatr           | 2011 | T    | Morph, DTI  | PPA       | (27)      |
| de Toledo Ferraz Alves et al. | J Alzheimers Dis             | 2011 | T    | Morph       | HE        | (28)      |
| Vasconcelos et al.            | Clinics                      | 2011 | T    | Morph       | AD        | (29)      |
| Tiel et al.                   | Dement Neuropsychol          | 2012 | T    | Quali       | Vasc      | (30)      |
| Lanna et al.                  | J Neurol Sci                 | 2012 | T    | Quali, SPECT| Vasc      | (31)      |
| Simon et al.                  | Neurosci Biobehav R          | 2012 | R    |             |           | (32)      |
| Alves et al.                  | PLoS ONE                     | 2012 | T    | Morph       | AD, MCI   | (33)      |
| Alves et al.                  | Dement Neuropsychol          | 2012 | R    |             |           | (34)      |
| Sudo et al.                   | Dement Neuropsychol          | 2012 | R    |             |           | (35)      |
| Borgio et al.                 | Arq Neuro-Psiqiatr           | 2012 | L    | Morph       | MCI       | (36)      |
| Squarzon et al.               | J Alzheimers Dis             | 2012 | T    | Morph       | HE        | (37)      |
| Pedro et al.                  | Dement Geriatr Cogn          | 2012 | T    | Morph       | AD, MCI   | (38)      |
| Foss et al.                   | Clinics                      | 2013 | T    | Morph, Other| HE        | (39)      |
| Menezes et al.                | Arq Neuro-Psiqiatr           | 2013 | T    | Morph, Other| AD, MCI   | (40)      |
| Radanovic et al.              | Expert Rev Neurother         | 2013 | R    |             |           | (41)      |
| Sudo et al.                   | Arq Neuro-Psiqiatr           | 2013 | T    | Quali       | MCI       | (42)      |
| Dubois et al.                 | Lancet Neurol                | 2014 | P    |             |           | (43)      |
| Lee et al.                    | Brain                        | 2014 | T    | fMRI, Morph | FTD       | (44)      |
| Teipel et al.                 | Psychiatr Res Neuroim        | 2014 | T    | Morph       | PPA       | (45)      |
| Weiler et al.                 | Curr Alzheimer Res           | 2014 | T    | fMRI        | AD        | (46)      |
| Andrade de Oliveira et al.    | J Alzheimers Dis             | 2014 | T    | Morph       | AD, MCI   | (47)      |
| Weiler et al.                 | Brain Connectivity           | 2014 | T    | fMRI        | AD, MCI   | (48)      |
| Rondina et al.                | Front Aging Neurosci         | 2014 | T    | Morph       | HE        | (49)      |
| Balthazar et al.              | Hum Brain Mapp               | 2014 | T    | fMRI        | AD        | (50)      |
| Prezzi et al.                 | Arq Neuro-Psiqiatr           | 2014 | OR   | Quali       | D-EPS     | (51)      |
| Weiler et al.                 | Psychiatr Res Neuroim        | 2014 | T    | DTI         | AD, MCI   | (52)      |
| Killmann et al.               | J Alzheimers Dis             | 2014 | L    | Morph       | AD, MCI   | (53)      |
| Ferreira et al.               | Rev Bras Psiquiatr           | 2014 | R    |             |           | (54)      |
| Vasconcelos et al.            | Clinics                      | 2014 | T    | Morph       | AD        | (55)      |
| Tovar-Mol et al.              | PLoS ONE                     | 2014 | T    | DTI         | D-EPS, FDT| (56)      |
| Balthazar et al.              | Psychiatr Res Neuroim        | 2014 | T    | fMRI        | AD        | (57)      |
| de Oliveira et al.            | Acta Neurol Belg              | 2015 | CR   | Quali, SPECT| FTD       | (58)      |
| Yokoyama et al.               | PLOS ONE                     | 2015 | T    | Morph       | HE        | (59)      |
| Prado et al.                  | Dement Neuropsychol          | 2015 | R    |             |           | (60)      |
| Caixeta et al.                | CP & EMH                     | 2015 | T    | Morph       | D-EPS, FTD| (61)      |

(Continued)
### TABLE 1 | Continued

| Author                        | Journal               | Year | Type | Methods | Pathology | Reference |
|-------------------------------|-----------------------|------|------|---------|-----------|-----------|
| Forner et al.                 | Neurology             | 2015 | T    | Quali   | CJD       | (62)      |
| Hayata et al.                 | Arq Neuro-Psiquiat    | 2015 | T    | Morph   | AD        | (63)      |
| da Rocha et al.               | Dement Neuropsychol   | 2015 | R    |         |           | (64)      |
| Balardin et al.              | Front Aging Neurosci  | 2015 | T    | fMRI    | MCI       | (65)      |
| Weiler et al.                | J Alzheimers Dis      | 2015 | L    | Morph, DTI | AD        | (66)      |
| Coutinho et al.              | Int Psychogeriatr     | 2015 | T    | Quali   | AD, MCI   | (67)      |
| Alves et al.                 | BioMed Res Int        | 2015 | R    |         |           | (68)      |
| Promteangtrong et al.        | Dement Neuropsychol   | 2015 | R    |         |           | (69)      |
| Promteangtrong et al.        | Dement Neuropsychol   | 2015 | R    |         |           | (70)      |
| Haziot et al.                | Dement Neuropsychol   | 2015 | R    |         |           | (71)      |
| Boots et al.                 | Arch Clin Neuropsych  | 2015 | T    | Morph   | HE        | (72)      |
| Diniz et al.                 | Mol Psychiatr         | 2015 | T    | Morph, Ami | MCI       | (73)      |
| Agosta et al.                | CNS Neurosci Ther     | 2015 | R    |         |           | (74)      |
| Hamelin et al.               | Neurobiol             | 2015 | T    | Morph, Ami | AD        | (75)      |
| Grothe et al.                | Cereb Cortex          | 2016 | T    | Morph, FDG | MCI       | (76)      |
| Leuzy et al.                 | Brain Struct Funct    | 2016 | T    | Morph, FDG, Other | FTD     | (77)      |
| Resende et al.               | eNeurologicalSci      | 2016 | T    | Quali   | AD, MCI   | (78)      |
| Corrêa et al.                | J Mag Reson Im        | 2016 | L    | Morph, DTI | HAND      | (79)      |
| McAleese et al.              | BMC Med               | 2016 | R    |         |           | (80)      |
| Corrêa et al.                | J Neuroimaging        | 2016 | T    | Morph   | HAND      | (81)      |
| Teixeira et al.              | AGE                   | 2016 | T    | Morph, DTI | MCI       | (82)      |
| Weiler et al.                | Neurosci Biobehav R   | 2016 | R    |         |           | (83)      |
| Wang et al.                  | P Natl Acad Sci       | 2016 | T    | Morph   | AD        | (84)      |
| Ribeiro et al.               | Dement Neuropsychol   | 2016 | R    |         |           | (85)      |
| Alves et al.                 | Dement Neuropsychol   | 2017 | R    |         |           | (86)      |
| Pascoal et al.               | Mol Psychiatr         | 2017 | T    | Morph, FDG, Ami | HE        | (87)      |
| Lajoie et al.                | Neuroimage Clin       | 2017 | T    | fMRI, Morph | AD        | (88)      |
| Vasconcellos et al.          | Parkinson's Disease   | 2017 | T    | Quali   | PD        | (89)      |
| Tascone et al.               | PLOS ONE              | 2017 | T    | Morph   | AD        | (90)      |
| Etadi et al.                 | Front Neurosci        | 2017 | T    | DTI     | AD, MCI   | (91)      |
| De Souza et al.              | Prion                 | 2017 | CR   | Quali   | CJD       | (92)      |
| Shigaeff et al.              | Arch Gerontol Geriat  | 2017 | L    | fMRI    | EMS       | (93)      |
| Squarzoni et al.             | Clinics               | 2017 | L    | Quali   | HE        | (94)      |
| Fragoso et al.               | RadioGraphics         | 2017 | R    |         |           | (95)      |
| Radanovic et al.             | Dement Neuropsychol   | 2017 | T    | Quali   | AD, MCI   | (96)      |
| Resende et al.               | Arq Neuro-Psiquiat    | 2017 | T    | DTI     | MCI       | (97)      |
| Weiler et al.                | J Psychiat Neurosci   | 2017 | T    | fMRI    | AD, MCI   | (98)      |
| Rabelo et al.                | Neuroradiol J         | 2017 | T    | Quali   | AD, MCI   | (99)      |
| Corrêa et al.                | Neuroradiol J         | 2017 | L    | fMRI, Morph, DTI | HAND | (100)     |
| Ramos Bernardes da Silva Filho et al. | Neuroimage Clin | 2017 | T    | Morph   | AD        | (101)     |
| Swardfager et al.            | Alzheimers Dement     | 2017 | T    | DTI     | AD        | (102)     |
| Swardfager et al.            | Neurobiol Aging       | 2017 | T    | Morph   | AD        | (103)     |
| Ferreira et al.              | Rev Bras Psiquiat     | 2017 | T    | Morph, FDG, SPECT | AD | (104)     |
| Maia da Silva et al.         | Front Neurol          | 2017 | R    |         |           | (105)     |
| Smagula et al.               | Am J Geriatr Psychiatr| 2018 | T    | fMRI, Morph | HE        | (106)     |
| Branco et al.                | Psychiat Res Neuroim  | 2018 | T    | Morph, DTI | MIND      | (107)     |
| Simon et al.                 | Front Aging Neurosci  | 2018 | CT   | fMRI, Morph | MCI       | (108)     |
| Teixeira et al.              | Alzheimers Dement     | 2018 | CT   | Morph   | MCI       | (109)     |
| Weiler et al.                | Front Aging Neurosci  | 2018 | T    | fMRI    | AD, MCI   | (110)     |
impairment particularly challenging in comparison with developed countries (148). Regarding specific biological characteristics, for example, we far from understand the particularities of Brazilians miscegenated population. The regional genomic distribution of Brazilians is linked with the different colonization history of each region. Genetic admixture has been influenced by the colonization process, resulting in Brazil becoming a genetically trihybrid population (genomic inheritance of European, African, and Amerindian groups have been traced) (147). Previous epidemiological studies have highlighted that overall dementia prevalence can vary substantially across different ethnic groups and geographical regions (149). These differences in dementia prevalence rates have been attributed to different susceptibility to pathological brain changes in each ethnicity (150). In this sense, neuroimaging research in Brazil should consider these aspects. Neuroimaging studies are required to better characterize how subclinical brain changes might differ among ethnicities, and whether such differences may help explain differences in cognitive performance.
Neuroimaging research has provided evidence that previous or current adversities, such as low socioeconomic status or low levels of educational attainment, may reflect on interindividual variations in brain imaging measurements. Analysis from elderly individuals, recruited in an economically underprivileged area of São Paulo, showed reductions in both regional brain volumes and glucose metabolism in subjects with disadvantageous socioeconomic backgrounds (151, 152). Furthermore, education has a great impact on cognitive performance in older adults (153). A population census found that in 2018 nearly 52.6% of Brazilians over 25 years old did not have finished elementary school, and around 7.2% were unable to read or write (2). Variations in regional brain volumes were verified depending on the level of previous educational attainment (154). In this sense, ecological cognitive tests adapted to Brazilian characteristics (ex: including a wide range of schooling levels, illiterates, and stratified into groups of age and education) are important to be applied to more sophisticated methods, like body fluid biomarkers and neuroimaging.

Among chronic non-communicable diseases, those of the circulatory system are also the main cause of mortality worldwide, including Brazil, which has one of the highest rates in LA (155). Cerebrovascular damage, produced by midlife hypertension, diabetes, dyslipidemia, among other factors, may contribute to the onset and progression of cognitive dysfunction and dementia (156). Besides, Brazilians may have more cerebrovascular damage than other populations, as shown by Grinberg et al. (157) in a clinicopathological study with 1,291 individuals. In Brazil, cerebrovascular damage is one of the most neglected diseases, due to poor control of cardiovascular factors, especially hypertension, the main risk factor (155). In this context, it is surprising that only 4.6% of Brazilian original neuroimaging research was focused on vascular cognitive impairment. Dementia neuroimaging research in Brazil is highly focused on AD. Although AD is the most prevalent form of dementia, our results showed a disproportionate predominance to dementia epidemiology (158). The widespread interest in new drugs for AD may partially explain this finding (159). However, our study also showed that research involving AD was more likely to be cited, potentially feeding a vicious cycle. The underrepresentation of vascular dementia is particularly worrisome, as vascular risk factors and vascular pathology—either exclusive or mixed—are highly prevalent in Brazil. Once improvements in neuroimaging techniques allow detailed and sophisticated evaluation of many manifestations of cerebrovascular diseases, this topic must be considered a priority among Brazilian researchers.

The need for studies with the Brazilian population in this research field is an urgent matter. Scientific research, in general, is far from being fully developed and widespread across the country. Nowadays, even though Brazil is the 13th largest producer of research publications globally, its citation impact has historically been below the world average (160). The present work highlights some of the virtues and faults of the dementia neuroimaging research scenario in Brazil. Most of our findings are consistent with the Brazilian general scientific research background: a significant growth during the first decade of the twenty-first century followed by relative stability. Furthermore, the trend toward a highly concentrated scientific production in the Southeast region along with average-to-low research impact also reflects the national tendency (160). Finally, health research is particularly affected by spatial restriction in the national territory, as the cultural, ethnic, and socioeconomic diversity is not captured by the published depictions of our reality.

Brazil has limited wherewithals, sequential financial crises, bad investment of financial resources, and a lack of priority in investing in science in the different governments. All these factors limit the quality of scientific research performed in Brazil and delay the incorporation of novelties to generate original scientific data of global relevance. One of the consequences of these facts was the failure to implement Brazilian ADNI. Lack of fundings, heterogeneity of resources, and lack of specialized centers across the different regions of the country have hampered the implementation of a large national multicenter study. Besides, only recently Brazilian researchers have started studying molecular neuroimaging, with only five amyloid PET studies, and no Tau PET studies in the last decade. Despite these difficulties, Brazilians are studying and refining new neuroimaging methods, such as functional and structural connectivity, DTI, and surface-based morphometry. Two Brazilian centers in São Paulo and Rio Grande do Sul are studying amyloid PET, and collaborative studies are taking place. Comparisons of Brazilian neuroimaging studies with other countries of Latin America are difficult, due to the lack of relevant studies in this research area as they share the same problems found in Brazil. However, our neighbor Argentina is moving forward in the field, with the establishment of the first ADNI of Latin America (161). This program currently accounts for approximately sixty participants that are evaluated by structural MRI analysis, and metabolic and amyloid PET scan (FDG and PiB). This kind of multicentric program notably will assist the development of neuroimaging studies in low- and middle-income nations in the future.
Fortunately, increasingly Brazilian researchers are working across country borders, within foreign partnerships, and the resulting papers contribute to the impact of Brazil's domestic research. Although the majority of foreign partnerships analyzed in this review were derived from North America and Europe, there are efforts to develop collaborations with our neighbors of LA. One promising group is the Latin America and Caribbean Consortium on Dementia (LAC-CD), which is a regional organization that oversees and promotes clinical and research activities on dementia. Collaborations like this certainly can set new networks to support research and increase the supply of regional and international grant proposals (162). Taken together, suggests that knowledge and technological exchange can drive the Brazilian research scenario toward a richer production. All the above-mentioned challenges require efforts toward solutions involving clinicians, researchers, and policymakers, to better understand and investigate the dementia context in a continental country such as Brazil.

**CONCLUDING REMARKS**

As illustrated along with this manuscript, neuroimaging research carried out in low- and middle-income countries, such as Brazil, are challenging. Nonetheless, they are extremely important to increase the global knowledge about brain impacts derived from the inherent characteristics of the population, and their relationship with the development of dementia. Neuroimaging researches performed in the native population regarding regional peculiarities and adversities are of pivotal importance, especially in a resource-limited country facing economic and political adversities. In this sense, neuroimaging studies should address dementia not merely from a clinical perspective, but also in a societal context, considering individuals’ environment and peculiarities. Despite the aforementioned limitations, Brazilian researchers in dementia should be encouraged to deepen neuroimaging studies in Alzheimer's spectrum and other prevalent conditions, such as vascular dementia.
Because our focus was neurodegenerative diseases that primarily affect cognition, we did not evaluate normal aging or other conditions that may secondarily lead to dementia, such as Parkinson’s disease, Motor Neuron diseases, Epilepsy, or infectious/parasitic diseases common in Brazil. Further studies might consider the whole spectrum of dementias.

**AUTHOR CONTRIBUTIONS**

All authors contributed to the preparation and writing manuscript and approved the submitted version.

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**SUPPLEMENTARY MATERIAL**

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/neur.2021.640525/full#supplementary-material
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