

Alzheimer's disease, gender and health: reflections on the place of difference in neuroscientific research

Doença de Alzheimer, gênero e saúde: reflexões sobre o lugar da diferença na produção neurocientífica

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Abstract

The aim of this essay is to reflect about the place of difference in scientific research on Alzheimer's Disease (AD), which becomes a growing public health problem as the Brazilian population ages. In this scenario, our intention is to explore gender issues in relation to other social markers, to understand the heterogeneity of experiences and perceptions regarding the disease. To this do so, we carried out extensive bibliographic review and conducted brief online research on the PubMed platform. Although many studies indicate that Alzheimer's Disease has a higher incidence in women, issues such as race/ethnicity, social class, and other conditions have not been appropriated by researchers. Regarding prevention of the disease, differences are little or not considered.

Keywords: Alzheimer's Disease; Gender Feminist Studies; Social Studies of Science and Technology; Health.

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Resumo

O objetivo deste ensaio é refletir sobre o lugar da diferença na pesquisa científica acerca da Doença de Alzheimer (DA), que se torna um problema de saúde pública crescente à medida que a população brasileira envelhece. Nesse cenário, nossa intenção é explorar a questão de gênero na sua relação com outros marcadores sociais, a fim de compreender a heterogeneidade de experiências e percepções em relação à doença. Para isso, foi feita uma vasta revisão bibliográfica e realizada uma breve pesquisa online na plataforma PubMed. Embora grande parte das pesquisas apontem uma incidência maior da Doença de Alzheimer em mulheres, questões como raça/etnia, classe social e outras condicionantes não têm sido apropriadas pelos pesquisadores. No que tange à prevenção da doença, as diferenças são pouco ou nada consideradas.

Palavras-chave: Doença de Alzheimer; Gênero; Estudos Feministas; Estudos Sociais da Ciência e Tecnologia; Saúde.

Introduction

*And when I've left your circle,
Time, time, time, time
I will not be, nor will you have been*
Caetano Veloso, *Oração ao Tempo (A Time Prayer)*
(1979)

In recent years, a better quality of life, associated with social, environmental, and political aspects,¹ has increased people's average life expectancy, casting another look at aging and chronic-degenerative diseases. In this context, Brazil – historically recognized as a “young” country – now faces a different reality which includes the increased incidence of Alzheimer's disease (AD),² linked to the aging of its population and the growing concern with its treatment and prevention. Although many health professionals associate AD with predispositions such as diabetes or hypertension, we can categorize its relation to age as a direct and specific characteristic of this disease. Thus, a growing number of studies have evaluated pharmacological treatments to delay symptoms, experimental treatment forms, occurrence of the disease in certain population “types,” and the genetic origin of the disease.³

This study aims to explore whether research on AD addresses gender and other social markers to understand how scientific research, which helps guide prevention policies and treatments, has considered difference as part of its variables of interest. This concern follows international Science, Technology, and Society authors, who have, for decades, explored how medicine research agendas interrelate identity, and difference.

A classic example of such studies is Epstein (2004, 2006). The author highlights how social groups pressure and influence research agendas,

1 Such as reducing mortality and global fertility and the emergence of a range of pharmacological and preventive treatments.

2 We are aware that the term has been contested and that “Alzheimer's syndrome” may be a more appropriate terminology (Leibing, 2018). However, since most studies use it, we have adopted Alzheimer's Disease (AD) as the nomenclature in the conducted bibliographic search, maintaining in our sight those which approach the issue from the point of view of a “syndrome.”

3 Historically, AD has included several types of dementia. Between 1940 and 1950, North American hospitals began testing various therapy types, such as electroshock and food therapies (Engel, 2019). At that time, many physicians insisted that dementia had an intrinsic relation to aspects of their patients' social life, such as isolation in older adults, loss of family ties, retirement, etc. Some experts still believe and reiterate this perspective, blaming the disease on their patients' behaviors and experiences.

more specifically gay people taking interest in participating in HIV clinical trials. He also reflects on the controversies surrounding research with gender and sexuality, evincing how social markers are an important factor in forming biomedicine research agendas.

It is important to remember that in the 1980s the Atlanta International Conference on HIV was marked by civil movement and gay activists' participation, becoming an annual calendar event unrestricted to doctors and scientists. From that moment on, organized social movements' actions were important for antiviral tests, showing that patients are active subjects of clinical trials and problematizing the control groups receiving the placebo (Collins; Pinch, 2010).

Another example of how biomedicine and difference are intertwined is the case of BiDil, a controversial drug specially formulated for the African American population. Patients' resistance to it highlighted race controversies in the debate (Branca, 2005). Recent authors have investigated the naturalized relation between race and genetics and how we understand and treat diseases which would be "racially specific," explaining the importance of considering such elements in reflections on health/disease and treatment/prevention (Jorde; Wooding, 2004; Yudell et. al, 2021).

Wade et al. (2014), in **Mestizo genomics: race mixture, nation, and science in Latin America**, show how the issue of difference is a historically structuring element of Latin American scientific agendas. Based on research conducted in three countries (Brazil, Mexico, and Colombia), the book shows how central the category of race is to conforming research agendas in human genetics in a context in which several "origin myths" of how racial mixture helps configure these nations helped found both national imaginaries and scientific efforts.

Current research reinvents these narratives - which have been structuring our imaginaries since the 19th century - again highlighting the race variable. A very visible example is geneticist Sérgio Pena, professor at Universidade Federal de Minas Gerais (UFMG). His research has been instrumental in reinterpreting the notion of miscegenation as foundational in Brazil,

based on research of genetic ancestry markers which would show the intense mixture of races originating our population. He argues that since biology fails to recognize race, so should politics (Pena, 2006). Thus, Pena opposed the Brazilian Statute of Racial Equality.

Such examples show the intense interrelation between scientific and political agendas and help illustrate the relevance of better understanding how this interpenetration conforms biomedical research and policies. We understand that denaturalizing the biological component of race is an achievement but depoliticizing the structural racism in Brazilian society is a huge setback. Following this logic, questioning biological differences should differ from ignoring the social, political, and cultural differences materially impacting the bodies which are differently affected by the intersection between gender, race, class, sexuality, and other social markers. The AD case is one of many which show the relevance of thinking about intersectionality and its role in research and policy agendas.

According to the medical literature (Prado et. al., 2007; Mosconi et al. 2017; Savolainen-Peltonen, 2019), Alzheimer's disease affects more women than men, thus generating a significant number of scientific articles conducted exclusively with women. However, are these differences considered when thinking about prevention? To what extent do research and diagnosis situate and reflect on the role of gender, race, and class, among other social markers? Since research has indicated that women are the most affected by the disease, it is impossible to not highlight gender.

We must understand how the production of scientific knowledge about diseases has sought to collaborate with prevention and to what extent this production is socially and politically situated. To this end, we rely on Annette Leibling's (2018) concept of "situated prevention." The author refers to the need to critically contextualize prevention, aiming both at a more nuanced analysis in research on dementia - problematizing what narratives the field has privileged - and an attention to what really matters to people in their aging process. Thus, prevention would need to consider the sociocultural aspects of diseases (including difference issues), avoiding science

and public policies which propagate a biologically reductionistic understanding of diseases.

Thus, it is important to understand whether these agendas have considered gender issues and their relations with other social markers, thus dealing with “difference in its broad sense to fit interactions between possible differences in specific contexts” (Piscitelli, 2008, p. 266).

Gender as a marker of difference: toward a situated embodiment

We rescued Crenshaw’s (2004; 2020) notion of intersectionality to think about embodiment and prevention as situated around the centrality of gender. Advocating for Black women’s place of intersection, the author argues that “Black women’s experiences cannot be separately framed in the categories of racial or gender discrimination” (Crenshaw, 2004, p. 8) – nor is it the case that social markers simply overlap (race over gender or gender over race) but rather an intersection since – as the author warns us – we are not dealing with distinct, closed groups. Moreover, other discrimination groups also exist, such as age or generation and disability, for example.

Our discussion also engages with decolonial feminist theories (Curiel, 2007; Martín, 2013), situating it in Latin America, productions of the various Brazilian feminisms, such as Black feminism (Carneiro, 2018), lesbian feminism (Fernandes, 2018), and all “peripheral feminisms” or “other-feminisms” (Martín, 2013), and issues from white, middle-class, and heterosexual feminism.

We bring feminism prominently to the fore due to how central gender is to think of a necessarily situated embodiment and prevention. The Brazilian anthropologist Daniela Feriani (2017), for example, in her ethnography of the paths toward constituting AD, problematizes the extent to which the questions in the tests to detect the disease assume gender stereotypes and may thus compromise results. However, the medical literature fails to problematize stereotypes and naturalizations.

According to an interview in the *Jornal da USP* (University of São Paulo Times)⁴ with Professor Vitor Tumas from the Department of Neurosciences and Behavioral Sciences at the Ribeirão Preto School of Medicine, hormones, genetics, and environmental factors are among the risk factors for the development of Alzheimer’s in women. Other studies have also evaluated this association with hormones, such as Baum (2005) and Savolainen-Peltonen (2019), which are part of new studies in the 21st century which contradict theses of the previous century on the possible benefits of hormone replacement to prevent AD in women.

Mosconi et al. (2017), for example, associate the development of AD with glucose oscillations during women’s different reproductive periods. Based on supposedly universal biological criteria involving the reproductive cycles of this group throughout life, the studied sample contained between 71% and 86% of white women in each analyzed cycle. In this case, we note that the research is based on groups of white women, illustrating both a specific genderification and racialization of these results. If glucose levels and reproductive cycles are important to understand AD, Mosconi’s research shows this reality for a white female majority, but not for those of African or Asian origin, for example. And yet, what white women are we talking about? The study selected its sample based on biomarkers (hypertension, cholesterol, triglycerides, body mass levels, etc.) but fails to relate these criteria to other social markers besides gender.

As with the HIV clinical trials which Epstein debated, AD test groups fail to necessarily include multiple ethnicities (Heidi, 2019), conditioning the type of result emerging from these studies. What is generically called “human body” or “brain” is a materiality constructed and reconstructed daily in relation to these social markers. If new forms of prevention entail drug administration and lifestyle changes, then financial resources, type of work activities, time available for physical exercise and leisure, etc., will directly affect patients. Thus, we think of “a bodily history, a persistent physicality

4 Available at: <<https://jornal.usp.br/atualidades/demencia-afeta-mais-mulheres-que-homens/>> Access at: July 02, 2019.

that is part of their identity” (Mol, 2008). The highlighted variables intervene differently in body histories, outlining different bodies for which prevention requires considering their particularities. Otherwise, only a portion of the population will benefit from it.

In her discussion of anemia, Annemarie Mol (2008) reminds us that “If medicine were to perform all deviances in individualized ways, a lot of ‘undeniable’ biological sex differences would simply disappear.” But how feasible, in practice, would this individualization be? Mol replies that this decision would involve not only the reality of the disease but also that of these groups classified differently as “women” or “men.”

From this logic, what would be the “reality” of this group, “women,” in research on AD? Gender helps us to think about prevention in a plan between an ontological policy (Mol, 2008) and generalist representations. From the concept of “ontological politics” (Law, 2002; Mol, 2008) - already celebrated in social studies of science - we can think that a disease is an often unstable and multiple entity with unsteady borders: as in her study on atherosclerosis, the disease, including its materiality, can be seen as multiple. The disease is experienced and performed in multiple ways as patients experience it, healthcare providers and patients measure and demarcate it, and, of course, medical and tests concepts name it.

Thus, it became necessary to question the multiple representations of reality, its sources (whether images or words), and how the reality of diagnosis is modeled. It is important to understand how patients represent themselves but also how scientists represent them (Mol, 2008). Beyond biomarkers, the diversity of social markers helps us to think about prevention in an intersection between ontological policy and certain neuroscientific universalizing representations of prevention. We understand that this intermediate place follows the implication that the reality of the disease is materially, historically, and bodily situated. Thus, an intermediate place makes and stimulates new realities which are always marked by issues of gender, race, class, and other determinants intervening in bodies which simultaneously perform these new realities in the most different ways.

We assume that these representations - intended as universalizers - fail to realize the complexity of the markers intersecting and delineating disease prevention and treatment. Moreover, the materiality of individual, situated bodies may react differently from pre-established medical standards. As we have previously argued (Souza; Monteiro, 2014), it is not only the awareness of oneself or the technique (or their combination) which makes the disease but the action which enables the disease to be made and patients to relate to it. In the words of Mol and Law (2004), the body is a “set of tensions” (p. 13) but importantly, a set of tensions daily performed from individual, social, historical, cultural, and political dimensions.

When a disease is associated with a gender, a biological predisposition is assumed to be linked to certain types of determinisms which supposedly depend on sexual dimorphism. First, this is a notion which gender studies and queer theory highly contest (Foucault, 1997; Butler, 2003; Preciado, 2018) since biological sex is also socially, historically, politically, and culturally situated. Thus, we note an important controversy for this study: if the representation of the sick assumes itself universal, why do different social expectations for men and women, for example, compromise this supposed universality?

Thus, we understand the production of knowledge on diseases as a partial perspective (Haraway, 1995). We assume that the bodies affected by diseases are specific and not universal (Esptein, 2004) since they are unequal, situated, and relational and always exist in relation to other knowledge and institutions. Moreover, another complexity concerns the relation between bodies and diseases: people and bodies with Alzheimer’s exist in specific contexts which are marked by gender, race, class, sexuality, and age issues, thus also situating the experience of the disease.

Studying the production of neurosciences is crucial to problematize the information and techniques (Mol, 2008) which help sustain a certain infantilization of people diagnosed with dementia in Brazil, as previous ethnographic studies have pointed out (Leibling, 2016). Note the tendency to present people with dementia as

completely dependent on the care of others (again, they are mostly women). Moreover, dementia, though a situated social and relational experience, is subtracted from patients' experience - considered incapable - who, consequently, have their autonomy reduced by caregivers and healthcare providers.

Since the supposed universality of brain morphology is unsuitable as the only reference for prevention and treatment, we obtain the importance of a cross-cultural, interdisciplinary, and intersectional view of the disease. The brain is an organ in constant interaction and tension with other organs (Mol; Law, 2004), present in a body socially situated in terms of its gender, race, class, and sexuality. Research conducted at the interface between science, gender, and technology has explained the fallacy of these determinisms and how a predefined and naturalized imaginary of genre constructed scientific facts (Haraway, 2009; Keller, 2006)

Lab mice and gender problems

Considering that Brazil mainly researches and treats AD via neurologists (who most prescribe drugs for the disease), we would also need to investigate the specific scientific production of this medical specialty in Brazil.

To test its explored hypotheses on how the scientific production on AD fails to reflect on social markers, this study briefly searched the PubMed platform. We used the terms "Alzheimer's prevention Brazil" with a one-year filter (from August 2019 to July 2020), retrieving 37 results. Brazilians authored and co-authored 29 of these,⁵ of which 25 recreated traditional research, involving biomarkers and cognitive and pharmacological aspects. Only four indicated a discussion sensitive to social factors.

This in itself is remarkable. The absence of any debate on the relevant difference in recent research

on Alzheimer's and a focus on biological markers indicates the predominance of certain research agendas, offering us clues as to how they construct and implement prevention and treatment. Of the four articles with some discussion on social factors, we found a longitudinal study conducted by eight Brazilian researchers (four women and four men) with a more diverse sample, considering "age, gender, number of assets, past hazardous drinking, exercise and self-report of heart disease" to think about the relation between tobacco consumption and the development of dementia (Otuyama et al., 2019); and two articles which used a "harmonization" methodology in large cross-cultural research, assuming that the differences between countries delayed the development of effective policies (Ferri; Oliveira, 2019) and aiming to "harmonize and adapt multidomain interventions across various countries and settings" (Kivipelto et al., 2020). Although we take the perspective of public policies, we question to what extent this so-called harmonization would further obliterate the cultural differences between countries and the class, gender, race, and ethnicity disparities within each nation.

Finally, of those four articles, one specifically drew our attention for reasons very different from the initial issue of our reflection. From a feminist perspective, we were interested in the fact that mostly women authored that article (Giacomelli et al., 2019). Of its six Brazilian authors, five were women; its only man was its fifth author. That study sought to investigate the benefits of curcumin⁶ (derived from turmeric) in treating AD, using aged female mice for this. We also found a very similar study (Giacomeli et al., 2020), written by six Brazilian authors - four women and two men - which, like the first study, uses aged female mice.

We return to one of the points of this study: the medical literature finds the 3/2 women to men prevalence of AD. We wondered if this assumption would have led scientists to opt for older female

⁵ Available at: <https://pubmed.ncbi.nlm.nih.gov/?term=Alzheimer%27s%20prevention%20Brazil&filter=datesearch.y_1>. Access at: July 30th, 2020.

⁶ Recent studies indicate that oxidizing therapies, such as curcumin, can function as a neuroprotective strategy, reducing the oxidative damage caused by Alzheimer's disease.

mice in their research to the detriment of male mice or younger females. For Beery (2018), researchers always opt for males in various biomedical studies for assuming that females would be more variable due to their estrogen cycles. As we know, this pathologizing argument (used both by medicine and common sense) refers to mood swings in fertile women. Thus, we found a controversy: would guaranteeing the use of female rodents in research “democratize” science or re-recreate differences? Beery (2018, p. 143) claims that

Female subjects are underrepresented in animal research across disciplines, however [...], and lack of pre-clinical research on female subjects has likely resulted in poorer treatment outcomes for women [...]. In 2014, noting potential human health consequences of this research bias, the NIH instituted policies to encourage use of both male and female animal research individuals, and consideration of sex as a biological variable [...]. Biological sex - classification as generally male or female based on genetic and physiological features - is typically distinguished from gender - one’s self-representation as man, woman or non-binary. Inclusion of both sexes in animal research studies should drive important discoveries in both basic and clinically relevant research [...].

Another argument, according to the author, shows the fear that differences overlap with “fundamental similarities” and increase variability. Her third argument concerns the fallacy of the model of gender differences in human health, “that may have important sociocultural components” (Berry, 2018, p. 143).

Since 1993, the U.S. National Institutes of Health (NIH) have required clinical research to include women, but Beery tells us that this requirement is often disregarded. In 2014, the NIH established policies to include “sex as a biological variable” (Beery, 2018, p. 143). In November 2017, it announced an amendment to require the registration of searches conducted explicitly from this marker. Sex, then, is considered a variable, but studies need not problematize its implications. At the same time, we know that just including women in clinical research

without, however, substantially improving their health is insufficient.

From Beery’s perspective (2018), including females in animal studies may foster important discoveries. She argues that male mice have shown more variability in research than females. Hamsters show no differences between males, females with ovaries producing estrogen, and ovariectomized females lacking estrogen. “Sex differences can be small or large, insignificant, or critical,” the author summarizes: “One concern about the reporting of sex differences in animal studies is that it may lead to overestimation of human sex/gender differences, especially in brain and behavior.” (Berry, 2018, p. 145-147).

In neurosciences, Beery reports that only 20% of studies use rodents of both sexes and 25% fail to specify gender. The analysis of the neuroscience literature suggests that the omission of the theme has decreased in recent years but the number of studies with male rodents has increased, and mixed-sex analyses remain infrequent (Beery, 2018). In a way, sex is understood as variable, but studies need not problematize its implications. From Beery’s data, we can see how naturalized binarism separating sex and gender still marks both male and female scientists’ gaze.

Final considerations

*Bodies only speak if and when
they are made heavy with meaning
Annemarie Mol (2002)*

As we have seen, studies assessing underlying behavioral mechanisms in people are rare, causing us to have little understanding of the impact of studies which start off with the assumption that differences are relevant (Beery, 2018). Still, we know that much of the difference between women and men is based on factors which go beyond sex biomarkers, such as culture, gender, specific body experiences, race/ethnicity, social class, etc.

The claim of a “science of women’s health” leads us to a clash. On the one hand, reclaiming women in research would be a way, within this logic, to demand that science care about their body and health specificities. On the other hand, this blurs

the problem from the social toward the strictly biological. If differences between women and men are more cultural than biological, guaranteeing the presence of female mice in experiments fails to ensure research results which favor women. Moreover, failing to question the exclusive use of male mice does not seem to us very feminist. Despite from however many “sides” we view it, we will slide in circles since we are looking at the wrong problem. Thus, we understand that the bigger issue is ensuring a sociocultural sensitivity in AD public policies rather than just a reductionist focus on biomedical factors since bodies with AD experience the disease and its consequences immersed in complex realities marked by gender, race, and class differences, among others.

The Brazilian medical, biological, and natural scientific literature contains only a few studies conducted beyond the traditional biology-cognition-pharmacology standard. If the concern of these studies toward gender (when it exists) is just ensuring sexual diversity between mice, we are still a long way from visualizing policies to prevent AD which consider “women” a category performed by scientists and laboratories ignoring their nationality, race, class and life experience diversity.

Thus, we believe that the intersection between feminist and social studies of science can support research aimed at producing a more humanized science which recognizes diversity in its complexity and understands that the woman category is performed, an abstract notion overlapping the materialities lived and acted in the bodies of different women, attained in different ways on their bodies and health. As Gayle Rubin (1993) wrote,⁷ after all, women are closer to men than to apes. The question is, will medicine and science understand that women are closer to men than to female rodents?

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7 Original from 1975.

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Author's Contribution

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