

Tentative Outline

Special Thematic Issue for the journal *Current Alzheimer Research*

Reflections on normal and pathological aging in underrepresented populations

Guest Editors: Felipe Botero-Rodríguez & Hernando Santamaría-García

- **Scope of the Thematic Issue:**

Worldwide, global initiatives have called for studying normal and pathological aging in underrepresented populations. Nevertheless, most previous studies have excluded underrepresented populations from low- and middle-income countries (LMICs), and they are mainly dedicated to evaluating pathological aging, neglecting forms of aging brain health. Pathological aging, which has been more studied and is primarily represented by neurocognitive disorders (NCD), comprises a group of incurable and progressive diseases that are becoming more prevalent. With an estimated three-fold increase in prevalence, mainly in underrepresented populations. On this matter, by 2050, the proportion of people living with dementia will increase by around 75% in western Europe, about 200% in Latin American countries, and 350% in African countries. Even though the increase is estimated mainly in underrepresented populations, the risk factors studies have been carried out mainly in HICs, widening the gap between countries worldwide.

The World Health Organization (WHO) fosters that at least 80% of countries will have at least one functioning intersectoral program for brain health promotion and the prevention of neurological disorders across the life course by 2031. In this line, aging brain health is defined by the WHO as “a state in which every individual can learn, realize their potential and optimize their cognitive, psychological, neurophysiological, and behavioral responses while adapting to changing environments.” It is a dynamic and multifactorial process along the life course underpinned by physiological processes and interactions. Brain health is influenced by social determinants of health, medical risk, and protective factors, including cardiometabolic state and lifestyle habits. Therefore, a new research plan is needed to know the aging brain health determinants in LMICs and establish potential contrasts with HICs. Moreover, studying aging brain health is critical in LMICs as they exhibit exclusive epigenetics, genetics, ancestry, and social determinants of health (SDH).

For instance, there is knowledge about ancestry factors related to early Alzheimer’s disease (in Colombia, it has been described that PSEN1 E280A mutation carriers have more odds of presenting it, as well as mutations in the PRNP gene, Gly114Val, and G114V). Also, it has been said that the APOE ϵ 4 allele has differential effects within African ancestry compared to Caucasians. The frequency of this mutation has been reported to vary between 5% in Sardinians to over 40% in Pygmies in Africa. Additionally, immigrants from these regions have been affected by isolation, and we know the impact of rare variants such as TREM2, PLCG2, and ABI3 imply a different risk than other populations. Despite the above, <3% of the polygenic risk scores have been developed from Latino, or indigenous populations.

The mixed genetic and SDH risk featured in LMICs populations, such as genetic clusters, low literacy and cognitive reserve, multilingual, multi-ethnic, and high levels of inequity, represents an opportunity to understand the impact of disparities on aging brain health and neurodegenerative disorders. Otherwise, social differences like less schooling, lower socioeconomic status, social deprivation, social stress, extreme poverty, and greater reported violence and forced displacement, among others, could represent another differential risk between LMICs and HICs.

There are critical gaps in understanding the associated risk factors and the role of SDH related to their presentation (including social adversities such as exposure to violence and restricted access to health resources), which are also different in LMICs compared to HICs. For example, European/North American and African/South American countries. In this way, we should understand the genetic and epigenetic forms of brain health and identify the particular polymorphisms related to cognitive resilience and particularities. Likewise, the Hispanic paradox or the role of working memory studied in South Africa facilitates cognitive resilience in older adults from disadvantaged contexts interacting with their environment.

Considering the above, the opportunity to study normal and pathological aging through different methodologies aiming to deepen the understanding of the variations in other populations and integrate genetics, epigenetics and social characteristics becomes necessary. Thus, we are interested in exploring these characteristics and the related factors with healthy aging in diverse populations around the world that have been neglected in most investigations.

This Research Topic aims to address issues related to brain health and expand knowledge on the biological, social, and clinical determinants of the forms of healthy and pathological aging in underrepresented populations. Furthermore, to promote public health policies and have evidence-based dialogues with stakeholders to achieve equitable care for NCDs worldwide.

Keywords: Dementia; Alzheimer's Disease; Brain Health; Screening; Public Health; Aging.

Sub-topics:

- Public Health concerns
- Brain Health promotion
- Normal aging
- Pathological aging and related factors
- Future research

Schedule:

- ✧ Thematic issue submission deadline: 31st December 2022

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