Computational brain models map diversity embedded in aging and dementia

This study explored how diverse factors including neurocognitive disorders, socioeconomic inequalities, pollution and gender disparities influence brain aging in underserved populations (groups with limited access to essential services such as healthcare and education). Using deep learning on EEG and fMRI data, we identified brain-age gaps as key markers of accelerated brain aging and their connections to macrosocial determinants of health.

This is a summary of:
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The question

Brain health, aging and dementia are shaped by numerous cumulative burdens, including socioeconomic, environmental and health disparities[1]. Factors such as socioeconomic inequality, pollution, health disparities and gender inequality might affect brain aging in both neurotypical individuals and individuals with neurocognitive conditions such as mild cognitive impairment (MCI), Alzheimer's disease and behavioral variant frontotemporal dementia (bvFTD). However, how these multimodal burdens affect health metrics of accelerated brain aging, such as brain clocks (which measure the gap between a person's brain age and their actual chronological age) remains unclear. We set out to address this gap by developing a computational framework that could assess how multimodal diversity shapes brain aging. Including underserved populations from Latin American and Caribbean (LAC) countries enhances our approach by capturing detrimental exposomes (internal and external exposures a person experiences throughout their life)[2], and socioeconomic disparities.

The solution

We analyzed two independent electroencephalography (EEG; $n = 2,353$) and functional MRI (fMRI; $n = 2,953$) datasets from 5,306 participants (aged 21–92 years) from 15 LAC and non-LAC to capture multimodal diversity within our datasets. Our datasets comprised 3,509 neurotypical individuals, and 517, 828 and 463 individuals with MCI, Alzheimer's disease and bvFTD, respectively. LAC are among the most unequal societies, with underserved domains across several areas including healthcare access, income and education. The data were processed by deep learning models using graph convolutional networks (GCNs) to capture higher-order interactions in brain networks. This design allowed us to quantify the modulation of brain-age gaps — differences between our model's prediction versus the participant's chronological brain age — by diverse factors such as neurocognitive status (being a neurotypical individual versus an individual with MCI, Alzheimer's disease or bvFTD), structural socioeconomic inequality, pollution, health disparities and gender inequality. GCNs captured higher-order interactions by analyzing both direct and indirect connections in brain networks. Unlike other models, GCNs process graph-structured data, enabling the detection of complex context-specific patterns embedded across multiple brain regions more effectively. We trained models separately for LAC and non-LAC to capture region-specific effects and used a robust validation framework to ensure the generalizability of results. We used separate training and test datasets for fMRI and EEG, with out-of-sample validation showing consistent results across regions, sex, sites and clinical conditions.

Both our EEG and fMRI findings indicated that participants from LAC, particularly women, exhibited larger brain-age gaps than participants from non-LAC, suggesting accelerated brain aging (Fig.1a,b). Socioeconomic inequality and pollution were the most influential predictors of accelerated brain aging in LAC, and health disparities also contributed. Furthermore, brain-age gaps increasingly progressed across neurotypical, MCI and bvFTD groups, indicating accelerated brain aging in neurocognitive disorders and positioning MCI as an intermediate stage between neurotypical aging and dementia. Together, these results highlight the influence of macrosocial factors on brain aging and the necessity of developing context-specific models to capture multimodal diversity.

The implications

Our findings suggest that context-specific computational models that can address multimodal diversity are necessary for understanding global brain health, aging and neurodegenerative disorders[3], as brain age markers from these models can help identify groups at higher risk of dementia progression. Using these models, combined with globally accessible data, our study paves the way for more inclusive tools to assess disparities and diversity in brain aging[1].

This framework should be applied to develop precision brain health strategies that address specific regional and gender disparities such as those found in our study. A limitation of our research is that it focused primarily on comparisons between LAC and non-LAC, which may not fully capture the diversity within either region. In addition, although we controlled for data quality and demographic factors, other unmeasured variables may also have contributed to brain-age gaps we identified and analyzed.

Developing macrosocial and aggregate-level metrics will strengthen our understanding of how social determinants shape brain health across the lifespan. In our future research, we hope to integrate genetic and environmental data to further refine brain-age models.

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EXPERT OPINION

"The authors conducted an interesting study with a large number of individuals to identify brain-age gaps in both the global north and south, using a complex statistical model to explore high-order interactions using EEG and fMRI. The study offers valuable insights into the neurobiological mechanisms of brain aging and the environmental effects on the aging process." **Wyllians Vendramini Borelli, Federal University of Rio Grande do Sul, Porto Alegre, Brazil.**

FIGURE

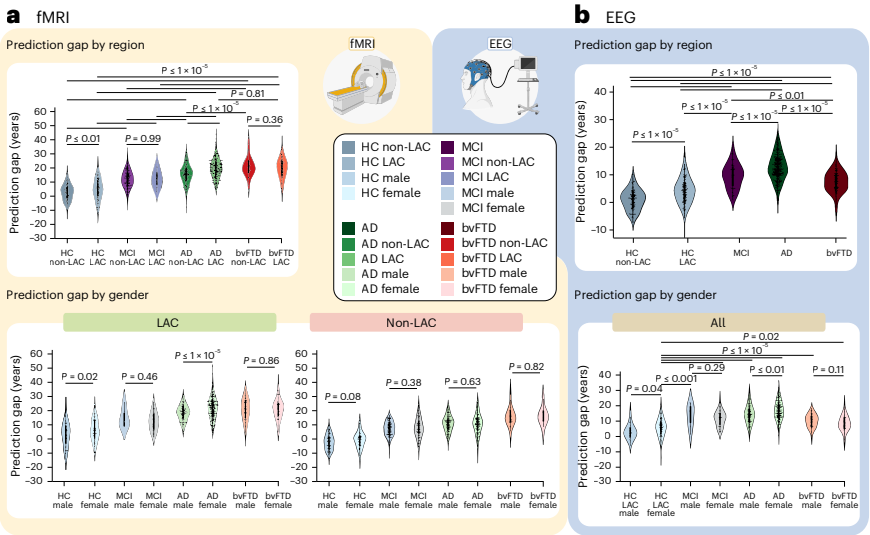

Fig. 1 | Neurocognitive and sex differences in brain-age gaps. a,b, We trained deep learning models using GCNs to capture higher-order interactions in brain networks obtained from fMRI (**a**) and EEG (**b**) datasets. The distribution of prediction gaps in years — or brain-age gaps — was stratified by region (LAC versus non-LAC; top) and further separated by gender (bottom) to create subgroups of neurotypical participants (healthy control, HC) and participants with a neurocognitive condition — MCI, Alzheimer's disease (AD) or bvFTD. We observed accelerated brain aging in individuals from LAC compared to non-LAC, and in HCs compared with individuals with neurocognitive conditions, with ascending brain age from HC to MCI and AD. For both fMRI (**a**) and EEG (**b**), women from the HC and AD subgroups in LAC showed accelerated brain aging compared with men. The fMRI and EEG device images were created with BioRender.com.

BEHIND THE PAPER

Studying Latino and/or Latina populations has always presented unique challenges[4], especially as we found that many models developed in other regions simply did not fit our data well[1,5]. This research was driven by the need to create models that capture the specific combination of multimodal diversity and tailored effects seen in Latino/Latino individuals, rather than forcing them into a single, universal framework. We are hopeful that these models can pave the way for future development of personalized, context-sensitive approaches. By addressing the complex forms of multimodal diversity, we aim to provide recommendations to policymakers and use population neuroscience to anticipate and mitigate factors that accelerate brain aging in different regions. Understanding how embodied and embedded brain health are influenced by multimodal burdens is crucial to fostering healthier brain aging trajectories worldwide[2]. **A.I. & S.B.**

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FROM THE EDITOR

"This is one of the most geographically diverse studies on brain aging, particularly including populations from Latin America and the Caribbean, which is underrepresented in aging and neurology research. The findings are important to highlight how diversity and disparities within populations from different regions with different levels of structural inequities and environments can impact brain health." **Editorial Team, *Nature Medicine*.**