

Structural brain ageing in Kenya

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Abstract

Establishing normative brain-ageing reference standards is essential for distinguishing healthy ageing from the emergence and progression of neurodegenerative disease. However, most normative references have been derived from cohorts in high-income countries (HICs), representing only ~ 20% of the world's population. Their generalisability to low- and middle-income countries (LMICs) with varying social and environmental exposures remains uncertain. Here, we present the first and largest Kenyan normative brain ageing model, based on structural MRI from 273 neurologically healthy adults aged 35–81 years. Age-related differences were most robust for cortical thickness and cortical volume, predominantly in association cortices, broadly mirroring patterns reported in European and North American samples. Critically, socio-environmental deprivations moderated the association with age for some brain measures, underscoring the impact of life-course exposures for brain health. These results enhance the global representativeness of brain ageing models and call for the development of LMIC-specific frameworks to support equitable brain health policy.

MAIN

Normative brain-age reference curves, which provide statistical benchmarks for typical brain morphometric changes across the lifespan, have been derived nearly exclusively from cohorts in high-income countries (HICs)^{1,2,3}. Paradoxically, 2024 estimates indicated that 80% of the world's population was concentrated in low- and middle-income countries (LMICs)⁴. Given the substantial differences in environmental exposures and socio-cultural contexts worldwide that influence healthy brain ageing⁵, the generalizability of these patterns is unknown, especially in the African context, where structural neuroimaging studies remain rare^{6–8}. Here, we address this gap by evaluating age effects on cross-sectional MRI morphometry data from neurotypical adults in Kenya (N = 273).

Characterising normative brain ageing reference curves is fundamental to contrasting healthy ageing with the onset and progression of neurodegenerative conditions. Healthy ageing is generally associated with gradual reductions in grey and white matter volumes, sulcal widening, cortical thinning, and ventricular enlargement⁹. In contrast, pathological atrophy is when changes exceed expected age-related trajectories. This is a core feature of neurodegenerative diseases, including Alzheimer's disease¹⁰, which is characterised by chronic neuroinflammation¹¹, vascular pathology¹², and accumulation of neurotoxic proteins¹³.

Therefore, scientific advances in ageing-related diseases, such as dementia, should be preceded by fundamental research on neuroimaging biomarkers of healthy brain ageing.

To characterise age-related changes, we used structural magnetic resonance imaging (MRI), a reliable neuroimaging tool that provides quantitative metrics of brain structure¹⁴. Using a semi-automated image-processing pipeline¹⁵ (Freesurfer v. 7.4.1), we derived cortical and subcortical features across individuals ranging in age from 35 to 81 years. Based on previous descriptions in HIC cohorts, we

expected to observe ventricular enlargement^{1,16}, cortical thinning^{17–19}, and volume loss across deep grey matter structures^{20,21} as standard features of ageing. We hypothesised that these morphological brain changes would occur linearly and non-linearly, depending on multiple factors, including stage-specific processes known as inflexion points, which tend to occur around middle and late adulthood^{22,23}. Critically, we expected to observe steeper age-related associations among individuals classified as multidimensionally poor, based on deprivations in education, health (food and water security), and living standards (e.g., clean cooking fuels, electricity, sanitation)²⁴.

Overall, we observed that cortical thinning and volume reductions, particularly in frontotemporal regions, were more robust markers of ageing, correlating more strongly with ageing than surface area. Furthermore, we observed linear age-related increases in ventricular volumes and decreases in cerebral tissue volumes, except for the amygdala, which showed a nonlinear downward trend. Altogether, these observations align with previous reports based on HICs, demonstrating similar rates and spatial patterns of healthy brain ageing. Critically, some of these ageing relationships were moderated by multidimensional poverty. Together, these findings

expand neuroanatomical knowledge of an understudied population and enhance the global representativeness of normative brain-age curves, as other initiatives^{25,26}.

RESULTS

To characterise age-related brain changes in a Kenyan cohort, we analysed 3T structural T1- weighted images from 273 healthy participants at a single time point, as part of the longitudinal Brain Resilience Kenya (BRK) Project at Aga Khan University in Nairobi, Kenya (Fig. 1A). Raw MRI data quality was ensured to be of high quality, as inspected by board-certified radiologists and quantitative approaches (**Supplementary Fig. 1**). Using Freesurfer version 7.4.1¹⁵, all scans underwent cortical reconstruction and segmentation. Cerebral reconstruction was inspected both quantitatively and qualitatively in accordance with ENIGMA standards (v.2²⁷).

Participant demographics

Participants were recruited from the urban area of Nairobi. The study was designed to investigate the impact of varying stress conditions on brain ageing by enrolling people with newly diagnosed breast or prostate cancer, alongside their self-identified caregivers and a large cohort of cognitively unimpaired community controls (CC). To address the current study objective of characterising normative brain ageing, analyses were constrained to the CC group. In addition, we excluded people with clinically significant incidental findings, as identified by radiologists, and those with poor MRI quality (**Supplementary Fig. 1**). The resulting sample consisted of 273 participants ranging in age from 35 to 81 years [155 females (median: 48, sd: 8.73) and 118 males (median: 49, sd: 11.54)]. Across sexes, 3.22% of females and 20.33% of males were over their respective life expectancies (**Supplementary Fig. 2A**).

Overall, the multidimensional characteristics of the sample were representative of the Nairobi County population (**Supplementary Fig. 2B-C**)²⁸.

Cortical features change with age

Cortical thickness declined with age, with the strongest effects in association cortex (Fig. 2A; **Supplementary Table 1A**). In vertex-wise analyses regressing out biological sex as a covariate, age was associated with widespread thinning, most pronounced in the dorsolateral and medial prefrontal regions, the lateral temporal cortex, and the inferior parietal/precuneus regions (permutation-based FWE-corrected $p < 0.05$). The largest effects were observed in superior frontal and pars triangularis, middle/inferior temporal, and precuneus and inferior parietal regions, with peak thinning rates of $\sim 4\text{--}6\%$ per decade expressed relative to the vertex-specific reference thickness (i.e., the sample mean thickness at each vertex; **Supplementary Fig. 3A**). Thinning was also detected in the precentral cortex bilaterally, indicating that age effects were not restricted to association areas.

In contrast to thickness, surface area was not consistently associated with ageing (Fig. 2B, **Supplementary Table 1B**). In the left hemisphere, we observed an age-related decline in the rostral medial frontal cortex at $\sim 4\%$ per decade (**Supplementary Fig. 3B**). In the right hemisphere, similar rates of reduction were observed in the middle temporal lobe. These results

were not unexpected as thickness consistently correlates more strongly with age than surface area across longitudinal and cross-sectional studies^{17–19}. Cortical volume declined strongly with age in a spatially concordant manner to that of thickness, mostly with robust changes in association cortex (Fig. 2C, **Supplementary Table 1C**). The largest effects were observed in the cingulate and rostral medial frontal, precuneus and inferior parietal cortex, and fusiform and inferior temporal cortex, with most volumetric losses ranging between $5\text{--}10\%$ per decade relative to the vertex-wise reference volume (**Supplementary Fig. 3C**). Volumetric atrophy was also detected in regions outside of the association cortex, such as the paracentral and precentral cortices.

Cerebrum tissue volume changes with age

Global cerebrum tissue volumes declined across adulthood, except for the ventricles, which increased in volume with age (Fig. 3; **Supplementary Table 2**; FDR-corrected for 7 regions, all $p < 0.05$). Generalised additive models (GAMs), controlling for biological sex and total intracranial volume, indicated predominantly linear age effects across tissues (edf ≈ 1 ; FDR $p > 0.05$). In contrast, amygdala volume showed modest evidence for a nonlinear decline (edf = 3.21; $F = 14.23$; $\Delta\text{BIC} = 8.3$). While such non-linear trajectories and transition points have been reported²², these estimates should be interpreted with caution, given the sparser sampling at older ages in our cohort (10th– 90th percentile: 38–64 years). Cortical grey matter showed the largest negative association with age, corresponding to a 3.11% decline per decade relative to the model-predicted reference volume (**Supplementary Table 3**). Subcortical grey matter volume exhibited a similar rate of decrease per decade (3.40%), while white matter showed a more modest decrease (2.07% per decade). Ventricular volume increased markedly with age (14.86% per

decade). For subcortical structures, thalamic volume (4.02% per decade) declined more steeply than hippocampal volume (2.57% per decade). More information on model stability and robustness is provided in **Supplementary Fig. 4**. Lastly, we present GAMs for the Desikan-Killiany atlas²⁹ (DKT)-based regional volumes in **Supplementary Fig. 5**.

Axes are scaled in units of 10,000 mm³ (10 ml). Points are coloured by biological sex. Solid lines indicate fitted curves, and shading represents 95% confidence intervals. (B) Model comparison for each tissue using generalised additive models with either a linear age term or a penalised smooth for age. Scatter plots of BIC (left) and AIC (right) scores for non-linear versus linear models, with dot size indicating the effective degrees of freedom (EDF). The point colour denotes the selected model, as shown in A.

Association between multidimensional poverty and cerebral integrity

While age-related associations were generally similar to those reported in cohorts from HICs, we explored whether participants exposed to multidimensional poverty would exhibit steeper age-related declines (N = 268 with available data; 98.2% of the total sample). As before, we modelled seven cerebrum tissue volumes using GAMs with age as a linear covariate, controlling for sex and intracranial volume, and included an interaction between age and multidimensional poverty at different deprivation thresholds (Fig. 4A). Exposure to at least 2 deprivations (55.6% of analytical sample) yielded three significant age by deprivation interactions: reduced age-related decline in the amygdala ($p = 0.01$, $\beta = 0.03$, crossover age = 56.9) and white matter

($p = 0.02$, $\beta = 0.03$, crossover age = 48.4), and a lower age-related increase in ventricular volume ($p < 0.01$, $\beta = -0.03$, crossover age = 52.6) relative to participants who were exposed to one or no deprivations (Fig. 4B). These findings are contrary to our expectation of a steeper age-associated decline and instead suggest greater stability in brain volumes among people with multidimensional poverty. Further characterisation of these interactions indicated that group differences were most apparent before the crossing points, with marginal differences in the amygdala ($\beta = -0.21$; $p = 0.065$) and ventricles ($\beta = 0.23$; $p = 0.10$). Collectively, these exploratory analyses suggest that among individuals surviving beyond average life expectancy, exposure to socioeconomic deprivation is associated with attenuated age-related cerebral tissue loss.

(A) Sensitivity analysis exploring various degrees of deprivation classification and their association with cerebrum tissue volumes. Tile plots depict standardised beta coefficients for the interaction effect between age and group for a corresponding volume. Asterisks denote FDR-corrected statistical significance (* $p < 0.05$, ** $p < 0.01$) (B) GAMs for amygdala, white matter, and ventricular volumes exhibited significant differences between groups of 0–1 against 2 or more deprivations. Points are coloured by the MPI score threshold, and their size is scaled to the total MPI sum. Axes are scaled in units of 10,000 mm³ (10 ml).

DISCUSSION

In the most extensive structural neuroimaging study to date in East Africa, we examined adult brain ageing curves in Kenya. The approximately 50-year age range from young to old adulthood revealed ageing patterns that overlap with those previously characterised in cohorts from HICs.

Association cortex showed the strongest signatures of ageing in cortical thinning and volumetric atrophy, while ventricular volumes expanded, and surface area did not correlate as strongly with age. Together, our data address a critical gap in the human neuroimaging literature on brain ageing.

In the cerebral cortex, we examined thickness and surface area independently, as they reflect distinct biological characteristics^{30–32} and tend to be more strongly associated with age and cognition, respectively^{33,34}. Consistent with previous reports^{17–19,34}, we observed that age explained variance in thickness across multiple regions. The association cortex showed the most pronounced atrophy at around 4–6% per decade. While heterogeneity exists in the degree and pattern of age-related cortical changes^{2,35}, we observed that the lateral temporal cortex^{2,36}, and prefrontal cortex¹⁷ were more affected. Separately, we observed cortical thinning signatures in the pre- and post-central sensory cortices. Although sensory cortices usually show more gradual changes with age³⁷, cortical thinning has been observed, near the primary motor cortex³⁵, and in sensory-motor areas in older adults³⁸. Our findings align with previous HIC cohorts, suggesting that cortical thinning occurs at a rate of at least 0.01 mm per year across the cortical mantle³⁹. Surface area, while not as strongly correlated with age as thickness, also declined with age, primarily in the association cortex, with most regions showing ~ 4% decreases per decade. While spatially similar to previous reports⁴⁰, the yearly rates of change we observed are on the higher than those observed in other studies, where yearly rates were around 0.15–0.4% (1.5–4.0% per decade)⁴¹. Volumetric reductions were observed throughout the cortical mantle, spatially similar to thinning patterns and of greater magnitude than surface- area reductions. Longitudinal research aligns with these findings and suggests that cortical thinning is the primary driver of age-related variance in volume⁴¹.

In addition to cortical changes, we sought to examine, across the entire cerebrum, rates of atrophy or enlargement in cerebrum-wide tissue and whether these changes followed linear or nonlinear dynamics. Across longitudinal and cross-sectional studies, cerebrum tissue volumes for grey matter, white matter, and subcortical grey matter decrease at a yearly rate of around 0.2–0.5% (2–5% per decade)^{42–45}, a range that overlaps with our findings. In the hippocampus, we observed a modest rate of atrophy of approximately – 2.57% per decade, which is lower than previously reported rates of 0.79–2.0% *annually* (7.9–20% per decade)^{42,43,46–48}. This apparent dissimilarity can be explained by two factors. First, hippocampal atrophy rates can vary with mean sample age, with estimated rates of 0.38% per year (3.8% per decade) in studies with mean ages of 55 or younger⁴⁹. Second, large cross-sectional studies reveal that the hippocampus and entorhinal cortex change minimally until the seventh or eighth decade of life in healthy aging^{37,50}. These late-life changes have been characterised as inflexion points at which

accelerated rates of change in brain morphometry occur^{1,22,23,51}. We found modest evidence for such non-linear volumetric decreases in the amygdala. It is possible that other

brain tissues did not exhibit nonlinear dynamics because late-life adults were underrepresented in the sample. Furthermore, many in this age range were older than the Kenyan life expectancy and may have been uniquely resilient agers⁵².

Broadly, our findings align with HIC cohorts and with the predominant hypothesis that healthy brain ageing reflects biological development, “first in, first out”, alluding to more pronounced age effects in association cortices⁵³. While these non-pathological morphological changes tend to be well-defined across the lifespan⁹, stressors distinct from ageing, such as socioecomic disparities, limited education and health care access, collectively termed the exposome⁵, can adversely affect brain health^{23,24,54} and be associated with premature life expectancy⁵⁵. Here, we found evidence of distinct age-related associations among people with few or no deprivations compared with those who experienced at least two deprivations. Contrary to our prediction, people with exposure to multidimensional poverty exhibited more stable amygdala and white matter volumes, as well as an attenuated association between age and ventricular volume.

These results argue for a hormesis-like mechanism in ageing, in which adaptive responses to external stressors may stimulate protective mechanisms in the brain⁵⁶. These findings must be interpreted in the context of a more pronounced survivor bias in people with poverty-associated shortened life expectancy⁵⁵. Longitudinal studies are needed to better characterise within-subject trajectories and their relationship to the socio-environmental exposome, particularly among those who survive beyond life expectancy.

Our study has multiple strengths. Given that cortical thinning and volumetric losses typically emerge around the second or third decade of life¹, the age distribution of this cohort is well-suited to addressing questions about brain ageing. Furthermore, these results are socially and clinically relevant within the sociodemographic context of a predominantly young Kenyan population (nearly 80% aged 35 years or below)⁵⁷ and the prediction that neurodegenerative diseases like dementia will increase up to 357% in Sub-Saharan Africa by 2050⁵⁸. Our purposive sampling approach enabled us to include participants across the adult lifespan with varying degrees of social and environmental exposure, reflecting relevant characteristics of the Kenyan population. However, most of our participants were recruited from the Nairobi urban area, and future studies should consider recruiting individuals from rural areas, as exposures can differ by context²⁸.

Several findings warrant future research. Inherent in ageing research is survivor bias, in which individuals live longer than their life expectancy (10.62% in our sample). While these individuals influenced the age-related associations we characterised, they also present an opportunity to understand resilience to ageing and how exposures such as multidimensional poverty may protect against decline *in those who*

survive. Second, processing tools and software, as well as the acquisition site, can influence the reproducibility of structural imaging results^{59–61}. We aimed to address this issue by collecting all imaging data from the same medical centre at similar daytime hours across participants, preprocessing the data with commonly used neuroimaging software (Freesurfer V. 7.4.1), and following global standards for data quality control (ENIGMA V.2²⁷). These strict controls may have enhanced detection of spatial patterns and rates of change that are broadly consistent with those observed in cohorts from HICs, but may also limit

generalizability to real-world clinicroadiologic data collection. Future research should evaluate the robustness of our findings to variations in scanners, sequences, and pre-processing decisions. Lastly, future studies could examine the impact of prevalent pathologies in the East African context on brain health, including vascular drivers⁶², potentially driven by untreated hypertension, hypercholesterolemia, and viral infections^{63,64}.

Overall, this study characterises spatiotemporal patterns associated with healthy brain ageing in Kenya, demonstrating broad concordance with patterns documented in HIC cohorts. These results call for sustained investment in larger multi-regional African samples, both to strengthen the representativeness of global normative brain charts and to build the local infrastructure and capacity essential for neuroimaging research. Future studies in LMICs should be designed with sufficient power and longitudinal duration to disentangle the complex interplay among life-span exposures, survivor bias, and brain structure, which may uncover distinct mechanisms underlying brain resilience. More broadly, systematic investigation of the exposome will be critical to understanding and promoting healthy ageing trajectories in resource-limited and otherwise vulnerable contexts.

METHODS

Ethics Approval and Consent

The study was conducted in accordance with Good Clinical Practice, the Declaration of Helsinki, and the local rules and regulations of Kenya. Ethical approval was obtained from the Aga Khan University Institutional Scientific and Ethics Review Committee (BRK: 2023/ISERC-125) and the National Commission for Science, Technology, and Innovation (BRK License #:NACOSTI/P/25/418163). Written consent was obtained from all participants.

Participant selection

Individuals were invited to participate in the Brain Resilience Kenya (BRK) study at Aga Khan University in Kenya. Healthy controls included in this study: I) were adults aged 35 years or older, II) spoke English or Kiswahili, III) had no visual or auditory impairment, IV) had no neurological or psychiatric conditions at the time of consent, and V) were established as cognitively unimpaired based on regionally validated cognitive screening procedures⁶⁵. A purposive sampling strategy was implemented to favour the

inclusion of diverse socio- demographic groups, including participants from informal settlements. The Multidimensional Poverty Index (MPI) was calculated for participants with available indicator data for 3 domains: education (highest level of schooling achieved); health (food security, water security), and living standards (access to indoor private toilet, clean cooking fuels, electricity, and common household assets), as described previously⁶⁶.

T1-MRI acquisition

Structural T1-weighted images were acquired on a Philips 3-Tesla scanner (Philips Achieva, 32- channel head coil) at the Aga Khan Medical Centre. A three-dimensional fast gradient-echo (FFE/MP-RAGE-type) sequence was used with the following parameters: echo time (TE) = 3.5 ms; repetition time (TR) = 7.9 ms; flip angle = 8°; field-of-view = 256 × 256 mm²; acquisition matrix = 256 × 256; in-plane resolution = 1 × 1 mm²; slice thickness = 1 mm (160 contiguous slices, no gap); voxel size = 1 × 1 × 1 mm³; bandwidth = 332 Hz/pixel; SENSE acceleration factor = 2; acquisition time ~ 3 min. A board-certified radiologist inspected the scans for motion and artefacts prior to processing and analysis. Scans were re-taken in cases of poor data quality and excluded in cases of severely poor quality. Additionally, subjects with clinical incidental findings were excluded from the analyses presented here and referred for further clinical care. Scans were de-identified and anonymised.

Structural neuroimaging

De-identified DICOM images were converted to NIFTI format using the dcm2niix library (version 1.0.20241211). Subsequently, NIFTI files were preprocessed with Freesurfer (version 7.4.1) for cerebral morphometric analyses. In brief, Freesurfer operates by 1.) skull stripping, 2.) intensity normalisation due to magnetic field inhomogeneities, 3.) gray-white matter boundary segmentation, 4.) volumetric labelling, 5.) surface extraction, 6.) surface atlas registration, and

7.) gyral labelling using anatomical atlases of interest. Features of interest, such as volume and thickness of cortical and subcortical structures, were automatically computed through Freesurfer. Estimated intracranial volume was controlled for when appropriate.

Following preprocessing, we further evaluated raw scan quality using Euler's index (EI⁶⁷), as provided by Freesurfer. EI was defined as the number of topological defects in the cortical surface (left and right hemispheres) before topological correction. Given the preceding radiologist review and ENIGMA-based postprocessing checks (see below), we used EI primarily to identify extreme failures rather than to apply a cohort-specific exclusion threshold. The EI distribution was approximately normal, with one extreme outlier detected (Grubbs test) that was excluded from the primary analyses. Additionally, we used GAMs to examine the relationship between image quality measured by EI and 4 cerebrum tissues: cortical, subcortical, and white matter volumes, and ventricular volumes.

Additionally, we performed quality control of the cortical parcellations and segmentations generated by Freesurfer, following the ENIGMA protocol version 2²⁷ (<https://enigma.ini.usc.edu/protocols/imaging->

protocols/). In brief, blind expert reviewers visually inspected the Freesurfer outputs for each subject (one review per subject). Analysts examined the placement of the white matter surface (the grey/white boundary), the pial surface (the grey matter/CSF boundary), the accuracy of subcortical segmentation, the completeness of skull stripping, and the correctness of the 34 bilateral cortical Desikan-Killiany atlas (DKT) parcellations. After error correction and reprocessing through recon-all, we excluded subjects from morphometrical cortical analyses (section: Morphometric analyses) if they had any DKT “failed parcellations”.

Morphometric analyses

For analyses performed at the cortical surface level, mean and standard deviation for thickness, volume, and surface area were resampled from each subject to fsaverage space ($n = 163,842$ vertices per hemisphere), and the data were smoothed using a 10 mm full-width at half-maximum⁶⁸ (FWHM) to reduce measurement variability^{69,70}. Measures of interest are mapped onto the ‘inflated’ surface of each participant’s reconstructed brain, thereby improving visualisation across the cortical surface^{68,71}. Morphometric properties from the insula were masked due to its known low signal-to-noise ratio.

At each cortical vertex ($n = 163,842$), we fitted a general linear model (GLM) to assess the relationships between thickness, volume, and surface area and age, while including sex as a covariate. Intracranial volume was not controlled for, in accordance with previous studies^{72–74}. We modelled surface-based features at each vertex as a function of age and sex using Freesurfer’s general linear model tool (mri_glmfit) with separate intercepts and slopes for males and females. This resulted in four model parameters: an intercept for females, an intercept for males, a slope for females, and a slope for males. To test the average effect of age across sexes while accounting for sex differences in baseline and age-related slope, we specified a contrast vector that equally weights the slopes of males and females ($[0\ 0\ 0.5\ 0.5]$). Thus, we tested whether the mean association between age and cortical thickness/volume/surface area across both sexes differs significantly from zero. From this analysis, we derived t - and uncorrected p -values for each vertex (two-tailed).

To address the multiple comparisons problem, we employed a cluster-wise correction using the Freedman and Lane⁷⁵ permutation method. In brief, a reduced GLM without age was fitted to the data to obtain residuals. At each iteration ($n = 5000$), these residuals were shuffled across subjects and then added back to the reduced-model predictions to generate the permuted dataset. The full GLM (with age) was fitted to the permuted data, and p -values at each vertex were thresholded using a cluster-forming threshold (CFT) of 0.001 (two-tailed, uncorrected).

Thus, a binary map of suprathreshold vertices was generated, and the area of the maximum cluster was recorded. This process was repeated 5,000 times to obtain a stable estimate of the empirical distribution of maximum cluster sizes. We then applied the same CFT ($p < 0.001$) to the original t -map, identified all clusters, and assigned each cluster an empirical p -value by comparing its size against the null distribution of maximum cluster sizes⁷⁶. Clusters with $p < 0.05$ were retained. Because the left and right

hemispheres were analysed separately, we applied Bonferroni correction by dividing each cluster's p-value by 2.

Age-related changes in cortical thickness, surface area, and volume were expressed as percentage change per decade, calculated by dividing each vertex's beta coefficient (units per year) by the corresponding vertex-wise mean across subjects, then multiplying by 10. This standardisation accounts for the large variability in regional size across the cortex⁴¹.

Cerebrum tissue and subcortical volumes

The relationships between cerebrum tissue volumes (subcortical grey matter, white matter, and total cerebrospinal fluid) and subcortical volumes (thalamus, hippocampus, and amygdala) with age were modelled linearly and non-linearly. For each tissue, we fitted two generalised additive models (GAMs) using maximum likelihood (ML) to compare models with different fixed-effects specifications. One linear model including age as a linear covariate, and a non-linear model replacing the linear age term with a penalised regression spline ($k = 6$). Both models included sex and estimated total intracranial volume as covariates.

Volume ~ age centered + sex + intracranial volume

Volume ~ s(age centered, $k = 6$) + sex + intracranial volume

To determine whether the non-linear model significantly improved fit over the linear model, we examined: (1) the approximate significance of the smooth term from the GAM summary, (2) AIC and BIC differences between models, and (3) the effective degrees of freedom (EDF) of the smooth term, where $EDF \approx 1$ indicates a linear relationship. A cerebrum tissue volume was classified as exhibiting a non-linear age association if the smooth term was significant after FDR correction (Benjamini–Hochberg, $q < 0.05$), the non-linear model had a lower BIC, and EDF exceeded 1.5.

To express age effects as percentage change per decade, we divided the estimated linear age coefficient (in volume units per year) by the model-predicted reference volume at the mean age and mean intracranial volume, and then multiplied the result by 10.

Declarations

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Author Contribution

Conceptualisation and study design: TT, KB Funding acquisition: CU, KB, MS Project management: CB Data collection: BA, CB, LM, JS, JO, JM, SP, SG Study implementation: BA, CB, LM, JS, JO, JM, SP, SG, MS, ZM, CU, TT, KB Manuscript writing: CC, BA, TT, KB Data cleaning and analysis: CC, BA, AS, JS, JO, JM, KB Approval of final manuscript and consent for publication: CC, BA, CB, AS, LM, JS, JO, JM, SP, SG, MS, ZM, CU, TT, KB

Data Availability

The datasets generated during the current study are not publicly available due to restrictions imposed by Kenyan data protection legislation, specifically the Kenya Data Protection Act (2019), which require that all data sharing, including deidentified data, comply with agreed protocols and authorization procedures but are available from the corresponding author on reasonable request and with the appropriate agreements in place. All data relating to this study are presented in the manuscript and supplementary materials.

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Figures

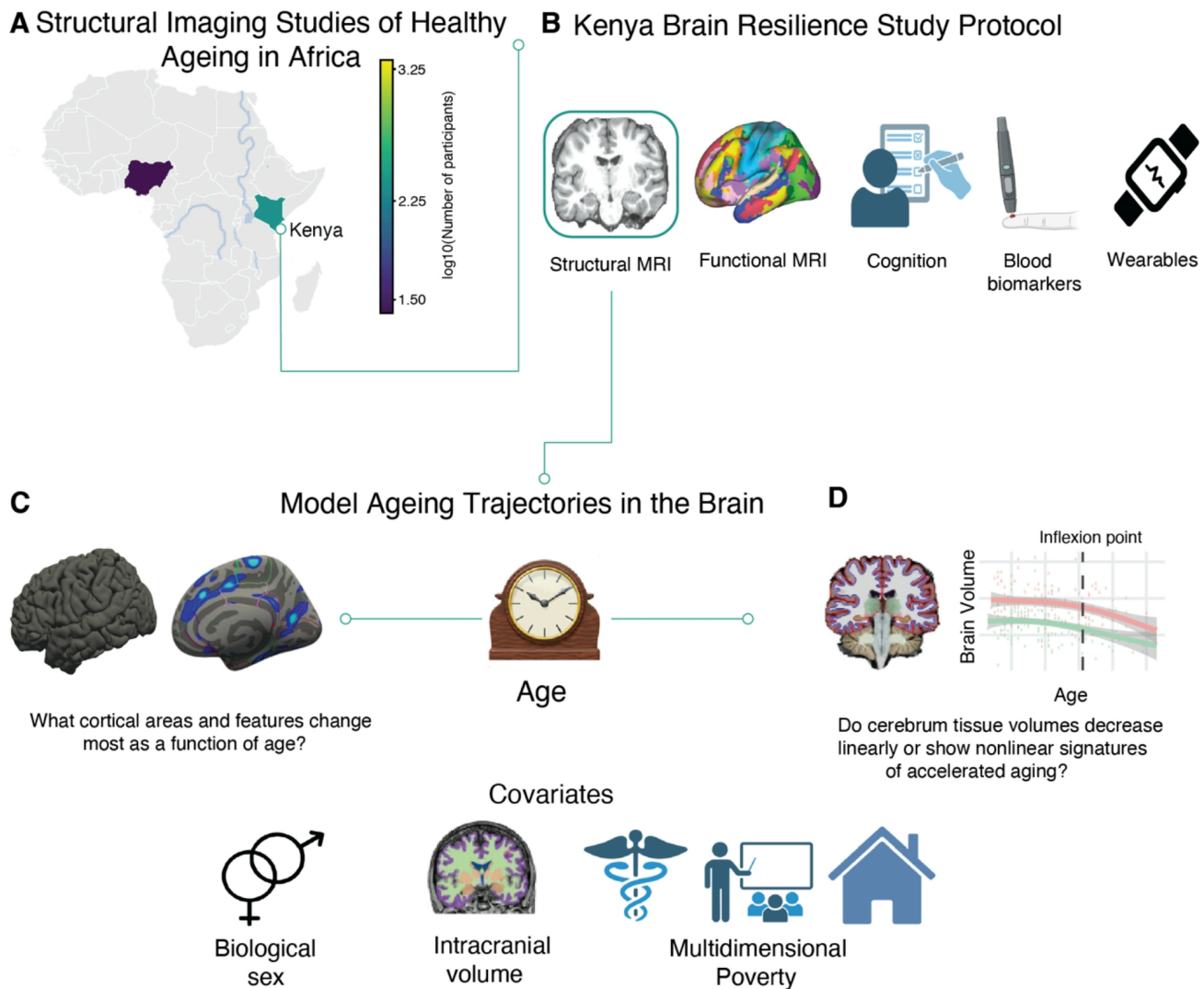
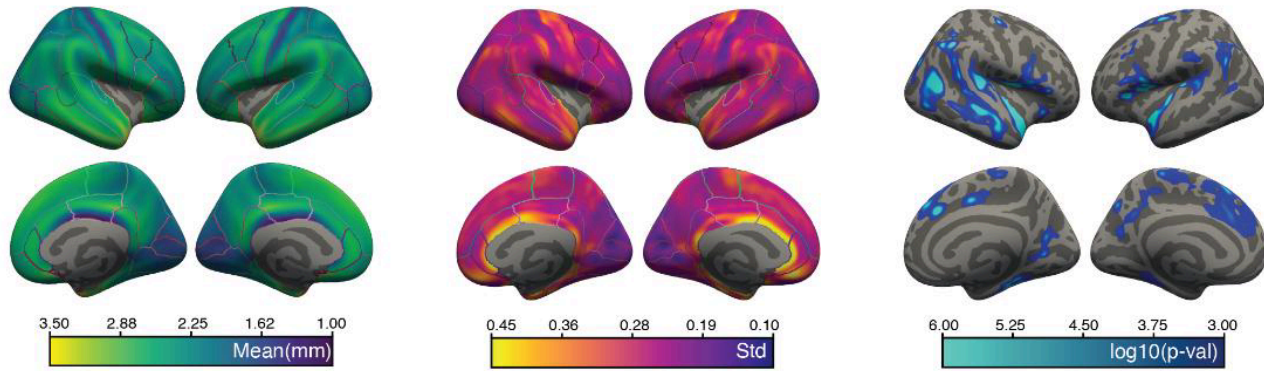


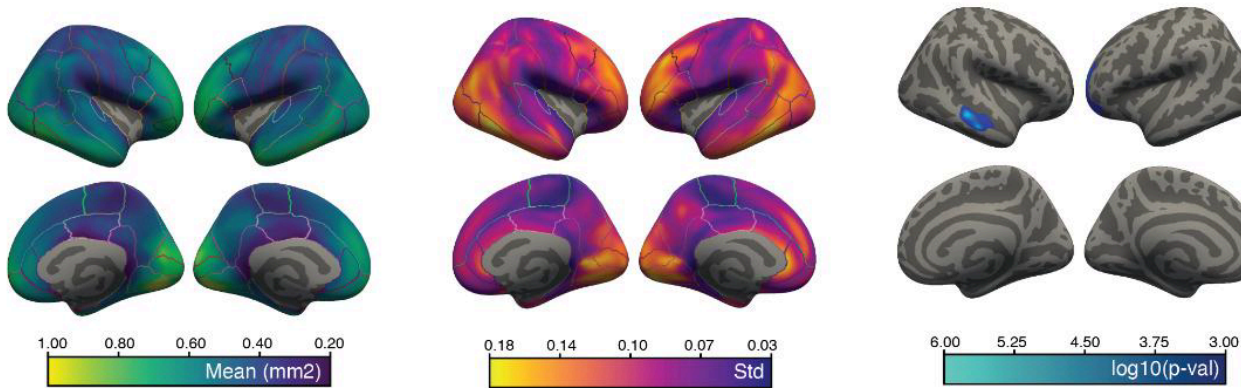
Figure 1

Overview of experimental paradigm and methods. (A) Few structural imaging studies of healthy adult brain ageing have been conducted and publicly released in Africa: Nigeria⁷ and our study in Nairobi, Kenya. (B) Description of the recording modalities in the longitudinal Kenya Brain Resilience Study, which investigates signatures of resilient ageing. The analyses presented here focus on a single time point in the structural imaging data. (C-D) Methodological approach. (C) Cortical features of thickness, volume, and surface area were modelled at each vertex to investigate regions most affected by ageing. (D) Cerebrum tissue volumes were modelled linearly and non-linearly to investigate possible signatures of accelerated ageing. Socio-environmental factors were examined as potential moderators of age-related brain trajectories.

A Thickness



B Surface Area



C Volume

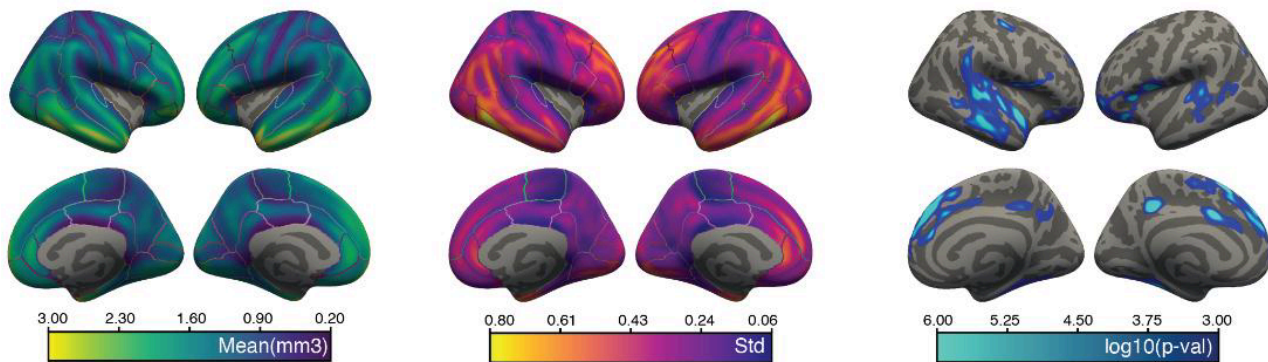


Figure 2

Ageing-related effects of cerebral reductions were predominant in the association cortex for thickness and volume. (A) Regional averages (left), standard deviation (middle), and significance maps with log10-scaled p-values for cortical thickness (right). Most cortical thinning occurred in fronto-temporal regions and the precentral gyrus. (B) Surface area was less strongly associated with age. Only the middle temporal lobe of the left hemisphere showed signs of atrophy. (C) Spatial patterns of volumetric

reductions were broadly consistent with thickness. Significance maps are thresholded to show p-values that survived multiple comparisons. Refer to **Supplementary Table 1A-C** for summary statistics of significant clusters.

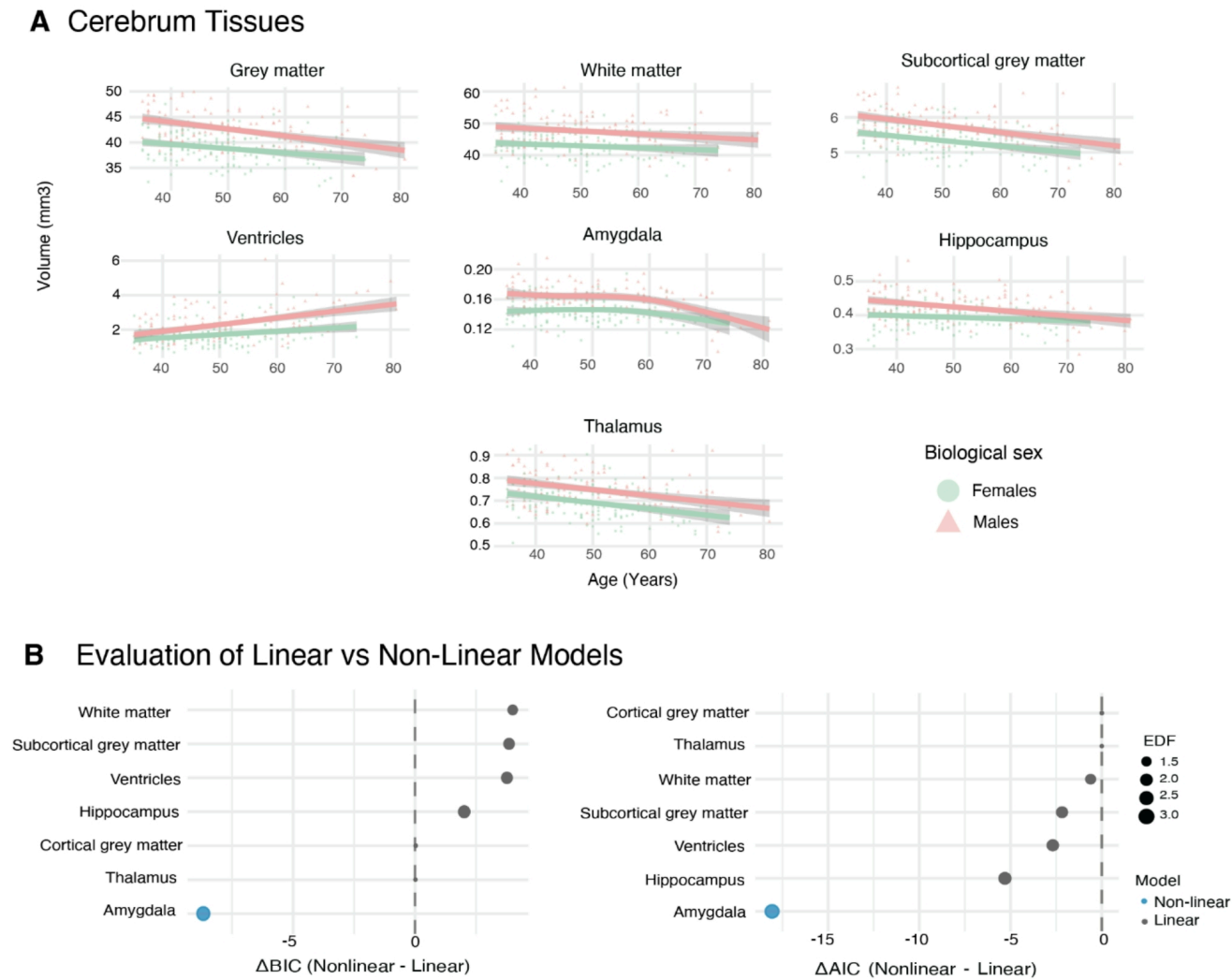


Figure 3

Cerebrum tissue volumes show predominantly linear ageing relationships. (A) Age-related changes for volumes in grey matter, white matter, subcortical grey matter, ventricles, amygdala, hippocampus, and thalamus.

Axes are scaled in units of 10,000 mm3 (10 ml). Points are coloured by biological sex. Solid lines indicate fitted curves, and shading represents 95% confidence intervals. (B) Model comparison for each tissue using generalised additive models with either a linear age term or a penalised smooth for age. Scatter plots of BIC (left) and AIC (right) scores for non-linear versus linear models, with dot size

indicating the effective degrees of freedom (EDF). The point colour denotes the selected model, as shown in A.

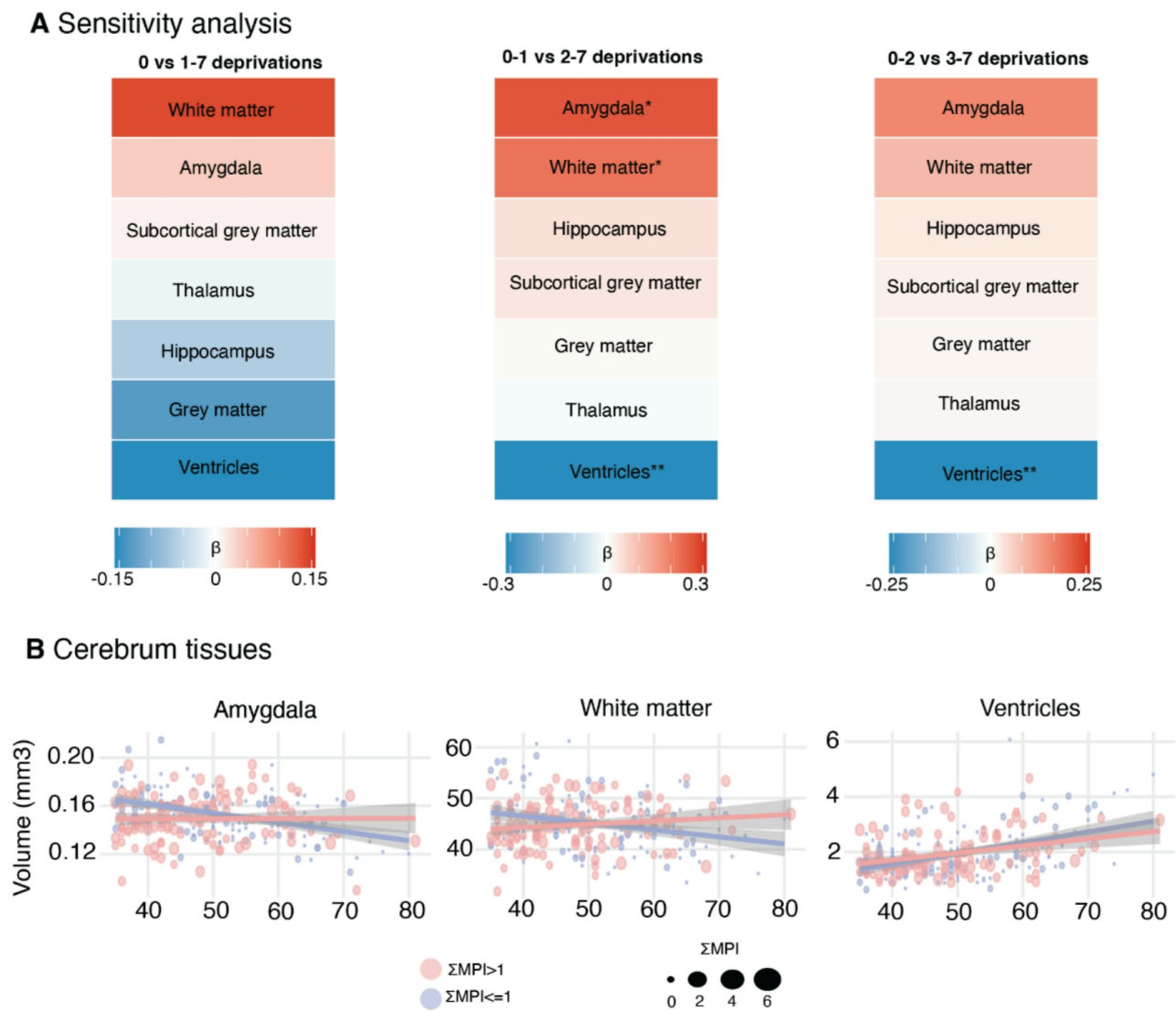


Figure 4

Socio-environmental deprivations are associated with distinct age-related trajectories of cerebral volumes.

(A) Sensitivity analysis exploring various degrees of deprivation classification and their association with cerebrum tissue volumes. Tile plots depict standardised beta coefficients for the interaction effect between age and group for a corresponding volume. Asterisks denote FDR-corrected statistical significance (* $p < 0.05$, ** $p < 0.01$) (B) GAMs for amygdala, white matter, and ventricular volumes exhibited

significant differences between groups of 0-1 against 2 or more deprivations. Points are coloured by the MPI score threshold, and their size is scaled to the total MPI sum. Axes are scaled in units of 10,000 mm³ (10 ml).

Supplementary Files

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- [SupplementaryMaterials.docx](#)