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Reevaluating the role of education on cognitive decline and brain aging in longitudinal cohorts across 33 Western countries

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Why education is linked to higher cognitive function in aging is fiercely debated. Leading theories propose that education reduces brain decline in aging and enhances tolerance to brain pathology or that it does not affect cognitive decline but, rather, reflects higher early-life cognitive function. To test these theories, we analyzed 407,356 episodic memory scores from 170,795 participants older than 50 years, alongside 15,157 brain magnetic resonance imaging scans from 6,472 participants across 33 Western countries. More education was associated with better memory, larger intracranial volume and slightly larger volume of memory-sensitive brain regions. However, education did not protect against age-related decline or weakened effects of brain decline on cognition. The most parsimonious explanation for the results is that the associations reflect factors present early in life, including propensity of individuals with certain traits to pursue more education. Although education has numerous benefits, the notion that it provides protection against cognitive or brain decline is not supported.

Although the total number of people with dementia will increase substantially due to population growth and aging[1], the incidence seems to be declining[2,3], and older adults have better cognitive function today than 20 years ago[4]. One hypothesis is that this reflects broad societal and individual lifestyle changes and that dementia incidence can be further reduced by promoting these[1,5]. Education has repeatedly been suggested to be one such potential protective factor[6,7], in line with observations of robust associations between education and higher cognitive function in aging as well as declines in dementia incidence with increasing population educational attainment[8,9]. However, results thus far are heterogeneous and point in different directions, and the specific mechanisms that could explain such a causal link are widely debated[10]. We, therefore, suggest addressing these questions by conducting a large mega-analysis of longitudinal brain and cognitive studies covering a wider geographical distribution of samples.

Education could result in better cognition in aging by contributing to a lower rate of age-normative brain decline[11]—that is, 'brain maintenance'—which has been associated with better episodic memory[12].

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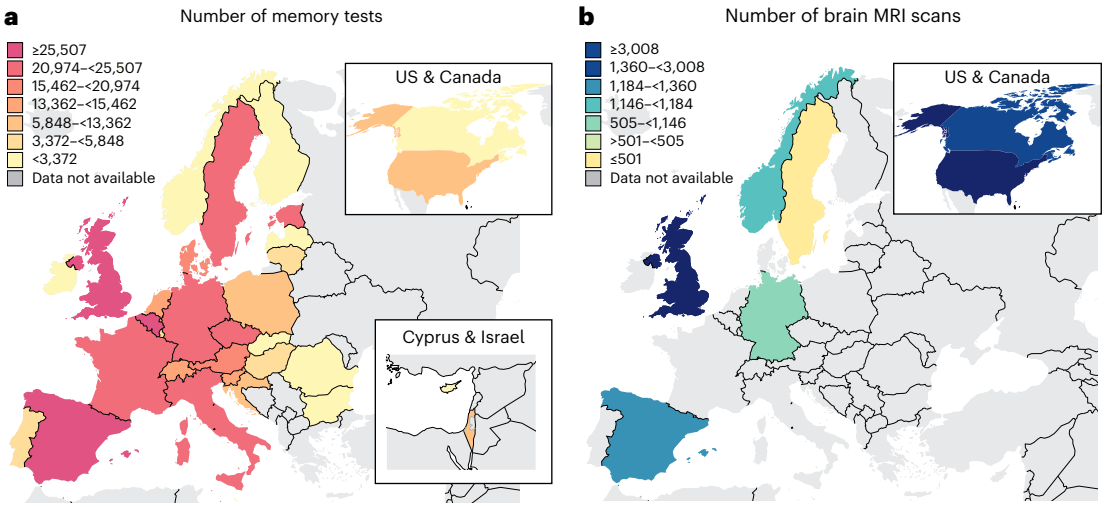

Fig. 1 | Geographical and age distribution of samples. a, Total number of completed memory test sessions per country. **b**, Number of brain MRI scans per country. Maps were generated using the IMAGE Interactive map generator (https://gisco-services.ec.europa.eu/image/).

Studies have reported that older adults with higher education have less brain pathology[13], less brain decline in presymptomatic dementia[14] and less accumulation of cerebrovascular lesions[15]. However, a recent longitudinal study investigating two independent samples did not find different rates of change in hippocampus and age-sensitive regions of the cerebral cortex in more educated participants[16]. Alternatively, education could make people more resilient to underlying brain pathology—that is, yielding higher 'cognitive reserve'[17]. According to this theory, education leads to more efficient processing of cognitive tasks, which, in turn, allows for higher performance despite age-normative levels of brain decline[18]. Although a popular theory[5,19], a longitudinal study found that education did not weaken the link between hippocampal atrophy and memory change[20]. Both the maintenance and the reserve accounts of education imply that education causally influences late-life cognition by reducing or postponing age-related decline. This is controversial, however, because even though education is associated with better cognitive function among older adults, it is not clear that more educated persons show less cognitive decline when measured longitudinally[21,22].

An alternative perspective holds that the association between education and cognitive performance is persistent across the adult lifespan. This contrasts with the more aging-centered views presented above. Under this alternative view, if education has a positive causal effect on cognition in aging, it would be by permanently boosting cognitive function earlier in life, causing persistent differences between educational groups. Increased compulsory schooling has been shown to elevate scores on tests of memory[23–25], intelligence[26,27] and general cognition[28], with effects detectable decades later[29]. This perspective could also be consistent with a lack of causal effects of education on cognitive function, however, as those with higher initial cognitive functioning would be expected to reach higher levels of education than their peers. Hence, the topic of the role of education in cognitive function and brain health in aging is riddled with controversies[30].

Nonetheless, contrasting predictions can be derived from the different theories. If education improves memory in older age by shaping brain aging, we expect better preservation of memory-sensitive brain regions among individuals with higher education. If education improves cognitive reserve, we expect more tolerance to brain pathology, indexed by a lower correlation between brain decline and cognitive decline. In contrast, if the education–memory–brain relationship reflects stable individual differences, education should not correlate with either memory or brain decline. In that case, we also would expect to see selection effects, in the sense that participants with specific traits, especially higher cognitive function, are more likely to pursue further education. It is also relevant to examine whether re-test effect—the tendency for performance to increase as a function of previous tests taken—is exaggerated with higher education. If more education yields cognitive reserve, this may manifest as a greater ability to take advantage of previous testing experience and to develop more efficient test-taking strategies.

A major challenge in addressing these questions is that large, representative and heterogeneous longitudinal samples with sufficient statistical power are needed. The geographic coverage is critical, because relationships may vary across time[31] and societies[32,33]. For example, the population attributable fraction (PAF) of dementia due to low education varied from 1.7% in Argentina to 10.8% in Bolivia in a study of seven Latin American countries[34]. We compiled data from 33 countries across Europe, the United States and Israel, including a total of 407,356 memory tests from 170,795 participants with up to seven follow-up sessions (Fig. 1a), ensuring that the results are not confined to one specific time and place. Still, because the samples come from Western, Educated, Industrialized, Rich, Democratic (WEIRD) countries, we compare the results to patterns from non-WEIRD societies in Africa, Latin America and East and South Asia[35].

Episodic memory is a unique memory system[36] that can be defined as the ability to recall information tied to a specific time or place, in contrast to semantic memory, which is recall of general knowledge and facts[37]. In research and clinical assessments of memory function, episodic memory is typically measured as the amount of newly acquired information that can later be explicitly recalled, such as the number of words remembered from a presented list. We focus on episodic memory because it is a particularly age-sensitive long-term memory system[38], and we assess it using a verbal recall test, one of the most employed methods.

To address brain mechanisms, we analyzed 15,157 brain magnetic resonance imaging (MRI) scans and concurrent memory tests from 6,472 participants across seven countries (Fig. 1b). Brain decline was defined as within-participant reductions over time in memory-sensitive brain regions. The primary data sources were the population-based multinational Survey of Health, Ageing and Retirement in Europe (SHARE) (https://share-eric.eu/)[39] and the Lifebrain consortium[40] (https://www.lifebrain.uio.no/), enriched with legacy databases. For sample representativity, SHARE uses the best available sample frame resources in each country to achieve full probability sampling, including access to population registers. The MRI populations vary

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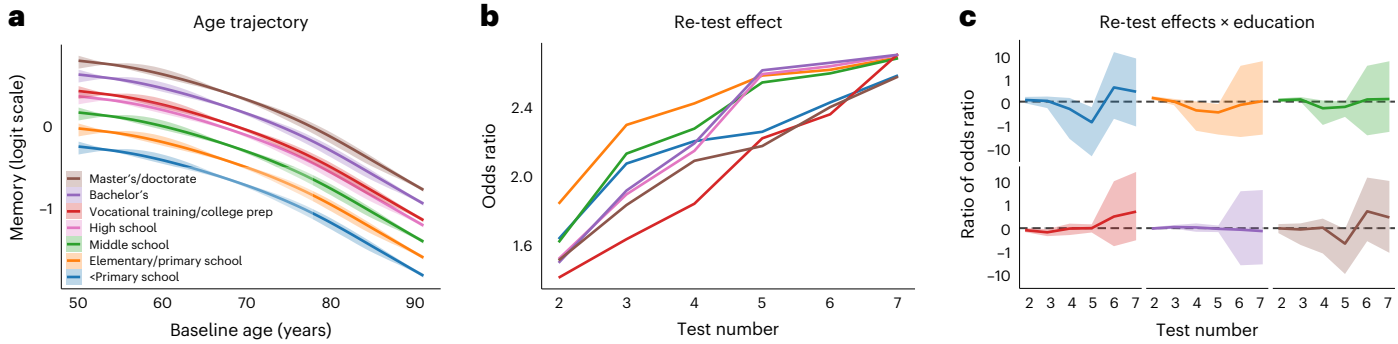

Fig. 2 | Age, education and practice effects on memory. a, Memory score trajectory over age. The *y* axis denotes memory score on the logit scale, and the lines show the predicted memory performance over baseline age for each education category. **b**, Re-test effects for each education group. **c**, Comparing re-test effects for each education group to the 'High school' group, lines show the ratio of odds ratio for the given education/odds ratio for 'High school' (dashed horizontal line). Shaded areas denote 95% confidence interval.

in representativity, and, hence, we validate the memory results from SHARE in the MRI samples before conducting the brain analyses.

Results

SHARE cohort results

Episodic memory was assessed with a 10-word verbal recall test, with two conditions (immediate and 5-minute recall), using multiple versions across waves and participants[41]. Each condition was separately included in the statistical models, yielding two observations per timepoint per participant. Generalized linear models (GLMs) with a binomial link were run using memory score as dependent variable, with the interaction between education and time since baseline as the critical term, using test type (immediate or 5-minute delay), a monotonic function of the number of previous tests taken (to control for re-test effects), education, self-reported sex, country, baseline age (smooth function), time since baseline and the age × time interaction as covariates. Individual-specific intercepts per participant were nested within country. *z*-transformed values for age and time were used in the model fitting and converted back to natural units when showing the results. Memory offset refers to the cross-sectional differences between groups—that is, main effect of education. Memory change was defined as change in memory over time within participants, with differences between education groups represented by the education × time interaction. The main outputs of the statistical model were the odds ratios of remembering a word compared to a reference group. For readability, we used simplified terms for education categories, with definitions, SHARE categorization and mapping to the International Standard Classification of Education (ISCED) presented in Supplementary Information.

Memory scores were lower with higher baseline age, showing slightly accelerating trajectories (smoothing parameter for the combined sample = 45.8, confidence interval: 20.7–81.5). Figure 2a revealed a perfect ordering of higher scores with more education across age. 'No education' had an odds ratio of 0.54 (Cohen's $d = -0.33$) compared to the reference category ('High school'), whereas 'Master's' had an odds ratio of 1.55 (Cohen's $d = 0.24$) (Fig. 3a and Extended Data Table 1), yielding an odds ratio range of 1.01 and a Cohen's *d* range of 0.57. This confirms the well-known positive association between education and episodic memory in aging and shows that the difference in memory score is almost identical with each increase in education category.

Re-test effects were substantial and, thus, essential to adjust for in analyses of change. Odds ratios increased almost linearly, from 1.5 compared to baseline at the first follow-up to 2.5 at the fifth follow-up (Fig. 2b). A small negative effect of time (1 year) was observed on memory scores (odds ratio = 0.963, confidence interval: 0.961–0.964), slightly increasing with age (age × time odds ratio = 0.9981, confidence interval: 0.9980–0.9982). These results

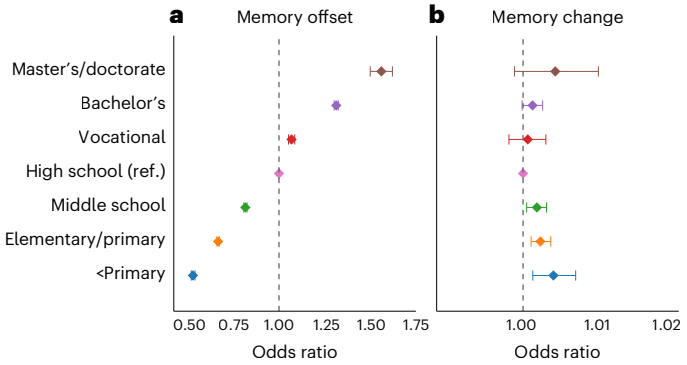

Fig. 3 | Associations among education, memory score and memory score decline. a, Associations between education and memory offset scores expressed by odds ratios. **b**, Associations between education and decline in memory scores expressed by odds ratios. 'High school' is used as reference (dashed line). Error bars denote 95% confidence interval and odds ratio. Results are based on 130,880 unique participants and 352,953 memory tests. ref., reference.

show that test scores increase when participants are tested repeatedly but that scores become lower over time when this is accounted for. Testing whether higher education was associated with less memory decline (Fig. 3b and Extended Data Table 2), we found negligible effect sizes—all odds ratios less than 1.005—meaning that there were no meaningful differences. Furthermore, no systematic differences were observed in re-test effects between participants of different education levels (Fig. 2c). Although the immediate and delayed recall conditions were highly correlated ($r = 0.74$), the delayed condition was more difficult and likely to a larger extent reflected long-term memory. We repeated the analyses for each condition separately, yielding identical results (Supplementary Figs. 5 and 6).

The first set of analyses showed that education was linearly associated with better memory scores but not differences in memory decline or re-test effects. To test the hypothesis that the education–memory associations reflect selection effects, we re-ran the analyses using 'relative' education as measure of interest. That is, for each participant, we calculated amount of education relative to the other participants from the same birth cohort, sex and country. This yielded a percentile score for each participant (0–100%), indexing amount of education relative to similar peers. This analysis provides a test of selection effects on education–memory associations—that is, that people with some unmeasured traits take more education—and this trait is correlated with late-life memory scores. Absolute level of education was used as covariate, as absolute and relative education would be correlated. By using relative education, we were able to partially account for these

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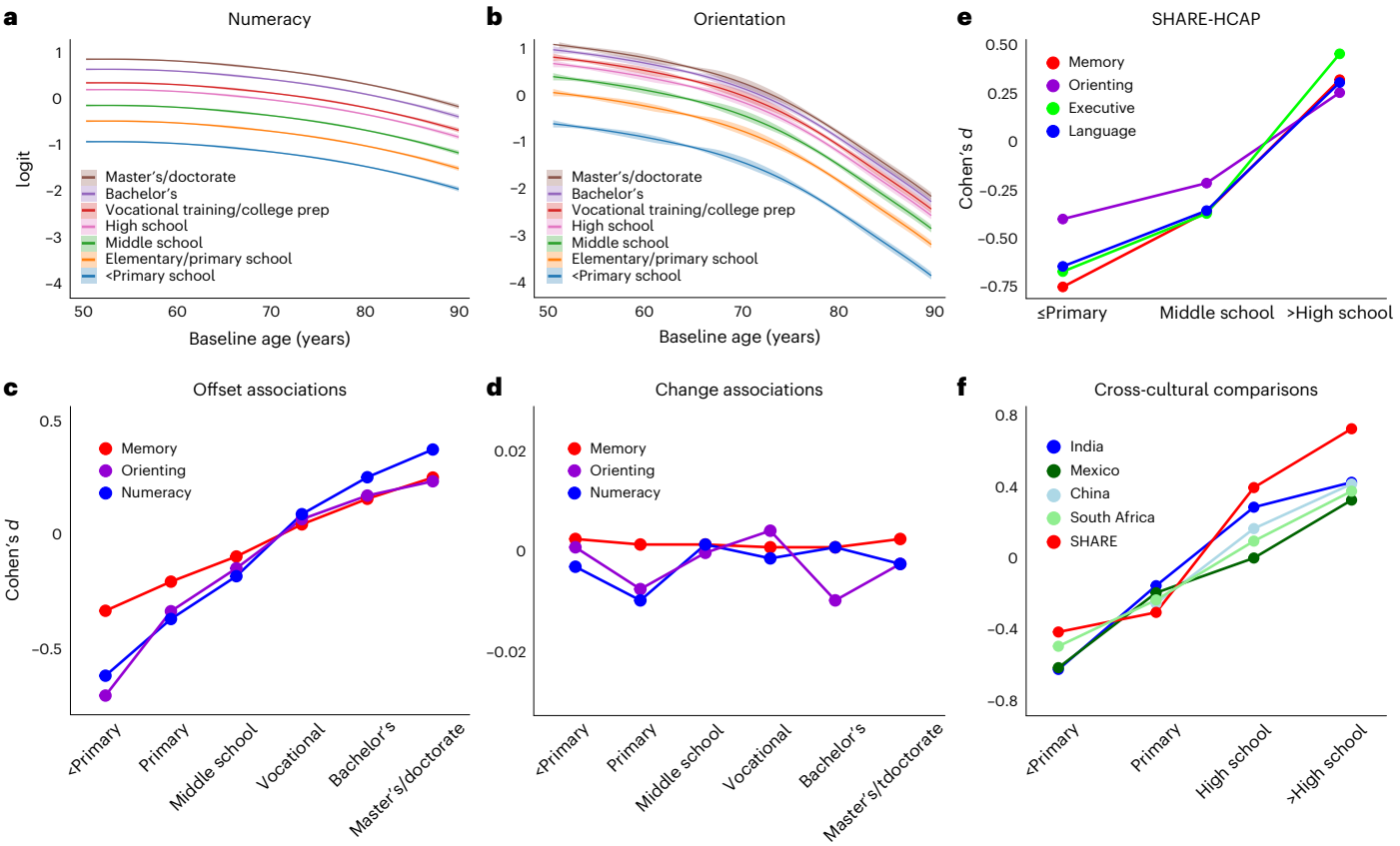

Fig. 4 | Sensitivity analyses. a, Numeracy score trajectory over age. The *y* axis denotes numeracy score on the logit scale, and the lines show the predicted numeracy performance over baseline age for each education category. **b**, Orientation score trajectory over age. The *y* axis denotes orientation score on the logit scale, and the lines show the predicted orientation performance over baseline age for each education category. Shaded areas represent 95% confidence intervals. **c**, Offset results: Cohen's *d* for each education category compared to the reference category ('High school') for three cognitive tests from SHARE. **d**, Longitudinal change results. **e**, Cohen's *d* compared to the 'High school' category in SHARE-HCAP. **f**, Effects for memory (HCAP) compared to the 'Middle school' category across culturally diverse samples.

selection effects that vary between men and women from different birth cohorts in countries with widely varying educational opportunities and experiences. Birth cohort was measured in bins of a decade (1900–1909, 1910–1919, …, 1960–1969). The results showed that including relative education in the model reduced the associations between absolute education and memory, whereas relative education showed an independent, positive association with memory. The effects were modest, as moving from the lowest (0) to the highest (100) percentile was associated with an odds ratio of 1.17 (confidence interval: 1.14–1.20)/ Cohen's *d* = 0.08 compared to the reference group ('High school') (Supplementary Fig. 10). This suggests that selection effects explain some of the association between education and memory in aging.

Further support for selection effects would be if variables reflecting individual differences in childhood, before or in the first years of schooling, could account for the associations later in life. We re-ran the analyses controlling for two proxies of earlier-life cognitive function—self-assessed mathematical and language skills at age 10 years—as well as a proxy of 'parents' scholarly culture'[42]— number of books in the house at age 10 years. If this reduced the association between episodic memory scores and education, this would support the hypothesis of selection effects. The three childhood variables were all significant confounders of the association between education and memory score (math: estimate = 0.104, confidence interval: 0.099–0.108; language: estimate = 0.118, confidence interval: 0.114–0.123; books: estimate = 0.083, confidence interval: 0.079–0.087). When controlling for them, the association was reduced: the odds ratio and Cohen's *d* ranges from the original model were 1.01 (0.54–1.55) and 0.58 (−0.34 to 0.24), respectively, whereas the adjusted model ranges were odds ratio 0.60 (0.65–1.25) and Cohen's *d* 0.36 (−0.24 to 0.12). This shows that a part of the late-life association between education and memory score could be explained by self-reported childhood cognitive function and home environment. For the analyses of intra-individual memory decline over time, controlling for each childhood variable further reduced the already minute associations with memory recall, rendering none of them statistically significant (full results in Supplementary Information).

Sensitivity analyses SHARE

To explore whether the results were specific to the verbal recall test, we first repeated the analyses for two additional tests from SHARE (Supplementary Information). 'Numeric skill' yields a measure of mathematical ability, and 'orientation for time and place' is a test sensitive to age-related cognitive decline. Similar to the verbal recall results, scores were perfectly ordered according to educational level for both tests (Fig. 4a–d), with effect sizes numerically slightly larger (orienting: odds ratio range = 1.0 (0.26–1.26), Cohen's *d* range = 0.86 (−0.74 to 0.12); numeracy: odds ratio range = 1.48 (0.31–1.79), Cohen's *d* range = 0.96 (−0.64 to 0.32)). Age slopes were parallel, with minute education–change associations: odds ratio range 0.982–1.007 for orientation and 0.982–1.002 for numeracy. Hence, the pattern of results for verbal recall generalizes to two other tests.

To explore whether the results could be replicated with a more comprehensive test battery, we analyzed the recently released comprehensive cognitive test protocol administered to a subsample of

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participants at the latest wave of the survey (SHARE-HCAP (Harmonized Cognitive Assessment Protocol); Supplementary Information). We screened out cognitive impairment and restricted the sample to participants older than 65 years, yielding 25 test scores from 1,380 participants, including 11 memory scores. Due to the smaller sample, four education categories were used (primary or less $n = 115$, middle school $n = 192$, high school $n = 608$, vocational or university level $n = 465$). We used principal component analysis (PCA) to extract individual-level scores for four cognitive domains (episodic memory, executive function, language and verbal fluency and orientation). Associations between education and performance were monotonously positive for all domains (orientation Cohen's d range (minimum, maximum) = 0.74 (−0.29 to 0.45); episodic memory range = 1.22 (−0.54 to 0.68); executive range = 1.03 (−0.24 to 0.79); language range = 1.00 (−0.36 to 0.64) (Fig. 4e)). The age trajectories were close to parallel (Supplementary Information), except for more complex curves for the lowest education level, probably due to few participants in this group. This demonstrates that the main results for verbal recall are generalizable to other cognitive tests and domains.

The data cover 33 countries in different continents but are restricted to WEIRD societies. To explore whether the results generalized to non-WEIRD societies, we plotted the memory component score from SHARE-HCAP against memory scores from a recent HCAP study of 16,524 older participants (59–78 years) in three non-WEIRD countries (China, India and South Africa) and one partially WEIRD country (Mexico)[35]. In these studies, substantial efforts were devoted to validating HCAP across widely different cultures. Although education and mean scores differed greatly compared to SHARE[42], with less than 10% of participants from South Africa and China having high school education or more, associations were remarkably similar (Fig. 4f). In all non-WEIRD samples, there were monotonous, almost linear relationships between education and higher memory scores, mimicking the SHARE-HCAP results. This suggests that the present cross-sectional education–memory associations are not restricted to WEIRD societies only.

Brain MRI cohort results

Thirteen datasets with longitudinal MRI, memory assessments and information about education were included from seven countries across the North to South of Europe, the United States and Canada (Fig. 1b). In addition to cohort-specific inclusion and exclusion criteria, all participants were older than 50 years without cognitive impairment or neurological or psychiatric disorders. The initial dataset included participants with 1–14 MRI acquisitions with follow-up intervals up to 15.8 years and 1–24 memory assessments with follow-up intervals up to 28 years. Sample characteristics are presented in Extended Data Table 2, and cohort-specific descriptions are presented in Methods.

First, we tested whether the main cognitive results from SHARE replicated in the MRI cohorts. As education coding varied, we could not use the SHARE coding scheme, and education was, hence, dichotomized based on the median split for each sample, with post hoc analyses using 'Higher education' (education after high school) versus 'Secondary education' (high school or lower) ('replication analyses'). A generalized additive mixed model (GAMM)[43] was run using memory (z-normalized based on the first observation per each dataset) as dependent variable, with education, time since baseline, sex and a dummy for re-test effects as fixed effects and baseline age as smooth term. Random intercepts were included per participant and dataset, and random slopes of re-test and time were included for each dataset. To test memory change, an education × time interaction term was added to the model.

Similar to the SHARE results, whereas high education was associated with better memory scores ($\beta = 0.33$, s.e. = 0.009, $P < 0.001$, Cohen's $d = 0.63$), the education groups showed close to parallel changes over time (Fig. 5d,e). Predicted change over 10 years was

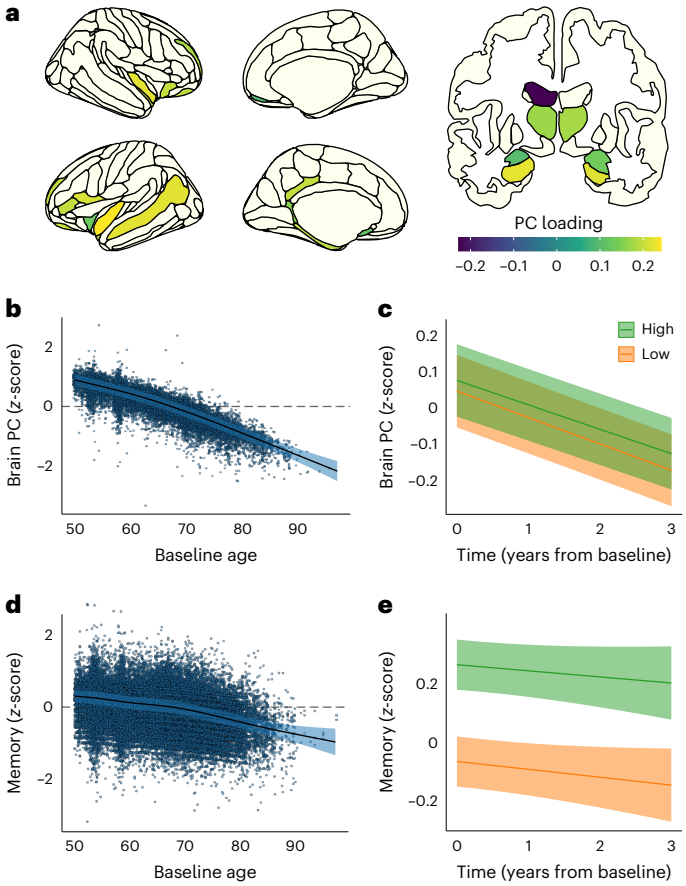

Fig. 5 | Education, brain measures and episodic memory. a, Brain regions where changes in structure and memory were related (FDR < 0.05) are highlighted, with color intensity reflecting the strength of each region's loading on the PC. The nucleus accumbens and left inferior lateral ventricle are not shown. **b**, Predicted brain PC score over baseline age. **c**, Three-year brain change (PC) for the high (green) and low (orange) education categories. The lines represent the predicted brain PC score as a function of time in each category. Shaded areas represent the s.e. of subject-level predictions. **d**, Predicted memory score over baseline age in the MRI cohorts. **e**, Three-year memory change for each education category. The lines represent the predicted memory score as a function of time in each category. Shaded areas represent 95% confidence intervals.

$z = −0.20$ for high education compared to $z = −0.26$ for low education (effect of education group on memory z-score change per year: $\beta = 0.006$, s.e. = 0.003, $P = 0.029$, Cohen's $d = 0.01$) (for complete results, see Supplementary Information). Similar results were seen when using the alternative education categorization. This confirmed that the main findings from SHARE were also seen for the memory tests in the brain MRI cohorts.

Next, we extracted a brain variable sensitive to memory change. For each participant, annual change in each of 166 brain regions was calculated and related to memory change by a series of linear mixed-effect models, yielding 29 false discovery rate (FDR)-corrected significant regions (Fig. 5a). These were entered into a PCA, yielding a memory-sensitive brain principal component (PC). This PC could then be used to test the specific hypothesis that high education has protective effects on brain change relevant for episodic memory and the prediction from the cognitive reserve theory that highly educated participants would experience less memory decline for a given level of brain decline.

To test the association between education and brain PC score (offset effects), a GAMM was run with education, time since baseline, sex and estimated total intracranial volume (eTIV) as fixed effects and

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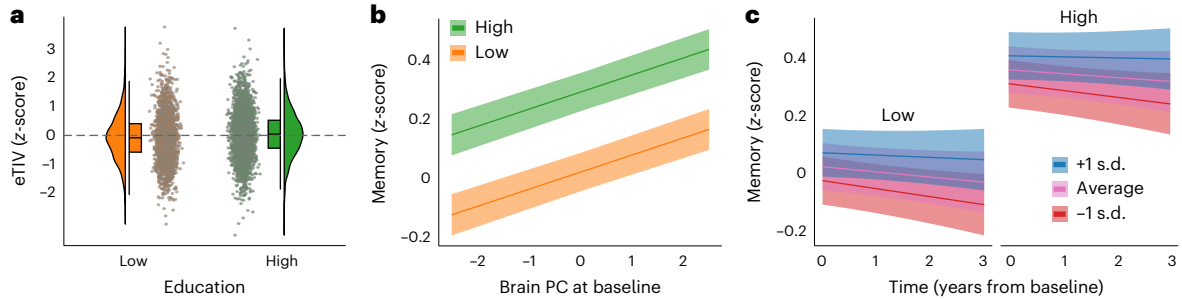

Fig. 6 | Relationships among brain, memory and education. a, eTIV in the high (n = 3,800) versus low (n = 2,672) education category. The center of the box is the median eTIV for each group, and the whiskers extend to ±1.5 s.d. × interquartile range. **b**, Predicted memory score as a function of baseline brain PC across education categories. **c**, Predicted memory score over time as a function of brain PC score for each education category. Shaded areas represent s.e. of subject-level predictions.

baseline age and sex × baseline age as smooth terms. Random intercepts were included per participant, scanner and dataset, and random slopes of time were included for each dataset. The brain PC showed the expected negative relationship to age, slightly accelerating from about 70 years (Fig. 5b), and time (β = −0.07, s.e. = 0.008, P < 0.001). Estimated loss in the high education group was z = −0.68 over a decade compared to z = −0.74 for the low group (interaction effect of education × time on brain volume: β = 0.005, s.e. = 0.002, P = 0.015, Cohen's d = 0.024), yielding close to parallel change slopes (Fig. 5c). Hence, brain decline across memory-sensitive brain regions was very similar in the two education groups.

In contrast, high education was slightly positively associated with the brain PC (β = 0.04, s.e. = 0.02, P = 0.049, Cohen's d = 0.17) and intracranial volume (β = 0.12, s.e. = 0.002, P < 0.001) (Fig. 6a). This means that participants with high education on average had slightly larger regional brain volumes, smaller ventricles and larger head size. The association with intracranial volume was numerically larger than the association with the brain PC. Intracranial volume is developed in childhood and undergoes minimal changes during school age, suggesting that this association reflects selection effects.

Finally, we tested whether the prediction from the cognitive reserve theory that the relationship between brain decline and memory decline is weaker in participants with higher education. First, a positive relationship was observed between the brain PC and episodic memory score (β = 0.073, s.e. = 0.013, P < 0.001). Because the brain PC was extracted from regions where brain change was related to memory change, the memory change–brain change relationship was given (β = 0.01, s.e. = 0.002). More importantly, no significant education × brain PC (β = 0.01, s.e. = 0.02, P = 0.60) or education × brain PC × time (β = 0.004, s.e. = 0.004, P = 0.43) interactions were observed. This means that the relationship between brain and memory, and the relationship between brain changes and memory changes, did not vary as a function of education (Fig. 6b,c), contrary to the prediction from the cognitive reserve theory.

Replication analyses

The main analyses were run using the alternative categorization of education (more/less than high school) and a different brain component derived using machine learning—that is, a regularized regression model (least absolute shrinkage and selection operator (LASSO)) used to predict memory based on an independent sample of 28,114 cross-sectional MRI scans from the UK Biobank, yielding four model specifications (Supplementary Table 8). Controlling for eTIV, cross-sectional education–brain associations were relatively weak although significant at P < 0.05 in three models. The education × time interaction was significant but with small effect sizes in the same three specifications. Effect size was largest for the PC brain measure and the high school categorization, with an interaction coefficient of 0.008 compared to 0.005 for the two other significant specifications. The brain × education × time interaction on memory was not significant in any specification.

As an additional set of control analyses, we tested whether the coefficients for the brain variables in predicting memory were affected by including education in the models (Supplementary Fig. 11). The coefficients changed only minimally, suggesting that the brain–memory relationships were largely independent of education.

Discussion

Education was only minimally associated with less age-related decline in episodic memory and rate of decline in memory-sensitive brain regions and did not increase resilience to the brain changes. The small magnitude of differences in brain and memory change across education groups contrasts with the much larger differences in baseline levels, highlighting a distinction between lifelong cognitive advantages and age-related trajectories. Additionally, we found evidence that selection effects account for parts of the associations, meaning that people with certain traits, such as larger brain volumes and higher cognitive function from early age, were more likely to pursue higher education. This selection process likely varies across social and demographic contexts and educational systems. Nevertheless, clear patterns emerged across diverse samples spanning multiple WEIRD societies and age cohorts. The findings aligned with trends observed in non-WEIRD societies, suggesting a certain degree of robustness across populations and historical contexts.

A role for education in brain and cognitive aging?

The idea that higher education reduces age-related cognitive decline is based on two complementary hypotheses. The first suggests that education protects against memory decline by influencing lifestyle factors that help preserve memory-sensitive brain regions—that is, by promoting brain maintenance. We found that less brain atrophy was linked to better episodic memory[12], yet differences in decline trajectories of memory-sensitive brain regions across educational groups were minimal.

This aligns with and extends previous findings[16] and provides a neurobiological explanation for why individuals with different educational attainment experience similar rates of age-related memory decline[21,44]. An implication is that behaviors associated with higher education may not be as protective against brain decline, as often assumed, because we would then expect accumulated effects over time, leading to diverging age trajectories and different rates of brain change between educational groups.

The second hypothesis proposes that education protects cognitive function by increasing resilience to brain decline, building a 'cognitive reserve'[5,18,19]. We found little support for this idea. Differences in aging trajectories for memory and memory-sensitive brain regions were minimal, and structural brain decline was associated with similar

amounts of memory decline across educational levels, aligning with previous research on hippocampal[20] and cortical[45] atrophy.

Additionally, more education was not linked to larger re-test effects, suggesting that higher education did not enhance the ability to benefit from test experience[46]. Re-test effects reflect the capacity to take advantage of previous testing to improve performance, and, although more educated individuals encoded new information more effectively—as reflected in their higher memory scores—this did not translate into greater gains from repeated testing. Similar findings have been reported for tests of mental speed and reasoning[47].

Taken together, these results suggest that education does not reduce brain decline or episodic memory in aging. Instead, the observed associations likely reflect differences established earlier in life.

How do associations among brain volume, cognitive function and education arise?

The results revealed relationships among education, memory function, slightly larger volumes of memory-sensitive brain regions and larger intracranial volume. The most straightforward explanation is that individuals with higher cognitive abilities and larger brain volumes are more likely to pursue higher education[48]. Although participants faced unequal opportunities and barriers to education[49], which may weaken the link between cognitive abilities and educational attainment, the findings suggest that selection may partly explain the associations:

First, consistent with selection effects, participants with higher education relative to their peers—matched by sex, birth cohort and country—had better memory function decades later even when accounting for absolute education.

Second, controlling for proxies of childhood cognitive function and 'scholarly culture'[50] attenuated the association between education and memory performance. Earlier-life cognitive function predicts cognitive ability and brain health in aging[51,52], limiting opportunities for causal effects of education beyond adolescence. This conclusion aligns with a systematic review of the effects of education on dementia risk, which suggested that low education is more strongly associated with dementia when it reflects cognitive capacity rather than privilege and when linked to other risk factors across the lifespan[53].

Third, larger intracranial volume confounded the education–memory relationship. Intracranial volume, a proxy for lifetime maximum brain size[54], is often considered a measure of 'brain reserve' and is linked to better cognitive function in aging, even after accounting for brain pathology[55]. Because intracranial volume is fully developed before adolescence, it is unlikely to be directly influenced by education.

Taken together, these findings suggest that earlier-life factors contribute to the lifelong associations between education and cognition. Still, these observations do not preclude the possibility of causal effects. Cognitive training can lead to improvements in memory and brain structure, even in older adults[56–58], and early education could similarly contribute to increased brain volumes of the magnitude observed here. Because part of the relationship between cognition and education can be explained by neuroanatomical differences from early childhood[33], brain structure may serve as a phenotype in the causal pathway linking genetic variation to differences in cognitive function and educational attainment[59].

However, training-induced effects on brain structure tend to be more transient than those on cognition[60,61], making it less likely that direct effects of youth education on brain volume would persist into old age. Accordingly, a study found no evidence of structural brain differences resulting from the increase in mandatory schooling in the UK from 15 years to 16 years, when assessed 50 years later[62]. Instead, intracranial volume has a stronger relationship to education than gray matter volume[33]. In fact, the association between education and intracranial volume was twice as large in the present study as the association with the brain component, and removing intracranial volume from the model strengthened the memory–brain relationship. This again points to selection effects. Furthermore, it is consistent with genetic evidence[63], although it is important to note that, despite education and cognitive function being genetically correlated[64], some of the predictive power of polygenic scores for these traits reflects environmental amplification of the genetic effects, which vary across environments[64,65].

Nonetheless, education could lead to improved cognitive scores without detectable brain structure effects. Natural experiments suggest impacts of education on cognitive function[26–28], including memory[23–25], although such effects could reflect improvements in test-taking skills rather than changes in brain structure or cognitive functions outside the testing environment[21]. Such effects could contribute to reductions in early dementia diagnoses, as recently shown in a study of the 1972 UK school reform[66], without necessarily reducing brain pathology. However, it would be surprising for the relationship between education and memory test performance to remain linear if test-taking skills were the main factor, as improvements would likely plateau at some point. Hence, test-taking skills are unlikely to be the major contributor to the superior memory performance in highly educated individuals.

The importance of childhood factors

The most coherent interpretation of the current results is that any positive effect of education on cognition in aging must stem from early schooling[29]. The parallel memory–education associations across the age range align with evidence that education enhances lifelong cognitive function without mitigating age-related decline. Still, most cognitive intervention studies have found that the positive effects on cognitive scores diminish over time[21,67]. Thus, any early effect of education on cognition would likely need to be sustained through some mechanisms that help maintain the initial benefits.

This idea aligns with the gravitational hypothesis, which suggests that the stability of individual differences in cognition is shaped by consistent exposure to the same environments over time, including social, educational and economic contexts[21,68,69]. Studies have shown that 'cognitive stimulation' in the workplace is associated with a lower risk of dementia diagnosis[70], although it does not fully account for the link between education and reduced risk[71]. Furthermore, individuals with higher cognitive function may naturally seek out cognitively stimulating activities, regardless of their formal education.

The linear association between memory performance and education is interesting. If education directly causes higher cognitive scores, one might expect diminishing returns with increasing years of schooling. This question has not been adequately addressed by quasi-experimental methods[29] and could reflect additive selection effects across the spectrum of educational levels. It is also noteworthy that this pattern holds across diverse samples from many countries and cohorts, suggesting robustness to societal variations.

Considerations and future research

Although we did not specifically examine variations across time[31] or societies[32–34], other studies have found relatively consistent education–cognition associations[72], in line with our comparisons with countries in Africa, Latin America and East and South Asia. SHARE employed probability sampling, but the MRI samples are generally less representative[73]. Although it is difficult to estimate the impact of this, we note that the relationships were replicated in the brain imaging cohorts.

Test scores correlate with important real-life indicators, such as work participation and independent living, but it remains unclear to what extent differences in scores reflect daily life function[66]. Education could improve test scores with minimal effect on the underlying cognitive construct, especially in crystallized or domain knowledge-based tests, but maybe less so in fluid tasks such as list recall[21], although

effects have been reported for compound (for example, the *g*-factor) measures of cognition[29]. One study found that the relationship between education and cognitive scores, after controlling for childhood cognition, involved direct effects on specific cognitive skills, including memory, rather than being mediated by the *g*-factor[74]. Still, we observed similar associations across several cognitive domains. Finally, although structural brain change is predictive of memory decline in aging[75], other measures could reveal different relationships.

Conclusion

In this large-scale, geographically diverse longitudinal mega-analytic study, we found that education is related to better episodic memory and larger intracranial volume and modestly to memory-sensitive brain regions. These associations are established early in life and not driven by slower brain aging or increased resilience to structural brain changes. Therefore, effects of education on episodic memory function in aging likely originate earlier in life.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-025-03828-y.

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Methods

The research complies with all relevant ethical regulations, and all participants provided informed consent. The main project was approved by the Norwegian Regional Committee for Medical Research Ethics South (approval no. 8122), and each substudy was approved by the relevant ethical review board, as specified in Supplementary Table 3.

Samples

SHARE cohort. SHARE is a research infrastructure for studying the effects of health, social, economic and environmental policies over the life course of European citizens and beyond (https://share-eric.eu/)[39]. SHARE contains observations of individuals from 50 years of age from 28 countries, recruited to be representative of the population in each country. Data for the present analyses were extracted from *easy*SHARE release 8.0.0 (10 February 2022, https://doi.org/10.6103/SHARE.easy.800); see refs. 76,77 for methodological details. *easy*SHARE release 8.8.0 is based on SHARE waves 1, 2, 3, 4, 5, 6, 7 and 8 (https://doi.org/10.6103/SHARE.w1.800, https://doi.org/10.6103/SHARE.w2.800, https://doi.org/10.6103/SHARE.w3.800, https://doi.org/10.6103/SHARE.w4.800, https://doi.org/10.6103/SHARE.w5.800, https://doi.org/10.6103/SHARE.w6.800, https://doi.org/10.6103/SHARE.w7.800, https://doi.org/10.6103/SHARE.w8.800)[39,78]. Participants included in the analyses participated in up to six waves of data collection. In total, we included data from 130,880 participants (mean age 64.9 years at baseline, 50.1–112.0, 59,363 males and 71,517 females), with an average of 2.7 waves (s.d. = 1.63) with a mean maximum follow-up interval of 6.53 years (0.9–15.9, s.d. = 3.93). In total, 352,953 memory test sessions were included, with two test results (immediate versus delayed recollection) for each—that is, 705,906 memory scores went into the analyses. Respondents aged younger than 50 years (individuals recruited due to being spouses of other participants) were excluded from the sample. An overview of the age distribution per country is provided in Fig. 1a. Sample distribution as a function of timepoints, education category and age is provided in Supplementary Fig. 3.

Memory was assessed with a 10-word verbal recall test. The word list is read out loud to the participants, and then recall is tested immediately after the presentation (recall 1) and then after a delay of approximately 5 minutes (recall 2). Multiple versions of the lists are assigned to the respondents[41]. The response distribution is shown in Supplementary Fig. 4. There were no ceiling effects, which is important when assessing longitudinal change for the best-performing participants. There were some floor effects for recall 2 but less for recall 1, suggesting that we can estimate longitudinal chance well for most baseline levels of memory. Because education is associated with differences in memory scores, ceiling and floor effects could potentially obscure real differences in change, but this is unlikely to have affected the current results given the response distribution below. Scores were lower for delayed than immediate recall (odds ratio = 0.535, confidence interval: 0.534–0.537), and females scored higher than males (odds ratio = 1.160, confidence interval: 1.153–1.168).

In addition to the memory measures, we extracted the variables age, sex, birth year, education (based on the ISCED 1997) and country of current residency.

MRI cohorts. We combined data from 13 datasets with longitudinal brain MRI scans and memory assessments: LCBC[79], Betula[80,81], UB[82,83], BASE-II[84,85] and Cam-CAN[86] datasets (from the Lifebrain consortium)[40] as well as the COGNORM[87], the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (https://adni.loni.usc.edu)[88], BBHI[89], the Harvard Aging Brain Study (HABS)[90], the UK Biobank (https://www.ukbiobank.ac.uk/)[91], PREVENT-AD[92,93], OASIS3 (https://sites.wustl.edu/oasisbrains/)[94] and VETSA[95]. Sample size was maximized for each analysis and, hence, varies due to data availability and missingness (see Supplementary Table 2 for an overview). In addition to cohort-specific inclusion and exclusion criteria, participants older than 50 years without cognitive impairment, Alzheimer's dementia or severe neurological or psychiatric disorders were included. Additionally, MRI data from scanners with fewer than 15 measurements were also excluded. The initial dataset included individuals with 1–14 MRI acquisitions with longitudinal structural MRI data spanning up to 15.8 years. Similarly, memory assessments range from one to 24 observations per individual with a follow-up up to 28 years. For detailed descriptions of general characteristics of each dataset, see the study-specific citations above. An overview of each dataset is given in Supplementary Information (Supplementary Table 1). The main sample descriptives are provided in Extended Data Table 2, but because the exact sample size varies somewhat between analyses depending on data availability, the specific characteristics for the samples used and their age distributions used to address the different research questions are provided in Supplementary Table 2 and Supplementary Fig. 1.

Education in the brain imaging cohorts. For each dataset, education was categorized as high or low using a mean split. We chose this approach because quantitative distributions of education were often highly non-Gaussian, and level-based codifications were somewhat arbitrary due to idiosyncratic reporting of years of education and variations in schooling systems across years and country. To ensure robustness, we conducted analyses with an alternative operationalization of education, categorizing individuals with or without tertiary education. When education data were provided as qualifications or categories, these were converted to years of education based on country-specific norms. Individuals were then grouped as having high or low education based on the median. For the tertiary education categorization, the reverse process was applied, converting years of education into education qualifications. For reporting consistency, a lower cap of 6 years and an upper cap of 20 years were applied to education years. An overview of education characteristics for each MRI sample is provided in Supplementary Table 4 and Supplementary Fig. 2.

Memory function in the brain imaging cohorts. For each sample, we operationalized memory performance as a *z*-normalized score based on the first timepoint and the different available memory tests. When multiple scores were available, we used the first component of a PCA with all measures as inputs. For each dataset, we regressed out age (as a smoothing term), sex and one or two dummy test–re-test regressors using GAMMs ('gamm4' R package)[43]. Individual identifiers were used as random intercepts, and the number of dummy test–re-test regressors depended on whether the dataset had two or three or more waves with memory function data. The residuals were used as an estimate of memory function in each observation. An overview of tests included in the memory performance score for each dataset is provided in Supplementary Table 5.

MRI acquisition and preprocessing. Structural T1-weighted (T1w) MPRAGE and FSPGR scans were collected using 1.5T and 3T MRI scanners. Information regarding scanners and scanner parameters across datasets are presented in Supplementary Table 6. We used the longitudinal FreeSurfer version 7.1.0 stream[96] for cortical reconstruction and volumetric segmentation of the structural T1w scans[97–99]. For sessions with multiple scans, data from the scanners were averaged. In brief, the images were processed using the cross-sectional stream, which includes the removal of non-brain tissues, Talairach transformation, intensity correction, tissue and volumetric segmentation, cortical surface reconstruction and cortical parcellation. Next, an unbiased within-subject template space based on all cross-sectional images was created for each participant, using robust, inverse-consistent registration. The processing of each timepoint was then reinitialized with common information from the within-subject template to increase reliability and statistical power. Except for the Betula dataset, all data were preprocessed on the Colossus processing cluster, part of the

Services for Sensitive Data (https://www.uio.no/tjenester/it/forskning/sensitiv/), University of Oslo. Memory-sensitive brain measures for each observation were derived using regional loadings based on the 'Destrieux' (cortical)[100] and 'aseg' (subcortical) atlases[101].

Memory-sensitive brain measures. We computed two complementary measures of brain structure sensitive to memory, capturing different aspects of memory function in older age. The primary measure was defined as a longitudinal brain component sensitive to memory changes inspired by Vidal-Piñeiro et al. (in preparation). The second measure, for the purpose of assessing the robustness of the results, was trained on independent scans to detect cross-sectional brain–memory relationships in aging. The components were highly correlated ($r = 0.71$), both decrease with age ($r = -0.67$ and $r = -0.64$, respectively) and include partially overlapping sets of brain regions. The first measure (brain PC) is optimized to be sensitive to memory changes in aging, whereas the second (brain LASSO) is optimized to detect also offset (that is, baseline) associations. See Supplementary Information for a full description of LASSO.

Brain PC as a change-based, memory-sensitive measure. This measure was derived from a sample largely overlapping with that used for the statistical analyses and the Australian Imaging, Biomarker and Lifestyle Flagship Study of Ageing in the present work but included participants down to age older than 18 years. Brain PC is based on a PC of longitudinal change in 20 cortical thickness and nine subcortical volume regions. Brain regions were harmonized using a normative modeling framework[102,103] with the PCNtoolkit (0.30.post2) in the Python3 environment[104] (version 3.9.5). This framework offers several advantages: (1) it is run independently across sites; (2) it can isolate site effects from other sources of variance associated with it; and (3) it produces site-agnostic deviation scores (z-statistics) adjusted for age and sex. PCNtoolkit uses a hierarchical Bayesian regression (HBR) technique[105] and pretrained models from 82 different datasets, including UK Biobank and Cam-CAN data. To avoid losing longitudinal observations, we performed this step recursively by iteratively ($n = 100$) holding out a calibrating sample and computing the estimates on the remaining data. The average scores of all iterations were used as the standardized scores for each observation. Scanners contributing with fewer than 12 unique individuals or fewer than 25 observations were excluded. For scanners contributing more than 12 and fewer than 32 unique individuals, we used a calibration sample consisting of all but two participants and estimate the harmonized scores in these two. For scanners with 32 or more unique individuals, we used, in each iteration, a held-out sample of 30 individuals while estimates were applied on the rest.

Next, we selected individuals with at least two observations and a minimum follow-up of 1.5 years. For both MRI and memory preprocessed data, we estimated yearly change for each participant by regressing data on follow-up time. Change data were then fed into separate linear mixed models as implemented in lme4 and lmerTest[106,107], one per brain region. Note that here we used estimates of change, and there was only one observation per individual. For each region, we predicted memory change by brain change, using dataset as random intercepts. Additionally, we used weights to account for potential heteroskedasticity. That is, individuals with short follow-up periods and fewer observations contribute with more unreliable, high-variance data and, thus, should produce an unequal spread of residuals. We used the square of reliability as weights as estimated in ref. 108. Longitudinal reliability is a function of variance in change and mean measurement error for a given region and number of observations and total follow-up time for a given individual. After FDR correction ($P < 0.05$), 29 regions showed significant associations between brain change and memory change, including nine volumetric subcortical regions (bilateral amygdala, hippocampus and thalamus, left lateral and inferior lateral ventricle and right accumbens area) and 20 cortical thickness regions (left G cingul-Post-dorsal, G cingul-Post-ventral, G insular_short, G oc-temp_med-Parahip, G front_inf-Opercular, G front_inf-Triangul, G subcallosal, S temporal_sup; right G Ins lg&S cent_ins, S circular_insula_ant, S oc-temp_med&Lingual, S suborbital; bilateral G temp_sup-Plan_polar, S orbital-H_Shaped, S front_middle, S circular_insula_inf). These regions were entered into the PCA to extract the PC of the memory-sensitive brain regions, yielding a brain measure sensitive to episodic memory change in aging. All regions except the ventricles showed positive loadings with the brain PC.

Statistics

SHARE. Analyses were performed in R (mostly version 4.2.1 (ref. 109)) using the brms package's[110] interface to the probabilistic programming language Stan[111]. To assess effects of education on memory and memory change, we ran logistic regressions with memory recall as dependent variable, yielding odds ratios as the most relevant model parameter to interpret. An odds ratio of 1 corresponds to a regression coefficient of 0. The main model was:

```
formula=recall|trials (10) ~ test + mo (past_tests)
+ sex + country + edu + time_since_baseline_z:edu +
s(age_at_baseline_z,bs="cr") + time_since_
baseline_z + age_at_baseline_z:time_since_
baseline_z + (1|country/mergeid)
```

Each memory test was used as a separate response, yielding two observations per timepoint, and the variable 'test' represents difficulty of condition 2 relative to condition 1. To control for practice effects, a monotonic function of the number of previous tests taken was included as covariate. We used a smooth function of age to allow nonlinear relationships. Individual-specific intercepts per participant were nested within country. Default priors were used for all parameters, and two parallel chains of Stan's No-U-Turn Sampler[112] were run for 1,500 iterations, discarding the first 1,000 as warmup. This yielded 1,000 post-warmup samples. For the offset/level analyses, education (edu) was the variable of interest, whereas, for the slope/change analyses, edu × time since baseline was the critical variable. z-transformed variables were used in the model fitting for numerical stability, and results were converted back to their natural units for easier interpretability—for example, age and time in years.

MRI cohorts. All the analyses were performed using the R environment (version 4.2.1)[109]. Visualizations were made with the 'ggplot2'[113] and 'ggseg'[114] R packages. Memory, brain variables and eTIV were z-standardized before inclusion in the models. Outlier values defined as values >5 s.d. from the mean were removed from the analyses. Analyses were run using GAMM models as implemented in the 'gamm4' R package[43], unless otherwise specified.

Memory score was modeled as a function of education, time since baseline, sex and a dummy regressor for test–re-test effects as fixed effects. Baseline age by sex was included as a smooth term. Random intercepts were modeled per participant and dataset, with random slopes of re-test effects and time from baseline at a dataset level. To test the effects on memory change, the model was re-run with an additional education × time interaction term. Education was operationalized either as mean-split or based on tertiary education in separate models.

Brain structure was modeled as a function of education, time since baseline, sex and eTIV as fixed effects. Baseline age by sex was included as a smooth term. Random intercepts were modeled per participant, scanner and dataset with random slopes of time included at a dataset level. To test effects on brain change, the model was re-run with an additional education × time interaction term. As control analyses, we re-ran the GAMM models without eTIV as covariate. Additionally, we ran a linear mixed model as implemented in lme4, with eTIV being modeled as a function of education, sex and baseline age as fixed effects,

and site and dataset were included as random intercepts. Only the first observation of each participant was included, as eTIV and education are time-invariant variables. Alternative operationalizations of education and brain structure were tested in separate, but otherwise identical, models.

We used a fuzzy join algorithm, as implemented in 'fuzzyjoin'[115], to link pairwise MRI and cognitive observations, as these were not necessarily collected on the same day. MRI observations were matched with the closest cognitive observations within a maximum time gap of 1 year. Unlinked observations were excluded from the analyses. The relationship among brain, memory level and education was assessed with several models. 'Brain level and memory level': Memory was modeled by brain structure, sex, time, eTIV and a dummy regressor for test–re-test effects as fixed effects. Baseline age by sex was introduced as a smooth term. Random intercepts were modeled per participant, scanner and dataset with random slopes of re-test and time modeled at a dataset level. 'Brain change and memory change': An additional brain × time term was added to the model. 'Moderating effect of education on level–level associations': Additional terms for education and education × brain were added in the first model. 'Moderating effect of education on change–change associations': A triple interaction term (brain × time × education) as well as its lower-order components were added in the first model. 'Control analyses': A main education term, without any interaction, was added to the models to assess level–level and change–change associations between brain and memory, to test whether the strength of these associations was affected by education level. As with other analyses, alternative operationalizations of education and memory-sensitive brain structure were tested in separate but similar models.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Each dataset has different owners. Contact information to be used for data access is specified in Supplementary Table 3. Parts of the data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (https://adni.loni.usc.edu/). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in the analysis or writing of this report. A complete listing of ADNI investigators can be found at https://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf. More information about the Vietnam Era Twin Study of Aging (VETSA), including a list of VETSA investigators, is available at https://psychiatry.ucsd.edu/research/programscenters/vetsa/index.html.

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Author contributions

A.M.F., K.B.W., O.R. and D.V.-P. conceptualized the study. A.M.F., O.R., D.V.-P. and Ø.S. analyzed the data. A.M.D. wrote the paper. All authors critically revised the paper and approved the final version.

Competing interests

A.P.-L. serves as a paid member of the scientific advisory boards for Neuroelectrics, Magstim Inc., TetraNeuron, Skin2Neuron, MedRhythms and AscenZion. He is co-founder of TI Solutions and co-founder and chief medical officer of Linus Health. A.P.-L. is also listed as an inventor on several issued and pending patents on the real-time integration of transcranial magnetic stimulation with electroencephalography and magnetic resonance imaging and applications of non-invasive brain stimulation in various neurological disorders as well as digital biomarkers of cognition and digital assessments for early diagnosis of dementia. The other authors declare no competing interests.

Additional information

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Extended Data Table 1 | Associations among education, memory score and memory score decline

Education level	Memory offset Odds Ratio (CI low – high)		Memory change Odds Ratio (CI low – high)	
None	0.54	0.53-0.55	1.004	1.001-1.007
Primary school	0.68	0.67-0.68	1.002	1.001-1.004
Middle school	0.83	0.81-0.83	1.002	1.000-1.003
High school	1		1	
Vocational training	1.07	1.05-1.08	1.001	0.998-1.003
Bachelor's degree	1.31	1.29-1.32	1.001	1.000-1.003
Master's degree	1.55	1.49-1.60	1.004	0.999-1.010

'High school' is used as reference. Memory change (odds ratio per year) results are presented with three decimals to allow inspection of the very weak effects. Confidence interval is 95%.

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Extended Data Table 2 | Sample characteristics for samples with MRI

Dataset	Total participants	Total test sessions	Sex Male/Female	Higher education (n)	Above median education (n)	Tests pr participant	Education years (mean)	Age (baseline)	Follow-up time (mean)	Participants with MRI	Total MRI sessions	Mean MRI scans pr. participant	Follow-up time between scans
ADNI	904	3824	405/399	657	438	4.23	16.5	72.5	3.4	768	3315	4.32	3.35
BBHI	596	801	303/293	411	411	1.34	14.6	57.7	0.8	579	766	1.32	0.75
HABS	287	1286	127/160	191	191	4.73	15.7	74.0	3.4	281	673	2.40	3.50
BASE-II	1328	2363	640/688	483	618	1.78	14.2	70.7	3.4	295	505	1.71	1.46
OASIS-3	647	3169	292/355	396	396	4.90	15.7	72.6	4.5	940	2013	2.14	2.88
OUS	114	667	54/60	48	55	5.85	14.6	73.5	5.2	113	388	3.43	4.99
Prevent-AD	306	1057	91/215	134	134	3.45	15.3	63.4	2.1	305	1360	4.43	2.17
UB	160	297	56/104	54	79	1.86	11.2	68.6	1.8	285	418	1.47	0.97
Cam-CAN	34	66	18/26	28	28	1.94	15.2	64.8	5.8	346	486	1.40	0.58
LCBC	185	435	73/112	151	83	2.35	16.5	61.1	5.0	316	758	2.40	3.18
UKB	33623	36212	16335/17288	22791	22791	1.08	14.5	65.4	0.2	1261	2522	2.00	2.25
Betula	139	612	71/68	20	53	4.40	11.1	58.0	16.6	252	501	1.99	4.12
VETSA	1592	3614	1592/0	450	834	2.27	13.9	57.8	7.5	731	1452	1.99	6.09
Total	39915	54403	20057/19858	25814	26111	1.37	14.6	65.5	0.9	6472	15157	2.34	2.81

N, number of unique participants. Higher education: more than high school education.

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☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No data was collected as part of the study.
Data analysis	Statistical analyses were performed in R v4.4.1 (SHARE) and v4.2.1 (MRI), including packages mgcv, gamm4, fuzzyjoin, brms, ggseg, ggplot2, dplyr, readr, missMDA, FactoMineR. Brain MRIs were analyzed with FreeSurfer v.7.1.0.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Data availability and ethical approvals
Each dataset has different owners. Contact information to be used for data access is specified in SI Table 3.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Number of males and females is specified for each sample Sex was used as covariate in all statistical analyses.
Reporting on race, ethnicity, or other socially relevant groupings	Race and ethnicity are not reported in the manuscript, as this information was missing for many samples
Population characteristics	Age, education, sex and country of origin is described for the samples included. Participants were generally cognitively healthy, but exact screening. Inclusion and exclusion criteria varied between studies and samples. This is described in detail in the manuscript for each sample, see Table 1, Table 2, SI nTable 1, SI Table 2, SI Figure 2.
Recruitment	Recruitement varied with sample and study. The Survey of Health, Ageing and Retirement in Europe is a research infrastructure for studying the effects of health, social, economic and environmental policies over the life-course of European citizens and beyond (https://share-eric.eu/). SHARE contains observations of individuals from 50 years of age from 28 countries, recruited to be representative of the population in each country. Participants in the 13 datasets with longitudinal MRIs were recruited following different procedures, detailed in SI Table 1.
Ethics oversight	The main project was approved by the Norwegian Regional Committee for Medical Research Ethics South (approval 8122), and each sub-study was approved by the relevant ethical review board, as specified in SI Table 3.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Sample size was maximized for each analysis and hence varies due to data availability and missingness (see Table 1 for an overview).
Data exclusions	In addition to cohort-specific inclusion and exclusion criteria, participants >50 years without cognitive impairment, Alzheimer's dementia or severe neurological or psychiatric disorders were included. The age criterion was imposed to match the lower age in SHARE. The other criteria were used to ensure that participants were generally cognitively healthy and did not suffer from specific brain diseases or conditions, which could potentially affect the results. Additionally, MRI data from scanners with fewer than 15 measurements were also excluded. This was done because too few measurements from a scanner sould make it difficult to statistically control for scanner effects. The exclusion criteria were pre-established.
Replication	Memory results from the SHARE data were replicated using memory data from the MRI cohorts. This was done by testing whether education level was associated with memory offset and memory change in the MRI-cohorts, which were independent from the SHARE cohorts. MRI brain results were replicated by using different categorizations of education, different covariates, and by use of a LASSO approach in addition to the GAMMs used in the main models. Hence, the MRI brain replications consisted of different analyses of the same sample, and are hence not independent replications. Replication was also done using data from four additional countries, by use of two additional cognitive tests, and in a subsample with extensive cognitive testing. See the main manuscript for details about the replication procedures.
Randomization	This was an observational study
Blinding	Blinding was not applicable because no experimental manipulation or intervention was done. The analyses were based on data from observational cohort studies, and all statistical modeling was performed using existing and anonymized data in R. As such, there was no contact with participants, and the outcome (memory performance) and exposure (education) had already been collected prior to analysis. Therefore, the potential for bias due to lack of blinding was not relevant to this design.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Plants

Seed stocks — *Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*

Novel plant genotypes — *Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*

Authentication — *Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*

Magnetic resonance imaging

Experimental design

Design type	NA (observational study using structural MRI)
Design specifications	NA (observational study using structural MRI)
Behavioral performance measures	NA (observational study using structural MRI)

Acquisition

Imaging type(s)	T1 weighted structural scans
Field strength	1.5T & 3T
Sequence & imaging parameters	The MRI sequences varied between samples. In total, 23 different MRI sequences were used. Exact sequence parameters are provided in SI Table 6.
Area of acquisition	Whole-brain aquisition

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	FreeSurfer v.7.1.0
Normalization	Normalization template = subject-specific unbiased within-subject anatomical average ("base" image). Normalization process = timepoints are aligned and normalized relative to this base, enhancing consistency and measurement precision. Base creation: Rigid (6 DOF), robust template. Talairach registration: Affine (12 DOF). Intensity normalization: mri_normalize using WM.
Normalization template	Talairach
Noise and artifact removal	mri_normalize used to correct for bias fields, primarily by standardizing white matter intensity. In lthe ongitudinal analyses the base template guides normalization to make correction consistent across time. No explicit motion correction is performed within FreeSurfer itself, but mri_robust_template used for base creation is resilient to moderate motion, using outlier rejection and robust averaging. WM and GM priors from the base help stabilize segmentation across time. Surface placement is also initialized from the base, reducing variability.
Volume censoring	NA

Statistical modeling & inference

Model type and settings	For SHARE, generalized linear models (GLM) with a binomial link were run using memory score as dependent variable, with the interaction between education and time since baseline as the critical term, using test type (immediate or 5-minute delay), a monotonic function of the number of previous tests taken (to control for retest effects), education, sex, country, baseline age, time since baseline, and the age × time interaction as covariates (see Methods for exact specifications). Individual-specific intercepts per participant were nested within country. Z-transformed values for age and time were used in the model fitting and converted back to natural units when showing the results. More details provided in the main text. For the MRI cohorts, First, to be able to study brain changes of relevance to episodic memory, we extracted a brain variable sensitive to memory change. For each participant, annual change in each of 166 brain regions was calculated and related to memory change by a series of linear mixed effects models, yielding 29 significant FDR-corrected significant regions (Fig 5A). These were entered into a PCA, yielding a memory-sensitive brain PC. This PC could then be used to test the specific hypothesis that high education has protective effects on brain change relevant for episodic memory, and the prediction from the cognitive reserve theory that highly educated participants would experience less memory decline for a given level of decline in memory-sensitive brain regions. For replication, we also used machine learning, i.e. a regularized regression model (LASSO: Least Absolute Shrinkage and Selection Operator), to predict memory based on an independent sample of 28.114 cross-sectional MRIs from UKB (Replication analyses). To test the association between education and brain PC score (offset effects), a GAMM was run with education, time since baseline, sex, and estimated total intracranial volume (eTIV) as fixed effects, and baseline age and sex × baseline age as smooth terms. Random intercepts were included per participant, scanner, and dataset while random slopes of time were included for each dataset.
Effect(s) tested	For SHARE, number of words recalled was each participant's memory score and used to index episodic memory function. How scores differed over age for each education category defined the memory trajectory for that category. A smooth function for age allowed non-linear memory trajectories. Memory offset refers to the cross-sectional differences between groups, represented by the main effect of education in the GLM. Memory change was defined as change in memory over time within participants and represented by the 'time' term in the model. Differences in memory change between education groups were represented by the education × time interaction term. The main outputs of the statistical model were the odds ratios (OR) of remembering a word compared to a reference group. More details provided in the main text. For the MRI cohorts, output was score on the brain PC in terms of volume or volume change.

Specify type of analysis: ☐ Whole brain ☒ ROI-based ☐ Both

Anatomical location(s)	Regions were defined based on the Destrieux (cortical) and aseg (subcortical) atlases, yielding whole-brain coverage, yielding 337 features in total (see main text and SI)
Statistic type for inference (See Eklund et al. 2016)	ROI-wise statistics and machine learning
Correction	false discovery rate < .05

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis