Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Use it or lose it: Sustained cognitive benefits following later-life education

Aidan Bindoff

aidan.bindoff@utas.edu.au

University of Tasmania https://orcid.org/0000-0002-0943-2702

Mathew summers

University of the Sunshine Coast https://orcid.org/0000-0002-3869-4920

James Vickers

Wicking Dementia Research and Education Centre, University of Tasmania, Australia

Article

Keywords:

Posted Date: November 27th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11304910/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: There is **NO** Competing Interest.

Abstract

A well-established evidence base has emerged to support a relationship between higher levels of education and resilience to cognitive decline against a background of neurodegeneration[1]. This concept has been formalized in the “cognitive reserve” hypothesis[2]. However, the role of education in cognitive reserve is confounded by inequalities in access to higher education and its benefits over a lifetime, which are themselves associated with cognitive reserve and improved health outcomes[3–5]. While the field has relied on evidence from retrospective cohort studies to inform preventative strategies for cognitive decline, the Tasmanian Healthy Brain Project is the first *prospective* cohort study with a university-level education intervention and control group. Here we provide some of the strongest evidence to date that higher education is associated with modest but sustained improvements in language processing and episodic memory, relative to trial controls, in a cohort of people aged 50 and over who completed a university education intervention with over 10 years of follow-up data.

Main

Over the past two decades, there has been an increasing interest in the potential of cognitive reserve (CR) to account for individual differences in susceptibility to neurodegenerative diseases. The theoretical concept of CR emerged to explain differences in cognitive function between individuals with similar brain injuries[2] . CR encompasses lifetime activities that accumulatively contribute to strengthening or enhancing cognitive functions, such as formal education, intellectual capacity, social engagement, and leisure activities that involve mental activity and challenge (e.g. puzzles, crosswords, reading, etc)[6] . CR potentially explains inter-individual differences in the rate and severity of cognitive changes in age-related neurodegenerative diseases such as dementia[1] . Hence, the cognitive and functional impacts of the underlying biological process of neurodegeneration in dementia may be ameliorated or offset by the level of a person’s CR, such that individuals with greater CR may exhibit milder cognitive and functional symptoms of dementia than an individual lower in CR despite the same degree of neurodegeneration. Retrospective studies support this potential, with the Nun Study[7] demonstrating a relationship between higher levels of education and later onset of dementia symptoms, and autopsy studies indicating a relationship between level of education and lower dementia symptoms in older adults with marked neuropathology of dementia[8,9] . While a proportion of CR may be explained by genetic factors (such as intellectual ability), or by early life experience (e.g., formal education, occupation), the notion of CR implies that developmental changes can improve or decrease CR across the lifetime.

The evidence base for education improving CR has weakened considerably over the past five years. Adjustment for cognitive ability measured in early adulthood removes the association between educational attainment and dementia[10]; multivariable Mendelian randomization attributes the association to intelligence rather than to schooling[11]; and an analysis of 407,356 memory assessments across 33 countries found that education did not protect against age-related decline, nor weaken the effect of brain decline on cognition[12]. The consensus reading is that education raises the level of

cognitive function but not its trajectory, and that even this reflects who pursues education rather than an effect of education.

Such a conclusion rests on a form of evidence which cannot, in principle, decide the question. Education received in youth is inseparable both from what precedes it (childhood ability, family circumstances, opportunity, etc.) and from the decades of occupational and social advantage it subsequently confers, so adjustment cannot recover the effect of education from a variable that indexes an entire life course. The definitive review of this literature explicitly sets aside the one exposure that escapes the problem: education undertaken in later life[13]. Education beginning after the age of fifty arrives once the causal chain that early education sets in motion has already run, so that chain is not an unobserved mediator but a measured baseline. Selection on health, motivation, self-efficacy and prodromal status remains, but the residual confounding is contemporaneous and measurable at baseline, whereas the confounding that defeats early-life studies is historical and largely unmeasured. This is a partial decoupling rather than an identification strategy, and it is the asymmetry the THBP was designed to exploit.

The Tasmanian Healthy Brain Project (THBP)

To test the potential malleability of CR in older adults, we commenced the Tasmanian Healthy Brain Project (THBP) in 2011[14]. The THBP was a prospective longitudinal study with intervention and control groups designed to examine the potential for formal education in older adults to enhance cognitive functions, thereby enhancing CR and protect against age-related cognitive decline and reduce the risk of dementia. This study is the first of its kind in a field that has relied almost exclusively on retrospective observation to guide meaningful prevention strategies to combat cognitive decline. In this paper, we report the final results of the THBP after participants who completed at least 12 months of University level underwent repeat cognitive assessment over a 10-year period. Participants were eligible to participate if they were aged 50–79 years at the time of entry into the study and were assessed as healthy without any significant acute or chronic medical or psychiatric conditions. On entry into the THBP participants opted (non-random assignment) to participate in the University-education group or a no-further education group (control). At entry into the study, each participant underwent comprehensive assessment across measures of cognitive and neuropsychological function as well as psychosocial measures[14]. For analysis, participants in the university-education group completed a minimum of 12 months of university study, with a minimum study load of two units per semester at undergraduate or postgraduate level. Each participant was invited for full assessment every year for the first 4 years of the study (Year 1 [baseline], 2, 3, 4) and biannually thereafter (Year 6, 8, 10). The full THBP protocol is described elsewhere[14]. At baseline (Year 1) a total of 562 participants were screened and completed full baseline assessment; 433 (77%) participants undertook university-level education and 129 (23%) served as controls. For this paper, only participants who had completed 4 or more assessments including the baseline assessment were retained. This resulted in a final sample of 416 participants, with 21.4% in the control group and 78.6% in the university-education group, with 64.2% of participants completing 6 or more assessments (see Table 1).

Table 1
Participant characteristics stratified by group

	Control	Education	Overall
	(N = 89)	(N = 327)	(N = 416)
Age at baseline (years)			
Mean (SD)	62.5 (6.46)	60.0 (6.54)	60.5 (6.60)
Median [Min, Max]	63.0 [50.0, 76.0]	60.0 [50.0, 78.0]	61.0 [50.0, 78.0]
Sex			
Female	55 (61.8%)	226 (69.1%)	281 (67.5%)
Male	34 (38.2%)	101 (30.9%)	135 (32.5%)
Number of assessments			
4	13 (14.6%)	53 (16.2%)	66 (15.9%)
5	21 (23.6%)	62 (19.0%)	83 (20.0%)
6	22 (24.7%)	85 (26.0%)	107 (25.7%)
7	33 (37.1%)	127 (38.8%)	160 (38.5%)
Prior education (years)			
Mean (SD)	13.9 (2.65)	14.2 (2.62)	14.1 (2.63)
Median [Min, Max]	14.0 [9.00, 21.0]	14.0 [8.00, 23.0]	14.0 [8.00, 23.0]
# APOE ε4 alleles			
0	55 (61.8%)	193 (59.0%)	248 (59.6%)
1	27 (30.3%)	76 (23.2%)	103 (24.8%)
2	1 (1.1%)	12 (3.7%)	13 (3.1%)
Missing	6 (6.7%)	46 (14.1%)	52 (12.5%)
HADS anxiety (at baseline)			
Mean (SD)	5.37 (2.99)	5.12 (3.09)	5.17 (3.07)
Median [Min, Max]	5.00 [0, 14.0]	5.00 [0, 17.0]	5.00 [0, 17.0]
HADS depression (at baseline)			
Mean (SD)	2.94 (2.48)	2.21 (2.13)	2.37 (2.23)
Median [Min, Max]	2.00 [0, 10.0]	2.00 [0, 11.0]	2.00 [0, 11.0]

	Control	Education	Overall
	(N = 89)	(N = 327)	(N = 416)
Age at baseline (years)			
WTAR full-scale IQ			
Mean (SD)	112 (4.80)	113 (5.48)	113 (5.34)
Median [Min, Max]	114 [97.0, 119]	114 [83.0, 123]	114 [83.0, 123]
Dementia Rating Scale			
Mean (SD)	140 (2.94)	141 (2.61)	141 (2.69)
Median [Min, Max]	141 [127, 144]	142 [128, 144]	142 [127, 144]

Cognitive domains

The THBP protocol[14] utilizes a comprehensive neuropsychological assessment battery spanning multiple cognitive domains. The protocol was designed to utilize multiple standardized cognitive tests of each cognitive domain, to ensure overlapping assessment of each major cognitive domain and across each modality (i.e. visual, verbal). A challenge in cognitive assessment is that a single cognitive test does not measure a discrete cognitive function, rather performance of a single cognitive task requires the individual to utilize multiple cognitive processes. For example, a word list learning task is commonly used to assess learning and recall of new information. As the task involves listening to a list of words presented aurally, retaining this information before reciting as many words as the individual can remember, the individual will utilize multiple cognitive processes other than those involved in memory encoding and retrieval, such as working memory, executive processes (such as attentional mechanisms), language processing, and auditory perception. Hence, while an individual with a lowered performance on such a memory task may be exhibiting a learning and/or recall deficit, it is possible that deficits to other sensory, perceptual, or cognitive processes (e.g. attention) may result in the same negative effect on task performance. For this reason, neuropsychological assessment involves the use of multiple overlapping measures of memory as well as multiple measures of other cognitive domains before determining that an individual has a specific deficit to a cognitive function such as learning and/or recall.

In previous work by our group, an investigation of the underlying factor structure of the cognitive test battery identified that the THBP test battery loaded onto four cognitive process domains: language processing, episodic memory, working memory (a component of executive function) and a more general executive function dimension[15]. For the present study the 4-factor structure previously identified was retained using the loadings reported by Ward *et al*[16] and supported in Thow *et al*[15].

The impact of late life education on cognitive performance over time

Earlier work by our group examined cognitive change over the first 4 years of the THBP and identified an initial early “growth phase” in the university-education group that was assumed to comprise a practice effect combined with performance effect attributable to the education intervention[3,15]. Theoretically, we predicted that following the initial cognitive improvement due to the education intervention participants would display ongoing age-related decline over the remainder of the study. To estimate the duration and slope of the growth phase in each group, and the slope of the decline phase (if any) in the current study, we fitted hierarchical piecewise regression models with an estimated transition point[17] (see Methods). Change-point models of this kind have been applied in cognitive aging almost exclusively in relation to the approach of death or of dementia onset[18]; here the transition is estimated on time since baseline, and locates the point at which initial improvement gives way to decline. Slopes were compared between groups using Evidence Ratios (ER), i.e. by taking the ratio of the posterior probability under the hypothesis against its alternative. The estimated standardized group difference between slopes is taken to be the effect of the intervention, after adjusting for measured confounding (refer to Methods for detailed description).

Evidence for distinct growth and decline phases

We analysed 2,156–2,198 domain-level observations from 416 participants, depending on the domain (Supplementary Table 1). For the control group, episodic memory improved at 0.10 [0.05, 0.15] z per year before transition, flattening to -0.02 [-0.06, 0.01] z per year after the transition. A similar trajectory was observed for language processing, improving at 0.06 [-0.01 0.18] z per year before reversing to decline by -0.08 [-0.19, -0.04] z per year after transition. Because the pre-transition slope is freely estimated, a linear trajectory is nested within the model as the case in which the change in slope, δ_1, is zero. For both domains, the 95% credible intervals for the post-transition change in slopes excluded zero; [-0.19, -0.05] for episodic memory and [-0.27, -0.04] for language processing. We take this as evidence of distinct growth and decline phases on these domains, while for working memory and executive function, the post-transition change in slopes was less certain; -0.06 [-0.13, 0.02] and − 0.09 [-0.26, 0.04] respectively (Fig. 1a-d).

The transition point was only sharply identified in episodic memory, at 2.85 [2.52, 3.18] years after baseline. Estimates for working memory (2.49 [1.31, 3.59]), executive function (2.78 [1.07, 5.65]) and language processing (2.23 [1.06, 5.17]) were consistent with a common transition near the third year but were sensitive to the prior bounds (Supplementary Table 8a); the transition point is thus data-identified in episodic memory, reasonably robust in working memory, and partly prior-informed elsewhere. Allowing it to differ by group gave a group term centred near zero on every domain (Supplementary Table 9).

Evidence for an effect of the intervention

The education group's pre-transition slope in episodic memory was steeper by 0.07 [0.02, 0.12] z per year (ER = 228.9, P(H) = 0.996), the only domain with a well-supported pre-transition contrast (working memory ER = 2.3, executive function 1.8, language processing 2.9; Table 2). After the transition the advantage attenuated but did not reverse (0.03 [− 0.01, 0.07] z per year; ER = 10.2, P(H) = 0.911). In language processing the groups differed in net post-transition trajectory (0.07 [0.03, 0.18] z per year; ER > 1000): the comparison group declined at about − 0.08 z per year while the education group was near stable. No post-transition group difference was supported for working memory (ER = 0.6) or executive function (ER = 2.3).

Table 2

Directional group contrasts by cognitive domain Hypothesis: education group > control group. Estimates are z per year, mean [95% CrI].

Domain	β_1 (pre-transition slope)	ER [P(H)]	$\beta_1+\delta_1$ (post-transition slope)[a]	ER [P(H)][b]
Episodic memory	0.069 [0.018, 0.122]	228.9 [1.00]	0.027 [− 0.013, 0.067]	10.2 [0.91]
Working memory	0.015 [− 0.043, 0.082]	2.3 [0.69]	−0.005 [− 0.040, 0.030]	0.6 [0.38]
Executive function	0.005 [− 0.131, 0.085]	1.8 [0.64]	0.010 [− 0.085, 0.064]	2.3 [0.70]
Language processing	0.027 [− 0.065, 0.127]	2.9 [0.74]	0.071 [0.027, 0.181]	> 1000 [1.00]

[a] Simulation-based calibration indicates that δ_1's marginal uncertainty is under-stated where the transition point is weakly identified (Supplementary Note 5); this affects the precision, not the direction, of the language processing post-transition contrast.

[b] Evidence ratios above 1000 are shown as "> 1000": in that range the ratio is determined by fewer than approximately 20 of 20,000 posterior draws and is not stable to Monte Carlo error (Supplementary Note 5). Such contrasts should be interpreted by their posterior interval.

Discussion

In this study we have prospectively examined the trajectory of cognitive changes across 4 cognitive domains over 10 years in adults 50–79 years of age who either completed at least 12 months of university-based education or did not undertake further education. Prior research examining factor-analytic derived cognitive domains spanning memory, information processing speed, reasoning, and spatial processing displayed non-linear decline in performance with age[19]. Hence, the normal aging process is associated with a non-clinical curvilinear decline in cognitive performance, whereas the

presence of neurodegenerative disease processes such as dementia represent a clinically significant acceleration of cognitive decline[20]. Previously, we identified a cognitive benefit for up to 3 years duration in older adults who attended university for at least 12 months[15]. In the present study, we examined the persistence of this earlier observed cognitive benefit over a decade. The results indicate that the benefit conferred by university level education in older adults is cognitive modality specific. Attending university for at least 12 months resulted in a short-term improvement in language processing, spanning vocabulary and comprehension. However, of greatest importance, the results indicate that following this short-term improvement there was no evidence of age-related decline in language processing capacity over the remainder of the decade in the university-education group, whereas the control group displayed a decline in language processing over the same period. A similar result was identified for episodic memory, with the university-education intervention group displaying an increase and stabilization of capacity over the ensuing decade. In contrast, the control group displayed evidence of decline in episodic memory over the ensuing decade consistent with evidence of age-related cognitive decline observed in other studies[19]. Of interest here is that the university-level education group did not display an improvement to working memory capacity, nor to general executive function, with only trivial differences observed between the intervention and comparison group over time.

The four cognitive domains examined in this study were derived from factor analysis of multiple standardized neuropsychological tests. The language processing domain is comprised of measures of vocabulary, comprehension and object naming and likely reflects a measure of underlying crystallized knowledge[15,21]. In contrast, the domains of episodic memory, executive function and working memory reflect underlying fluid cognitive processes[15,21]. Crystallized cognitive functions reflect accumulated knowledge whereas fluid cognitive functions reflect underlying skills and capacity to perform skills (e.g. working memory, processing speed, attention, etc). The results of the present study indicate that university education in older adults acts most strikingly as a booster for crystallized knowledge, creating a level of cognitive capacity that appears to resist age-related decline. This finding is consistent with the notion of “use or lose it”, whereby knowledge can be lost through a lack of reactivation by use.

In contrast, the results indicate that university-education in later life did not alter the trajectory of age-related decline in the fluid domains of working memory capacity and general executive function, but appears to have conferred some improvement and potential resistance to age related decline to episodic memory capacity. These differential effects may reflect the nature of formal education, and the underlying cognitive skills utilized when formal education is undertaken. Hence, the nature of university education and assessment requires the individual to learn and recall new semantic information. Increasing evidence suggests that formation and retrieval of semantic and episodic memories are interdependent[22]. This suggests the possibility that university-education requiring the formation and retrieval of semantic memory may also benefit episodic information processing and retrieval, which resulted in sustained improvement in episodic memory in older adults attending university.

The THBP commenced in 2011, with participants engaging in at least 12 months of university-level education[14]. The education programs undertaken occurred before the COVID pandemic which affected Australian universities from 2020 resulting in transition from predominantly on-campus classes to online classes. On-campus university education involves a range of social and interpersonal activities in addition to the academic activities of learning. To attribute any cognitive changes seen in the THBP solely to mental activity from education-based learning would be misleading, as social engagement is known to be associated with improved cognitive function in older adults[23]. Arguably, the intervention provided by university-education provides enrichment of mental activity through learning and academic skill development as well as through social, emotional and interpersonal activity. The cognitive benefits to the individual observed in the THBP are likely the result of different combinations of effects from these elements.

A recent matched analysis of self-reported continuing education in the English Longitudinal Study of Ageing (ELSA), using a piecewise before-and-after design on a comparable time scale, found no evidence of improvement in memory or verbal fluency trajectories[24]. That result and the present one are not directly comparable because the exposures are not the same construct: the ELSA measure is a self-reported item on attendance at a formal education or training course in the preceding 12 months, whereas the exposure here is completed enrolment in accredited, assessed university units amounting to at least one FTE year – a nominal workload of some 1200–1500 hours, and in many cases considerably more. Whether the difference in findings is attributable to dose, to the outcome domains assessed (language processing has no close counterpart in ELSA), or to residual selection in non-randomized cohorts cannot be settled here.

It is important to recognize that the THBP is not a randomized control trial. Participants elected on entry to undertake either the education or the no-education arms on entry into the study[14], and group membership for analysis was confirmed by an audit of enrolments. The analysis is therefore per-protocol rather than intention-to-treat, conditioning on a variable realized after baseline. Due to ethical constraints, it was not possible to randomly allocate participants to university education as an intervention condition. Further, existing university admission requirements made conditions of dose or level of dose of university-level education impractical to apply. Therefore, as the THBP is not a randomized control trial, there is a risk that the study protocol may have introduced bias in groups in the THBP. That is university admission requirements, or a difference in desire to undertake university-level education, may have biased the self-selection of participants into either group. Despite these pre-conditions to participation in the THBP, the estimated full-scale IQ of each group were very similar, with a baseline mean FSIQ of 113 in the education-group and 112 in the comparison group. Both groups also displayed similar levels of prior education completed, with the education group completing a mean of 14.2 years and the comparison group completing 13.9 years of prior education. This suggests that despite the self-selection of participants into the two conditions, there is no evidence of a selection bias on the basis of underlying intellectual capacity or prior level of formal education. Furthermore, using statistical methods, we carefully controlled for previous education, full-scale IQ, age, gender, scores on the Dementia Rating

Scale (DRS) and also anxiety and depression on the Hospital Anxiety and Depression scale (detailed in Methods and Supplementary Table 2), addressing some of the potential biases in capacity to undertake university study which may otherwise affect results.

On the episodic memory and language processing domains there was clear evidence of distinct growth and decline phases, read from the posterior of the estimated change in slope. Evidence of non-linearity in cognitive trajectories is well supported in the literature[19,25,26], however in our study it is important to recognize that group comparisons were made on the linear coefficients that estimated the slopes of the growth and decline phases, and the location of the smoothed change-points. Assuming confounding was appropriately accounted for (accepting that this will always be up for debate), any observed difference in slopes must be assumed to reflect a difference in exposures to university education, since both groups had approximately equal practice at test taking, completing a mean of 5.84 and 5.87 assessments in control and education groups respectively. On episodic memory and language processing domains, the observed difference in slopes both in growth and decline phases is consistent with the notion that cognitive reserve can be built and maintained throughout the lifespan[27].

The location of the transition itself is of interest. In episodic memory it was estimated at 2.85 years after baseline, insensitive to the choice of prior. From an unrelated design using between-person variation in retest interval, Salthouse predicted that change in word recall would reach zero at 2.5 years[28]; the two analyses concern different estimands so the agreement is read as independent convergence rather than a replication. The practical implication is general, a longitudinal study of cognitive aging in healthy older adults which observes its cohort for less than approximately three annual assessments is likely measuring the net practice and aging over an interval in which practice predominates. This may account for the observation that estimates of cognitive change obtained from fewer than four waves, or fewer than eight years of follow-up, differ systematically from those obtained from full follow-up[29]. Practice effects persist well beyond the first follow-up,[30,31] so the transition is a crossover of the net trajectory.

A question that arises upon any critical review of the cognitive reserve literature is the extent to which the observed benefits of reserve-building can be attributed to assets such as education or job complexity, to cognition in later-life and resilience to brain pathology, when these assets are heavily confounded by genetics, intelligence, better access to healthcare, occupations with fewer health risks and so on[32–34]. It bears repeating that these cognitive benefits are observed after the fact and the field has limited evidence from studies with an intervention and control group, and all of these are either multi-domain or employ “brain training” exercises rather than higher education.[35,36] In this study we have presented prospective evidence, from a verified and sustained educational exposure followed over a decade, that education may independently leave an enduring mark on cognitive function. These benefits were observed over a duration with meaningful consequences in terms of cognitive function in the later years of life. Confronted with an ageing population, increased workforce pressures in providing adequate care for and protection of elder members of society, there is a need for evidence-based approaches to

improving and maintaining cognitive health. It may be that education at any stage of life plays an important role in preserving cognitive function into the later years.

Methods

Participants and study design

The Tasmanian Healthy Brain Project is a prospective longitudinal cohort study established to examine whether university-level education undertaken in later life alters the trajectory of age-related cognitive change; the protocol is described in full elsewhere[14]. Of 562 participants who completed baseline assessment, the 416 who completed at least four assessments are analyzed here (89 comparison, 327 education), contributing four to seven assessments each over up to 11 years, with a median follow-up of 7 years (range 2–11). Baseline characteristics are given in Table 1. All participants were cognitively healthy at entry and residents of Tasmania, therefore eligible for a Commonwealth Supported Place at the University of Tasmania in the course of study of their choosing (subject to entry requirements). Group membership was defined at entry by intention, and for this analysis enrolment records were audited: participants who completed at least one year of full-time-equivalent study load were retained in the education group, and participants in the control group were confirmed not to have undertaken further study. Study was undertaken in accredited, assessed units of the participant's own choosing at undergraduate level. One year of full-time-equivalent study at the host institution corresponds to a nominal student workload of approximately 1200 hours, comprising scheduled contact and directed independent study. A scholarship was available to off-set student co-contributions, this amounted to a fee-waiver for one unit per academic year.

Time (quantized to years) was measured as elapsed time at assessment per participant since baseline. The estimated transition point is therefore interpretable as a transition time.

The THBP was approved by the University of Tasmania Human Research Ethics Committee (H11070) in accordance with the National Health and Medical Research Council of Australia ethical code. Written informed consent was obtained from all participants and reconfirmed at each assessment point.

Cognitive composites

Composite domain scores were fixed-weight linear combinations of z-scored sub-tests: episodic memory from immediate and delayed logical memory, RAVLT total across trials 1–5, and CANTAB paired-associate learning; working memory from letter–number sequencing, digit span, spatial span length and CANTAB spatial working memory between-search errors; executive function from Stroop colour-word time, Trail Making Test B time and CANTAB rapid visual information processing A; and language processing from the Boston Naming Test, WAIS comprehension and WAIS vocabulary. Weights were fixed a priori from the published cross-sectional factor solution in this cohort[15,16]. The executive

function composite was sign-reversed after construction for consistency across the four domains, higher values indicating better performance.

Missing data

A participant-wave was excluded from a domain's analysis if it lacked a valid composite score, which occurs whenever any constituent sub-test is missing for that wave. This is an available-case analysis; exclusions ranged from 0.5% to 2.4% of participant-waves by domain (Supplementary Table 1). Attrition is characterized in the online content.

Statistical model

For each domain we fitted a smooth piecewise regression, an adaptation of the Bacon–Watts model[17], in which the rate of change may shift at an estimated transition point ω:

$\mu = \beta_0 + \beta_1 d + \delta_1 \cdot d \cdot s(d; \rho)$, where $d = t - \omega$ and $s(d; \rho) = [1 + e^{-d\rho}]^{-1}$

Here t is time in years since baseline and s is a logistic smoothing function, used in place of a sharp change-point, which is both intuitively and computationally unappealing. Participant-level random intercepts $u \sim N(0, \sigma^2_u)$ account for between-subject variation. Away from the transition the mean is asymptotically linear, so β_1 is the pre-transition rate of change and $\beta_1 + \delta_1$ the post-transition rate; for consistency with the broader literature we refer to ω as the transition point, being the mid-point of a smooth transition. We estimated group effects on the intercept β_0, the pre-transition slope β_1 and the slope change δ_1, with age (standardized), sex, years of prior education (standardized), baseline HADS anxiety and depression, and baseline cognition (WTAR, DRS) entered on β_0. Residuals and random effects were assumed to be normally distributed.

The transition point was specified as common to both groups. Models allowing it to vary by group were fitted as a robustness check: the group term was adequately identified in episodic memory, working memory and language processing ($\hat{R} \leq 1.01$, bulk effective sample size > 500) but not in executive function ($\hat{R}$ = 1.03–1.04, bulk effective sample size 152–213), and its posterior was centered close to zero on every domain. We therefore report a common transition point per domain as the primary specification.

The sharpness parameter ρ was fixed at 3, chosen to correspond to a transition running from 10% to 90% complete over ~ 1.5 years, approximately one inter-assessment interval. An earlier specification estimated ρ under a weakly informative prior; its posterior reproduced the prior in three of four domains while substantially degrading sampling geometry. Conclusions are unchanged across fixed $\rho \in \{2, 3, 5\}$ (Supplementary Table 5).

Priors

Parameter	Prior	Rationale
β_0 and covariates	N(0, 2)	Weakly informative on the z-scored composite scale
β_1 (pre-transition slope)	N(0, 2)	Freely estimated; the linear model is the nested null
δ_1 (slope change)	N(0, 1)	Conservative weakly informative width; its posterior answers the transition question
ω (transition point)	N(3, 2), bounded [1, 6]	Practice effects plateau 2–5 years post-baseline; sensitivity to the bounds in Supplementary Table 8
ρ (sharpness)	Fixed at 3	Transition completes over approximately one inter-assessment interval; see above
σ (residual SD)	InvGamma(2, 1)	Weakly informative
σ_u (random-intercept SD)	InvGamma(2, 1)	Matches σ; set explicitly rather than left at the software default of InvGamma(1, 1), whose prior mean is infinite

The bounds on ω were carefully considered. The upper bound disallows models estimating a growth phase beyond 6 years, since by the principle of parsimony one might select a linear model anyway; the lower bound prevents the transition being placed before observation begins.

Inference

Inference on reported effects is derived from the joint posterior of a single univariate model per domain. The existence of a piecewise transition is taken from the posterior of δ_1: a credible interval excluding zero was interpreted as evidence of a change in rate.

Two group contrasts were specified before fitting and are summarized as directional posterior probabilities P(H | data) and the corresponding evidence ratios, ER = P(H) / (1 − P(H)):

- a group effect on β_1, i.e. a steeper pre-transition slope in the education group; and
- a group effect on $\beta_1 + \delta_1$, i.e. a steeper decline after the transition.

Each is a linear combination of posterior draws. As posterior-odds quantities these are insensitive to the width of weakly informative priors, unlike marginal-likelihood Bayes factors. Coefficients are reported with 95% credible intervals and are not corrected for multiple comparisons.

Selection into groups and adjustment for confounding

To address selection bias caused by self-selection into education and control groups, we considered two established approaches: direct adjustment for confounding, and inverse probability weighting (IPW) using propensity scores (PS). IPW attempts to construct a “pseudo-population” by weighting observations to adjust for selection bias. While this approach is readily interpretable in the frequentist tradition, the posterior distribution drawn from a Bayesian analysis does not have a Bayesian interpretation if the weights used are not drawn from the posterior distribution of a group selection-bias

model. While methods exist to facilitate a truly Bayesian analysis using IPW[37], the computational cost is heavy, and IPW has other disadvantages compared to direct adjustment for confounding[38]. We therefore adjusted directly for confounding, entering all measured baseline covariates on the intercept.

We computed a Bayesian logistic regression of group membership on seven baseline variables to characterize selection into the education group (Supplementary Note 2). Age and baseline depressive symptoms showed the clearest group differences (evidence ratios 1332 and 92); the remaining five covariates showed comparatively little (evidence ratios 1.4 to 3.5). All seven were retained as pre-specified confounders in the trajectory models irrespective of the strength of their association. The model explains only approximately 7% of the variance in group membership, so most of what distinguishes the two groups is not captured by measured baseline variables, motivating the sensitivity analyses reported in Supplementary Note 8.

Allocation to the education group was by self-selection, so we avoid any causal claims. Sustained voluntary university study cannot be compelled, comparison participants cannot be prevented from studying, and randomizing the offer of enrolment would estimate the effect of encouragement - mediated by self-efficacy, financial capacity and prior ability - rather than of education itself. The appropriate comparison is therefore not against a hypothetical trial but against other observational evidence, where this study's single-modality intervention, decade-long follow-up and effortful exposure are unusual.

A second and distinct limitation follows from the classification rule. Because group membership is confirmed by study completed, the contrast conditions on a variable realized after baseline, this is a per-protocol analysis, not an intention-to-treat comparison. The concern this raises is the reverse-causality objection made of this literature more broadly, operating through completion rather than through enrolment: a participant whose cognition was declining might for that reason have failed to complete a full-time-equivalent year, in which case the classification sorts participants partly by cognitive trajectory and not only by education received.

Software, computation and validation

All models were fitted with smoothbp v0.2.8[39], which implements a Metropolis-within-Gibbs sampler in Rust, combining conjugate updates for linear terms with Hamiltonian Monte Carlo for the non-linear location and sharpness parameters. Each model was run as 4 chains of 10,000 iterations, of which 5,000 were warmup, with target acceptance 0.99, giving 20,000 posterior draws. The Bayesian logistic regression of group membership was fitted with the brms package[40] in R[41] using Stan[42]. Convergence diagnostics for every fit are reported in Supplementary Note 4.

The exact model configuration reported here — all priors as specified, ρ fixed at 3, σ_u as specified — was assessed by simulation-based calibration[43,44] over 500 replicates, using a bootstrapped design matrix drawn from the real covariate data so that covariate collinearity and the group imbalance are realistic. Marginal rank calibration for δ_1 did not fully pass; the mechanism was localized to the

conjugate update of δ_1 conditional on a single draw of ω, and per-replicate uncertainty in ω predicted δ_1's calibration error in two independent simulation runs, while β_1, whose design lacks the coupling, showed no such relationship. The residual limitation therefore bears on the precision of contrasts in domains where ω is weakly identified, and least on episodic memory, where it is sharply identified.

Declarations

Acknowledgements

We would like to thank Dr Nichole Saunders, Dr David Ward, Dr Megan Thow, Dr Shannon Klekociuk, Dr Kimberley Stuart, Dr Hannah Fair, Dr Katherine Franks, Dr Gongbu Pan, and Dr Edward Roccati for their contributions to data collection and work on the THBP.

Funding

The Tasmanian Healthy Brain Project was funded by National Health and Medical Research Council (NHMRC) Project grants (1003645 and 1108794) as well as the JO & JR Wicking Trust (Equity Trustees).

Author Contributions

MJS: Writing, study design, data curation, editing; ADB: Writing, formal analysis, editing; JCV: Study design, reviewing, editing

Use of AI disclosure

Anthropic Claude models (Opus 5.0 and 5.5) were used to assist in the preparation and editing of Supplementary Materials, and to review Methods for accuracy and omissions.

References

1. Stern, Y. Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol.* **11**, 1006–1012 (2012).
2. Stern, Y. Cognitive reserve. *Neuropsychologia* **47**, 2015–2028 (2009).
3. Bindoff, A. D., Summers, M. J., Hill, E., Alty, J. & Vickers, J. C. Studying at university in later life slows cognitive decline: A long-term prospective study. *Alzheimers Dement. Transl. Res. Clin. Interv.* **7**, e12207 (2021).
4. Glymour, M. M. & Manly, J. J. Lifecourse Social Conditions and Racial and Ethnic Patterns of Cognitive Aging. *Neuropsychol. Rev.* **18**, 223–254 (2008).
5. Cutler, D. M., Lleras-Muney, A. & Vogl, T. Socioeconomic Status and Health: Dimensions and Mechanisms. Working Paper at https://doi.org/10.3386/w14333 (2008).
6. Foubert-Samier, A. *et al.* Education, occupation, leisure activities, and brain reserve: a population-based study. *Neurobiol. Aging* **33**, 423.e15-423.e25 (2012).

7. Mortimer, J. A., Snowdon, D. A. & Markesbery, W. R. Head circumference, education and risk of dementia: Findings from the Nun study. *J. Clin. Exp. Neuropsychol.* **25**, 671–679 (2003).
8. Bennett, D. A. *et al.* Education modifies the relation of AD pathology to level of cognitive function in older persons. *Neurology* **60**, 1909–1915 (2003).
9. Brayne, C. *et al.* Education, the brain and dementia: neuroprotection or compensation? *Brain* **133**, 2210–2216 (2010).
10. Bratsberg, B., Fjell, A. M., Rogeberg, O. J., Skirbekk, V. F. & Walhovd, K. B. Differences in cognitive function at 18 y of age explain the association between low education and early dementia risk. *Proc. Natl. Acad. Sci.* **121**, e2412017121 (2024).
11. Anderson, E. L. *et al.* Education, intelligence and Alzheimer's disease: evidence from a multivariable two-sample Mendelian randomization study. *Int. J. Epidemiol.* **49**, 1163–1172 (2020).
12. Fjell, A. M. *et al.* Reevaluating the role of education on cognitive decline and brain aging in longitudinal cohorts across 33 Western countries. *Nat. Med.* **31**, 2967–2976 (2025).
13. Lövdén, M., Fratiglioni, L., Glymour, M. M., Lindenberger, U. & Tucker-Drob, E. M. Education and Cognitive Functioning Across the Life Span. *Psychol. Sci. Public Interest* **21**, 6–41 (2020).
14. Summers, M. J. *et al.* The Tasmanian Healthy Brain Project (THBP): A prospective longitudinal examination of the effect of university level education in older adults in preventing age-related cognitive decline and reducing risk of dementia. *Int. Psychogeriatr.* **25**, 1145–1155 (2013).
15. Thow, M. E. *et al.* Further education improves cognitive reserve and triggers improvement in selective cognitive functions in older adults: The Tasmanian Healthy Brain Project. *Alzheimers Dement. Diagn. Assess. Dis. Monit.* **10**, 22–30 (2018).
16. Ward, D. D. *et al.* APOE and BDNF Val66Met polymorphisms combine to influence episodic memory function in older adults. *Behav. Brain Res.* **271**, 309–315 (2014).
17. Bacon, D. W. & Watts, D. G. Estimating the Transition between Two Intersecting Straight Lines. *Biometrika* **58**, 525–534 (1971).
18. Karr, J. E., Graham, R. B., Hofer, S. M. & Muniz-Terrera, G. When does cognitive decline begin? A systematic review of change point studies on accelerated decline in cognitive and neurological outcomes preceding mild cognitive impairment, dementia, and death. *Psychol. Aging* **33**, 195–218 (2018).
19. Salthouse, T. A. Shared and unique influences on age-related cognitive change. *Neuropsychology* **31**, 11–19 (2017).
20. Sperling, R. A. *et al.* Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement. J. Alzheimers Assoc.* **7**, 280–292 (2011).
21. Hartshorne, J. K. & Germine, L. T. When does cognitive functioning peak? The asynchronous rise and fall of different cognitive abilities across the life span. *Psychol. Sci.* **26**, 433–443 (2015).

22. Greenberg, D. L. & Verfaellie, M. Interdependence of episodic and semantic memory: Evidence from neuropsychology. *J. Int. Neuropsychol. Soc.* **16**, 748–753 (2010).
23. Krueger, K. R. *et al.* Social engagement and cognitive function in old age. *Exp. Aging Res.* **35**, 45–60 (2009).
24. Bloomberg, M., Sabia, S., Bu, F., Gong, J. & Steptoe, A. Cognitive decline before and after mid-to-late-life continuing education in England: a matched longitudinal analysis of a prospective cohort study. *Lancet Reg. Health - Eur.* **60**, 101513 (2026).
25. Verhaeghen, P. & Salthouse, T. A. Meta-Analyses of Age-Cognition Relations in Adulthood: Estimates of Linear and Nonlinear Age Effects and Structural Models. *Psychol. Bull. 122, 231–249* (1997).
26. Swagerman, S. C. *et al.* The Computerized Neurocognitive Battery: Validation, aging effects, and heritability across cognitive domains. *Neuropsychology* **30**, 53–64 (2016).
27. Stern, Y. *et al.* A framework for concepts of reserve and resilience in aging. *Neurobiol. Aging* **124**, 100–103 (2023).
28. Salthouse, T. A. When does age-related cognitive decline begin? *Neurobiol. Aging* **30**, 507–514 (2009).
29. Thoma, M. C. *et al.* Are we there yet? Estimating the waves of follow-up required for stable effect estimates in cognitive aging research. *Am. J. Epidemiol.* **195**, 758–767 (2026).
30. Elman, J. A. *et al.* Practice effects persist over two decades of cognitive testing: Implications for longitudinal research. *medRxiv* 2025.06.16.25329587 (2025) doi:10.1101/2025.06.16.25329587.
31. Sanderson-Cimino, M. *et al.* Misinterpreting cognitive change over multiple timepoints: When practice effects meet age-related decline. *Neuropsychology* **37**, 568–581 (2023).
32. Boyle, R. *et al.* Verbal intelligence is a more robust cross-sectional measure of cognitive reserve than level of education in healthy older adults. *Alzheimers Res. Ther.* **13**, 128 (2021).
33. Le Carret, N. *et al.* The Effect of Education on Cognitive Performances and Its Implication for the Constitution of the Cognitive Reserve. *Dev. Neuropsychol.* **23**, 317–337 (2003).
34. Schmand, B., Smit, J. H., Geerlings, M. I. & Lindeboom, J. The effects of intelligence and education on the development of dementia. A test of the brain reserve hypothesis. *Psychol. Med.* **27**, 1337–1344 (1997).
35. Rosenberg, A., Mangialasche, F., Ngandu, T., Solomon, A. & Kivipelto, M. Multidomain Interventions to Prevent Cognitive Impairment, Alzheimer's Disease, and Dementia: From FINGER to World-Wide FINGERS. *J. Prev. Alzheimers Dis.* **7**, 29–36 (2020).
36. Simons, D. J. *et al.* Do "Brain-Training" Programs Work? *Psychol. Sci. Public Interest* **17**, 103–186 (2016).
37. Lin, J. & Lin, J. Incorporating propensity scores for evidence synthesis under bayesian framework: review and recommendations for clinical studies. *J. Biopharm. Stat.* **32**, 53–74 (2022).
38. Wang, J. To use or not to use propensity score matching? *Pharm. Stat.* **20**, 15–24 (2021).

39. Bindoff, A. D. smoothbp: Fast Bayesian Hierarchical Piecewise Regression with Smoothed Transitions and Spike-and-Slab Model Selection. Preprint at https://doi.org/10.48550/arXiv.2606.19044 (2026).
40. Bürkner, P.-C. **brms**: An *R* Package for Bayesian Multilevel Models Using *Stan*. *J. Stat. Softw.* **80**, (2017).
41. R Core Team. R: a language and environment for statistical computing and graphics. R Foundation for Statistical Computing, Vienna, Austria (2024).
42. Carpenter, B. *et al.* Stan: A probabilistic programming language. *J. Stat. Softw.* **76**, 1–32 (2017).
43. Talts, S., Betancourt, M., Simpson, D., Vehtari, A. & Gelman, A. Validating Bayesian Inference Algorithms with Simulation-Based Calibration. Preprint at https://doi.org/10.48550/arXiv.1804.06788 (2020).
44. Modrák, M. *et al.* Simulation-Based Calibration Checking for Bayesian Computation: The Choice of Test Quantities Shapes Sensitivity. *Bayesian Anal.* **20**, 461–488 (2025).

Figures

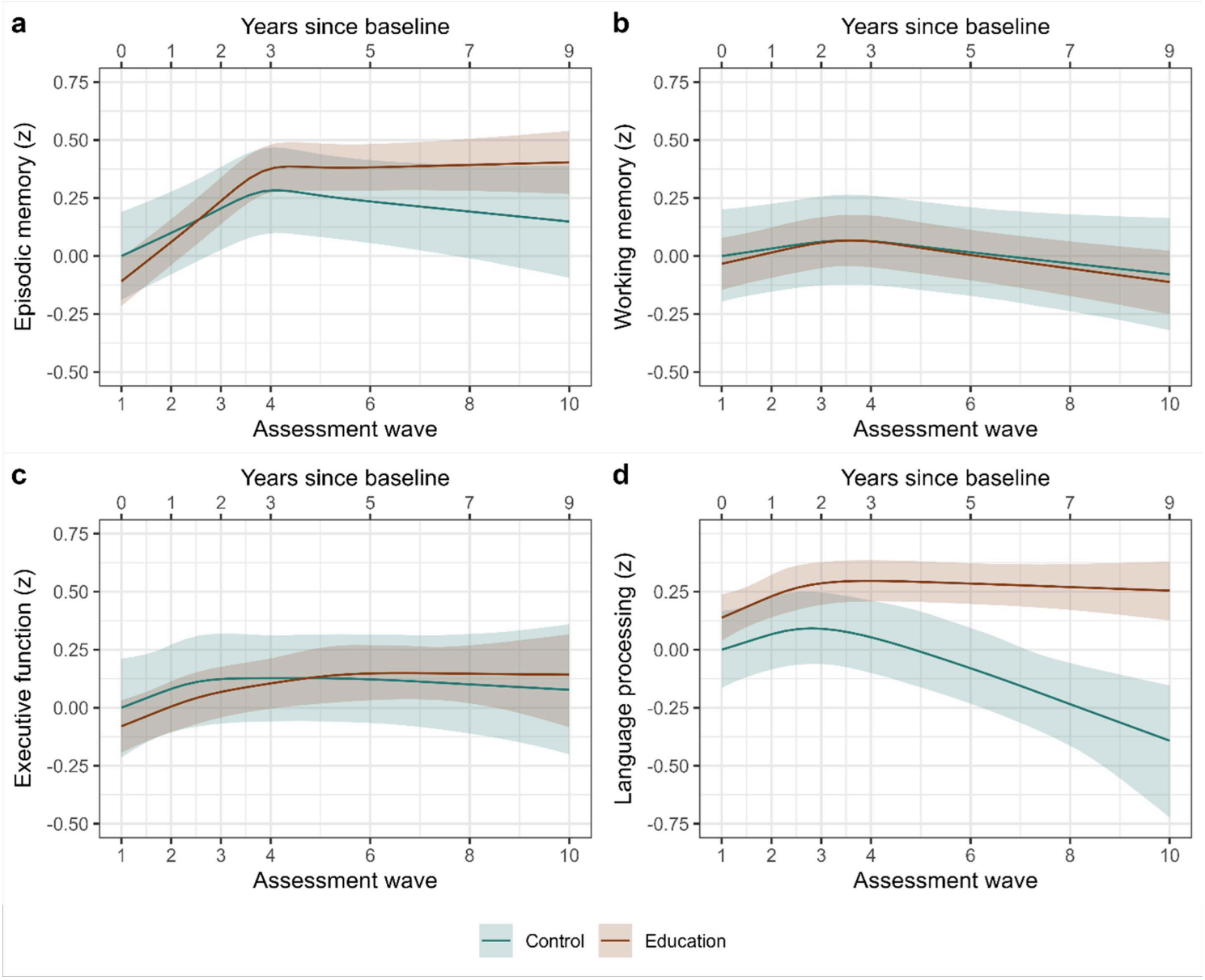


Figure 1

Estimated piecewise regression curves for scores on each cognitive domain: a, episodic memory; b, working memory; c, executive function; d, language processing. Shaded areas represent 95% credible intervals. Predictions have been off-set so that control group scores are zero at baseline. Y-axis ranges have been scaled alike so that standardized effect sizes are visually comparable between panels a–c; panel d is on its own scale. Covariates are held at population means (female, mean age, prior education, mood and baseline cognition). The lower axis gives the nominal assessment wave and the upper axis the corresponding years since baseline, the scale on which the transition point is estimated. Predictions are shown over 0–9 years, the common support of both groups; comparison group follow-up extends to 11 years but is not extrapolated here for the education group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementary.pdf