Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Psychology

Review

Cognitive aging and the life course: A new look at the Scaffolding theory

Patricia A. Reuter-Lorenz[1] and Denise C. Park[2]

Abstract

Our understanding of human neurocognitive aging, its developmental roots, and life course influences has been transformed by brain imaging technologies, increasing availability of longitudinal data sets, and analytic advances. The *Scaffolding Theory of Aging and Cognition* is a life course model, proposed originally in 2009, featuring adaptivity and compensatory potential as lifelong mechanisms for meeting neurocognitive challenges posed by the environment and by developing or declining brain circuitry. Here, we review the scaffolding theory in relation to new evidence addressing when during the life course potentially enriching and depleting factors exert their effects on brain health and scaffolding, and we consider the implications for separable, and potentially reciprocal, influences on the level of cognitive function and the rate of decline in later life.

Addresses

[1] University of Michigan, Ann Arbor, MI, USA
[2] University of Texas, Dallas, TX, USA

Corresponding author: Reuter-Lorenz, Patricia A (parl@umich.edu)

Current Opinion in Psychology 2024, **56**:101781

This review comes from a themed issue on Late Adulthood 2024

Edited by Alexandra M Freund and Jonathan Rolison

For a complete overview see the Issue and the Editorial

Available online 14 December 2023

https://doi.org/10.1016/j.copsyc.2023.101781

Keywords

Compensation, Neuroplasticity, Brain aging, Resilience, Cognitive intervention.

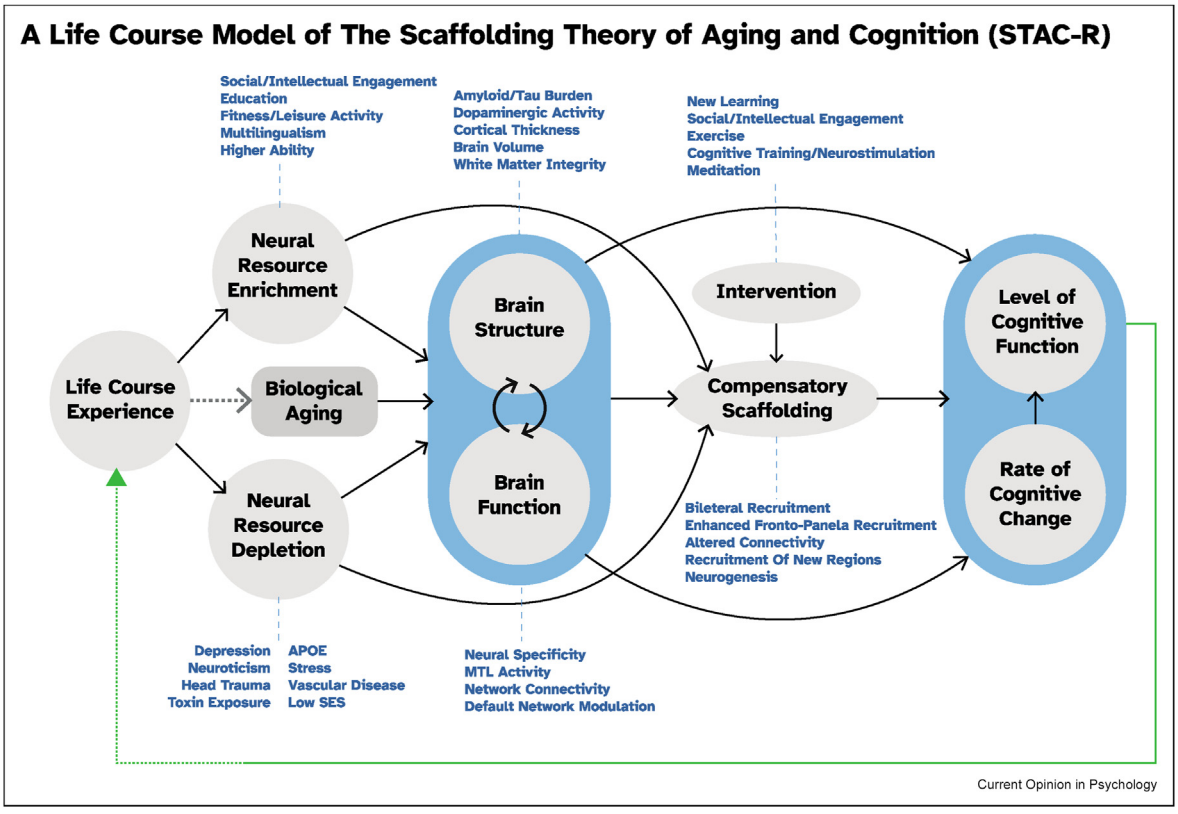
Introduction

In many respects, all aging people are alike: compared to one's younger self, the body becomes less able, the senses less acute, and the mind less sharp. And yet, every person ages in their own way. Beyond one's inherited endowment and family of origin, a life time of behaviors, experiences, and exposures chart the course of aging through the elder years. The Scaffolding Theory of Aging and Cognition (STAC; [1]), and its longitudinal life-course sibling, STAC-r ([2]; collectively STAC-R), were an early effort to integrate the general behavioral findings on aging with emergent evidence in cognitive neuroscience. This brief review takes stock of some new developments relevant to key facets of STAC-R, reassesses these and other features of the model, and considers future directions in the cognitive neuroscience of aging informed by STAC-R.

According to STAC-R, scaffolding is the forging of new neural pathways or circuitry that relies on the brain's inherent neuroplasticity in the face of cognitive challenge across the entire lifespan. Evidence suggests that the cognitive challenges of mastering the complex world faced in early development are particularly instrumental [3,4]. In addition, the challenges met by scaffolding may be posed by new skill acquisition [5] or by the challenges of maintaining fulfilling and effective levels of cognitive, behavioral, and socio-emotional functioning in the face of neurobiological declines that accompany increasing chronological age. STAC-R emphasizes the dynamic adaptability of the brain to engage supplementary neural circuitry to support developing or declining core task networks.

A key innovation of STAC-R [2] is its specification of two broad categories of life-course experience, referred to as neural resource 'enriching' and 'depleting' factors, that impact brain structure, brain function (collectively *brain health*), and the capacity for compensatory scaffolding, which in turn affect the model's outcome variables—the level of cognitive ability and rate of cognitive change (see Figure 1). Coupled with "biological aging", these features determine individual trajectories of aging and their potential for mutability. To date, scaffolding theory has broadly influenced the cognitive neuroscience of healthy aging; a recent bibliometric analysis based on the Web of Science [6] identified it as the most frequently cited, impactful, and potentially transformative work in healthy cognitive aging over the past twenty years. Informing large-scale predictions and new theories about the aging brain (e.g. Refs. [7–10]), with impact as far reaching as microgravity environments in outer-space [11], the influential status of STAC-R has been attributed to its multifaceted framework [12] and its unique emphasis on the notion of adaptivity [6]—the brain's lifelong capacity to adapt to its own development and aging [13].

Figure 1



This figure depicts the life course framework of the Scaffolding Theory of Aging and Cognition (STAC-R; Reuter-Lorenz & Park, 2014). Through life course experience, variables that enrich or deplete neural resources influence brain structure, brain function, and scaffolding, which is the brain's adaptive and neuroplastic response to cognitive challenge (see text for more details). These jointly influence the level of cognitive function and rate of cognitive change. Some examples are listed for neural resource enrichment and depletion factors, age-related indices of brain structure, brain function, and scaffolding, as well as types of interventions that can affect scaffolding. These lists are not exhaustive and will warrant continual updating as new empirical evidence emerges. STAC-R recognizes that different enrichment and depletion factors may operate independently, additively, or have interactive effects. Moreover, they are likely to exert their effects via different mechanistic pathways (e.g. inflammation, systemic biological processes, and/or processes within the central nervous system) and at different stages of the life course (genetic, prenatal, early to late childhood/adolescence, early, middle, late adulthood). Brain structure and function are jointly referred to in the text as 'brain health', which can also be characterized by level of brain resources and rate of neural change. The figure includes two noteworthy updates from Reuter-Lorenz and Park (2014). First, the influence of life course experience on biological aging is now depicted in the model, whereas this was assumed in the earlier account. Second, the likelihood that level of cognitive ability plays a causal role in life course experience (and thus, the type and magnitude of enrichment and depletion factors) is depicted by the dotted feedback arrow (see text for more details; illustration credit Stephen Alvey).

While predating recent consensus treatments of "risk and resilience" (Stern et al., 2023 [14]), maintenance and reserve [15,16], the STAC-R model offers a dynamic framework characterizing lifelong influences on the preservation (i.e. maintenance; [15]), enhancement, and decline of brain health, and compensatory scaffolding (see the publication by Oosterhuis et al. [12] for a comparison of STAC-R and cognitive reserve). The term *brain reserve* is also used to characterize individual differences potentially present from birth [17], which may set an upper boundary on the level and quality of brain resources (e.g. brain volume, cortical area/thickness, connectivity etc.) available to an individual. *Brain endowment* might constitute a more fitting term for the brain resources one is born with, because "reserve" connotes something unused unless needed. According to STAC-R, the extent to which brain resources are augmented, maintained, diminished, and engaged adaptively is influenced by life course factors, and are thus intricately related to brain health and biological aging.

The life course model

The ultimate goal of STAC-R is to predict an individual's level of cognition along with trajectories of cognitive change over time. We revisit several of STAC-R's core assumptions about aging cognition by considering recent studies that address enriching and depleting effects on level of cognition and rate of change, the time course and dynamics of influence,

specificity of cognitive impact, as well as influences on neural resources, brain maintenance, and scaffolding.

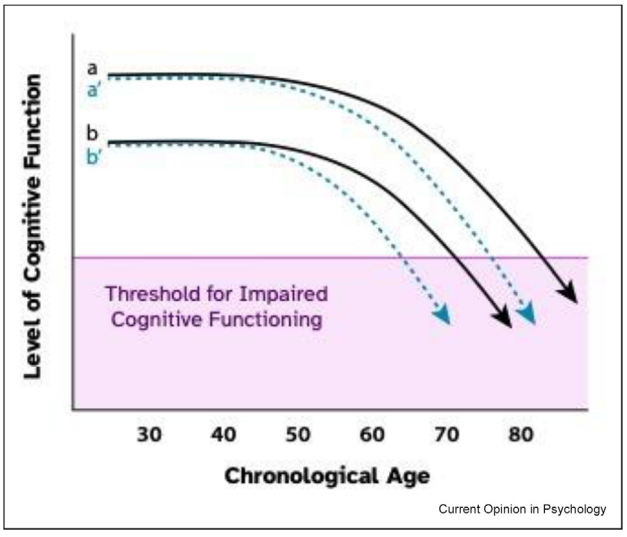
Level of cognition, rate of cognitive change, or both?

Figure 1 depicts "level of cognition" and "rate of cognitive change" as independent components of the STAC-R model. Recent evidence indicates that some enriching and depleting variables may influence these outcomes differentially. For example, consider education, a variable that figures prominently in early development, and in theories of adulthood such as STAC-R and cognitive reserve [18]. Whether measured by years in school or degree attained, education has a well-established positive relationship with level of cognitive ability: more education is associated with better cognitive performance throughout life (i.e., between-person differences), including in older age (see e.g. the publication by Lövdén et al. [19]). Indeed, there is even evidence that a higher *quality* high school education is associated with better cognition 58 years later [20]. Thus, the amount and quality of education raise the bar of cognitive performance. Evidence also indicates that cognitive ability can influence educational attainment [19] suggesting the influence is bidirectional, as we discuss further below.

However, is education associated with the *rate* of cognitive decline over time (i.e. within-person change)? Does education confer protection and resilience to the effects of aging? Apparently not, according to multiple studies reporting strong associations between education and the level of cognitive ability in older age, but not the rate of cognitive decline [19,21–24]. Similar effects of childhood education are found for indices of brain aging [25,26]. Likewise, at least one study reports that early childhood socioeconomic status affects general cognitive ability but not rate of decline in later life [27]. These relationships are of considerable consequence because they indicate that some powerful forms of early enrichment affect one's distance above a functional threshold in later years (as depicted in Figure 2), but their influence on the rate of aging is the same over the life course. The functional threshold may be breached at an earlier age with a poor education but the magnitude of the between-person difference is at least partially determined in youth (i.e. "preserved differentiation", [28]).

Indeed, compelling evidence from the Lothian birth cohorts indicates that individual differences in cognition measured at age eleven persist until at least age 80; however, early life ability did *not* predict later-life change (e.g. 29; c.f., 17). Nevertheless, numerous variables (i.e. depleting factors), including sedentary lifestyle, depression, smoking, and alcohol consumption [30], have been shown to affect the rate of later decline.

Figure 2



A graphical illustration of sample cognitive trajectories over the life course from early to late adulthood (after Lövdén et al., 2020, with permission). The figure depicts four hypothetical trajectories, labeled a/a' and b/b. The pairs have different intercepts, representing initial higher and lower levels of cognitive ability, respectively, in early adulthood that likely originates in early childhood or earlier. Throughout adulthood and into older age, the higher initial level of trajectories a/a' manifests as better relative cognitive ability and descent to the dysfunctional threshold at older chronological ages than trajectories b/b'. As others have noted, this illustrates that some aspects of "successful" aging can begin early in life. In early adulthood trajectories, a' and b' have levels of cognition comparable to their a and b counterparts. However, the dashed lines change more rapidly than the solid lines leading to comparably lower levels of cognitive functioning, and ultimately dysfunction at a younger chronological age for a' and b' compared to their respective a and b counterparts. Accordingly, comparing a and a' (or comparing b and b') illustrates trajectories characterized by different rates of change, despite initial equivalent levels of cognitive ability, whereas comparing trajectories a and b (or comparing a' and b') illustrates initial differences in level that are preserved throughout the life course (no differences attributable to differences in rate of change). As reviewed by Lövdén et al. [19], education is one form of enrichment that affects level of cognitive ability but evidently not the rate of cognitive change. Finally, comparing trajectories a and b' (or comparing a' and b) illustrates differences in initial level of cognitive ability as well as differences in cognitive change over the course of adulthood. Some forms of activity engagement have been shown to affect both the level of cognitive ability and rate of cognitive change (e.g. Corley et al., 2018; Frank et al., 2020) (Illustration credit Stephen Alvey).

Moreover, recent evidence indicates that greater gains in cognition (i.e. rate of change in visuospatial ability, memory, processing speed) prior to age 70 predict slower decline after age 70, even controlling for level of cognition in childhood, suggesting early determinants of cognitive *change* may be influential in later life [31], a property potentially related to plasticity and scaffolding. Of importance, STAC-R also captures the independence of cognitive level and rate of decline, which is essential for the model's account of life course influences and their dynamics over time.

Cognitive domain and model dynamics

STAC-R treats cognition as a global construct, and indeed, meta-analytic evidence of longitudinal change indicates sizeable correlations within an individual in the magnitude of decline across different ability domains [32]. Nevertheless, crystalized cognitive abilities, measured by vocabulary and world knowledge, age more slowly than fluid abilities, like memory, speed of processing, spatial reasoning, and executive functions, which may also have different trajectories of decline (e.g. the study by Park et al. [33] and Schaie and Willis [34]). Accordingly, some evidence suggests that enriching and depleting factors can have domain-specific effects (e.g. the study by Zaninotto et al. [30] and Aartsen et al. [35]). For example, Meister and Zahodne [36] examined the effects of social network properties (network size, contact frequency, quality) on memory, executive function, speed, and language. Contact frequency had positive effects across all domains, whereas domain-specific effects were associated with supportive or straining relationships with family or friends. Likewise, fitness interventions are reported to have greatest impact on executive functions, although as noted by Erikson et al., measurement limitations could contribute to this result [37].

STAC-R specifies a unidirectional effect of change rate on cognitive level due to limited evidence for reciprocal influence. However, we should consider the likelihood that cognitive ability influences education as well as individual life-style choices, and thus has consequences for the types and magnitudes of enriching and depleting factors experienced throughout the life course, such that advantages or disadvantages are cumulative (i.e. "differential preservation" ([28,38]). A modification to STAC-R now includes feedback connections from cognitive level to some modifiable factors including education, occupation, and health behaviors (e.g. [19,20,23,29,39,40]).

Time-dependency of enrichment and depleting effects

The temporal dynamics of aging are currently implicit in STAC-R. The framework does not explicitly represent the likelihood that various enriching and depleting factors may have 'sensitive periods' whereby their influence on the brain, and ultimately on cognition, may be greater during some phases of the lifespan than others, or that such periods and the biological locus of their influence may vary depending on the factor in question. For example, evidence indicates that educational benefits to cognitive ability are established early in life [19,21] and persist into later life. Further, the enrichment effects from engaging in a wide variety of childhood lifestyle activities, such as playing an instrument, team sports, vacationing, and volunteering, are associated with greater hippocampal volumes in older at-risk individuals, even when accounting for educational attainment and current lifestyle activities [41].

While the positive and negative long-term impacts of early life experiences (e.g. the study by Gehred et al. [42] and Kucharska-Newton et al. [43]) likely stem from greater neuroplasticity during early development [44], evidence indicates that benefits of enrichment can continue to accrue throughout the life course [45,46]. In particular, participation in enriching activities during one or more phases of the life span, from childhood to early, middle, and late adulthood has been found to influence the level and rate of cognitive decline (e.g. Gow et al. [39]). For example, based on a retrospective life history and current life style questionnaires from the longitudinal Health and Retirement Study, Frank et al. [8] report that high levels of enriching activities during early, mid, and late periods of the life course, independently predicted higher cognitive performance in adults age $\geq$65, while enrichment levels both early and later in life predicted the rate of cognitive decline over a subsequent 8 year period.

Scaffolding, neural resources, and brain maintenance

STAC-R assumes that aging successfully entails maintaining brain health with increasing age [47], which impacts cognitive ability and rate of cognitive decline (Figure 2, trajectories a and b). Enrichment and depletion factors can influence brain health and compensatory scaffolding. Compensation can be engaged when neural resources in core task networks are inefficient or insufficient to meet task demands [1,2]. Interventions that pose sufficient mental challenge can improve task performance, and presumably network efficiency by *reducing* reliance on compensatory scaffolding as indexed by decreased brain activity and increased modulation to task demand, post-training ([48,49]; see also the study by Tao and Rapp [50]). Because cognition across the life span is jointly determined by brain health and associated neurocognitive compensation [21,51], according to STAC-R some degree of 'cognitive maintenance' is possible even in the face of brain decline. For example, Chen et al. [52] identified subgroups of successful and average agers in the Dallas Lifespan Brain Study based on multidomain performance over a 4-year period. Then, despite some reduction in successful memory retrieval relative to young adults, successful agers showed a more youth-like activation pattern than average agers of the same chronological age, consistent with better functional brain maintenance, while also displaying higher activation outside the core task regions, including areas of prefrontal cortex, consistent with compensatory scaffolding.

STAC-R distinguishes between brain resources and neurocognitive scaffolding, although they are related and influenced similarly by life course factors (see also

Figure 1 in the publication by Cabeza et al. [15]). A significant percentage of individual variation in brain resources in older age has early developmental origins associated with genetic characteristics, birth weight, intracranial volume, and childhood intelligence (IQ) [29, 53–55]. Thus, while some constraints on brain structure and function may be determined prenatally (i.e. brain endowment) and in early development, the brain's adaptivity and compensatory potential through scaffolding may be a crucial target for modification throughout the life course [29,31].

Conclusions: aging and predicting the future

These are exciting times for the prospect of understanding the bases and modifiers of human neurocognitive aging and much more is to come. The availability and collective use of increasingly international longitudinal data sets, buttressed by targeted small-scale investigations, can address longstanding questions about why some people age better than others, trajectories of decline, as well as the neurobiological underpinnings and mechanisms of endowment and change. Greater and continued efforts to study representative and diverse life span samples are needed to understand societal variation and heterogeneity in life course influences [56,57]. Advances in brain imaging and biomarkers to measure disparities in chronological and (neuro)biological age [53,58–60], especially in early adulthood and middle age, hold promise for identifying targeted interventions that may alter the course of decline. STAC-R provides a framework for a more detailed delineation of enrichment and depletion pathways and a mechanistic understanding that can specify their temporal dynamics, selective influence, and targets of life-course modifiers to promote brain health and successful cognitive aging.

Funding

This work was supported by The National Institutes of Health: National Institute on Aging grants AG0-06265 (DCP) and R35-AG0-72262 (PARL).

Credit roles

Patricia Reuter-Lorenz: Conceptualization, original draft, review and editing; Denise Park: Conceptualization, review and editing.

Declaration of competing interest

The author declares no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data were used for the research described in the article.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Park DC, Reuter-Lorenz P: **The adaptive brain: aging and neurocognitive scaffolding**. *Annu Rev Psychol* 2009, **60**: 173–196.

2. Reuter-Lorenz PA, Park DC: **How does it STAC up? Revisiting the scaffolding theory of aging and cognition**. *Neuropsychol Rev* 2014, **24**:355–370.

3. Rosen ML, Amso D, McLaughlin KA: **The role of the visual association cortex in scaffolding prefrontal cortex development: a novel mechanism linking socioeconomic status and executive function**. *Dev Cogn Neurosci* 2019, **39**:100699.

4. Zelazo PD, Carlson SM: **The neurodevelopment of executive function skills: implications for academic achievement gaps**. *Psychol Neurosci* 2020, **13**:273–298.

5. Petersen SE, van Mier H, Fiez JA, Raichle ME: **The effects of practice on the functional anatomy of task performance**. *Proc Natl Acad Sci USA* 1998, **95**:853–860.

6. * Jiang J, Fan L, Liu J: **The knowledge domain of cognitive neuroscience of aging: a scientometric and bibliometric analysis**. *Front Aging Neurosci* 2023, **15**:999594.
A quantitative analysis of the published literature on the cognitive neuroscience of aging using bibliometric software that identifies networks of co-citations and other indices to detect intellectual trends, foundations and innovations.

7. Bernard JA, *et al.*: **Shaky scaffolding: age differences in cerebellar activation revealed through activation likelihood estimation meta-analysis**. *Hum Brain Mapp* 2020, **41**: 5255–5281.

8. * Frank CC, Mundy LM, Smith J: **Life course engagement in enriching activities: when and how does it matter for cognitive aging?** *Psychol Aging* 2023, **38**:263–276.
A recent report examining when in the life course enriching activities exert beneficial effects on later life level of global cognition and rate of cognitive decline.

9. Oschwald J, *et al.*: **Brain structure and cognitive ability in healthy aging: a review on longitudinal correlated change**. *Rev Neurosci* 2019, **31**:1–57.

10. Rao SM, *et al.*: **Genetic risk for Alzheimer's disease alters the five-year trajectory of semantic memory activation in cognitively intact elders**. *Neuroimage* 2015, **111**:136–146.

11. Hupfeld KE, McGregor HR, Reuter-Lorenz PA, Seidler RD: **Microgravity effects on the human brain and behavior: dysfunction and adaptive plasticity**. *Neurosci Biobehav Rev* 2021, **122**:176–189.

12. Oosterhuis EJ, Slade K, May PJC, Nuttall HE: **Toward an understanding of healthy cognitive aging: the importance of lifestyle in cognitive reserve and the scaffolding theory of aging and cognition**. *J Gerontol Ser B Psychol Sci Soc Sci* 2022, **78**:777–788.

13. Chen SHA, Goodwill AM: **Third international handbook of lifelong learning**. *Spring Int Handb Educ* 2023:763–781, https://doi.org/10.1007/978-3-031-19592-1_43.

14. Stern Y, *et al.*: **A framework for concepts of reserve and resilience in aging**. *Neurobiol Aging* 2023, **124**:100–103.

15. Cabeza R, *et al.*: **Maintenance, reserve and compensation: the cognitive neuroscience of healthy ageing**. *Nat Rev Neurosci* 2018, **19**:701–710.

16. Stern Y, *et al.*: **Mechanisms underlying resilience in ageing**. *Nat Rev Neurosci* 2019, **20**. 246–246.

17. ** Walhovd KB, *et al.*: **Brain aging differs with cognitive ability regardless of education**. *Sci Rep* 2022, **12**:13886.
A large scale study of multiple longitudinal adult cohorts finds that general cognitive ability, controlling for education, is associated with

cortical volume and to a lesser extent change in brain resources with age.

18. Stern Y: **Cognitive reserve**. *Neuropsychologia* 2009, **47**: 2015–2028.

19. Lövdén M, Fratiglioni L, Glymour MM, Lindenberger U, Tucker-Drob EM: **Education and cognitive functioning across the life span**. *Psychol Sci Public Int* 2020, **21**:6–41.

20. Seblova D, *et al.*: **High school quality is associated with cognition 58 years later**. *Alzheimer Dement Diagn Assess Dis Monit* 2023, **15**, e12424.

21. Berggren R, Nilsson J, Lövdén M: **Education does not affect cognitive decline in aging: a Bayesian assessment of the association between education and change in cognitive performance**. *Front Psychol* 2018, **9**:1138.

22. Wilson RS, *et al.*: **Education and cognitive reserve in old age**. *Neurology* 2019, **92**:e1041–e1050.

23. Cheval B, *et al.*: **Initial status and change in cognitive function mediate the association between academic education and physical activity in adults over 50 years of age**. *Psychol Aging* 2023, https://doi.org/10.1037/pag0000749.

24. Zahodne LB, *et al.*: **Education does not slow cognitive decline with aging: 12-year evidence from the Victoria longitudinal study**. *J Int Neuropsychol Soc* 2011, **17**:1039–1046.

25. ** Lövdén M, *et al.*: **No moderating influence of education on the association between changes in hippocampus volume and memory performance in aging**. *Aging Brain* 2023, **4**:100082.
Reductions in hippocampal volume with age are associated with reductions in episodic memory performance, even in healthy older adults. This study asks whether education level moderates this association, and finding no evidence for such effects, questions the contributions of education to cognitive reserve.

26. Nyberg L, *et al.*: **Educational attainment does not influence brain aging**. *Proc Natl Acad Sci* 2021, **118**, e2101644118.

27. Ericsson M, *et al.*: **Childhood social class and cognitive aging in the Swedish Adoption/Twin Study of Aging**. *Proc Natl Acad Sci* 2017, **114**:7001–7006.

28. Salthouse TA: **Mental exercise and mental aging**. *Perspect Psychol Sci* 2006, **1**:68–87.

29. Corley J, Cox SR, Deary IJ: **Healthy cognitive ageing in the Lothian Birth Cohort studies: marginal gains not magic bullet**. *Psychol Med* 2018, **48**:187–207.

30. Zaninotto P, Batty GD, Allerhand M, Deary IJ: **Cognitive function trajectories and their determinants in older people: 8 years of follow-up in the English Longitudinal Study of Ageing**. *J Epidemiol Community Heal* 2018, **72**:685.

31. ** Conte FP, *et al.*: **Cognitive change before old age (11 to 70) predicts cognitive change during old age (70 to 82)**. *Psychol Sci* 2022, **33**:1803–1817.
This study is the first to assess whether the magnitude of improvement in cognitive performance from childhood to age 70 is related to the rate of decline thereafter. Regardless of cognitive level at age 11 or 70, those who showed greater increases in early life, showed more gradual decline after age 70, a pattern consistent with notions of scaffolding and reserve.

32. Tucker-Drob EM, Brandmaier AM, Lindenberger U: **Coupled cognitive changes in adulthood: a meta-analysis**. *Psychol Bull* 2019, **145**:273–301.

33. Park DC, Lautenschlager G, Hedden T, Davidson N, Smith AD, Smith P: **Models of visuospatial and verbal memory across the adult life span**. *Psychol Aging* 2002, **17**:299–320.

34. Schaie KW, Willis SL: **The Seattle longitudinal study of adult cognitive development**. *ISSBD Bull* 2010, **57**:24–29. PMID: 23536918; PMCID: PMC3607395.

35. Aartsen MJ, *et al.*: **Advantaged socioeconomic conditions in childhood are associated with higher cognitive functioning but stronger cognitive decline in older age**. *Proc Natl Acad Sci* 2019, **116**:5478–5486.

36. Meister LM, Zahodne LB: **Associations between social network components and cognitive domains in older adults**. *Psychol Aging* 2022, **37**:591–603.

37. Erickson KI, *et al.*: **Physical activity, cognition, and brain outcomes: a review of the 2018 physical activity guidelines**. *Med Sci Sports Exerc* 2019, **51**:1242–1251.

38. Bielak AAM, Gow AJ: **A decade later on how to "use it" so we don't "lose it": an update on the unanswered questions about the influence of activity participation on cognitive performance in older age**. *Gerontology* 2023, **69**:336–355.

39. Gow AJ, Pattie A, Deary IJ: **Lifecourse activity participation from early, mid, and later adulthood as determinants of cognitive aging: the Lothian birth cohort 1921**. *J Gerontol Ser B* 2016, **72**:25–37.

40. Schrempft S, *et al.*: **Associations between life-course socioeconomic conditions and the pace of aging**. *J Gerontol Ser A* 2021, **77**:2257–2264.

41. Moored KD, *et al.*: **Engagement in enriching early-life activities is associated with larger hippocampal and amygdala volumes in community-dwelling older adults**. *J Gerontol Ser B* 2018, **75**:1637–1647.

42. Gehred MZ, *et al.*: **Long-term neural embedding of childhood adversity in a population-representative birth cohort followed for 5 decades**. *Biol Psychiatry* 2021, **90**:182–193.

43. Kucharska-Newton AM, *et al.*: **Association of childhood and midlife neighborhood socioeconomic position with cognitive decline**. *JAMA Netw Open* 2023, **6**, e2327421.

44. Power JD, Schlaggar BL: **Neural plasticity across the lifespan**. *Wiley Interdiscip Rev Dev Biol* 2017, **6**:e216.

45. Hertzog C, Kramer AF, Wilson RS, Lindenberger U: **Enrichment effects on adult development**. *Psychol Sci Publ Int* 2009, **9**: 1–65.

46. Mather M: **How do cognitively stimulating activities affect cognition and the brain throughout life?** *Psychol Sci Publ Int* 2020, **21**:1–5.

47. Nyberg L, Lövdén M, Riklund K, Lindenberger U, Bäckman L: **Memory aging and brain maintenance**. *Trends Cogn Sci* 2012, **16**:292–305.

48. Iordan AD, *et al.*: **Neural correlates of working memory training: evidence for plasticity in older adults**. *NeuroImage* 2020, **217**:116887.

49. McDonough IM, Haber S, Bischof GN, Park DC: **The Synapse project: engagement in mentally challenging activities enhances neural efficiency**. *Restor Neurol Neurosci* 2015, **33**: 865–882.

50. Tao Y, Rapp B: **How functional network connectivity changes as a result of lesion and recovery: an investigation of the network phenotype of stroke**. *Cortex* 2020, **131**: 17–41.

51. * Smith ET, *et al.*: **Longitudinal changes in gray matter correspond to changes in cognition across the lifespan: implications for theories of cognition**. *Neurobiol Aging* 2023, **129**: 1–14.
In a lifespan sample ranging from ages 21 to 88+ and tested over an ~9 year period, this study demonstrates that decreases in brain volume are related to decreases in cognitive performance across the lifespan, although cognitive decline accelerated in later years while the rate of atrophy did not.

52. Chen X, Rundle MM, Kennedy KM, Moore W, Park DC: **Functional activation features of memory in successful agers across the adult lifespan**. *Neuroimage* 2022, **257**: 119276.

53. ** Vidal-Pineiro D, *et al.*: **Individual variations in 'brain age' relate to early-life factors more than to longitudinal brain change**. *eLife* 2021, **10**, e69995.
Disparities between chronological age and measures of biological age, including 'brain age' may index risk or protection related to subsequent

decline. This study documents how pre-existing individual differences can contribute to measurements of brain age, underscoring the lifelong impact of early developmental factors.

54. Karama S, *et al.*: **Childhood cognitive ability accounts for associations between cognitive ability and brain cortical thickness in old age**. *Mol Psychiatry* 2014, **19**:555–559.

55. * Walhovd KB, *et al.*: *Back to the future: omnipresence of fetal influence on the human brain through the lifespan*. 2023, https://doi.org/10.7554/elife.86812.
This study demonstrates remarkably stable positive associations between the early life measure of birth weight, and brain measures (volume and cortical area) across a lifespan sample ranging from age 4–82 years of age, followed for ~8 years. Brain changes were not found to be associated with this early life measure.

56. Tucker-Drob EM, Bates TC: **Large cross-national differences in gene × socioeconomic status interaction on intelligence**. *Psychol Sci* 2015, **27**:138–149.

57. Walhovd KB, *et al.*: **Education and income show heterogeneous relationships to lifespan brain and cognitive differences across European and US cohorts**. *Cereb Cortex* 2021, **32**:bhab248.

58. Ebaid D, Crewther SG: **Time for a systems biological approach to cognitive aging? A critical review**. *Front Aging Neurosci* 2020, **12**:114.

59. ** Elliott ML, *et al.*: **Disparities in the pace of biological aging among midlife adults of the same chronological age have implications for future frailty risk and policy**. *Nat Aging* 2021, **1**:295–308.
This work uses a range of biomarkers to characterize the longitudinal "pace-of-aging" in a population-representative birth cohort from New Zealand across a ~20 year period of adulthood to age 45. Faster agers also showed lower brain health, cognition and greater cognitive decline even in mid-adulthood.

60. Ryan L, *et al.*: **Precision aging: applying precision medicine to the field of cognitive aging**. *Front Aging Neurosci* 2019, **11**:128.