Environmental influences on the pace of brain development

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Abstract | Childhood socio-economic status (SES), a measure of the availability of material and social resources, is one of the strongest predictors of lifelong well-being. Here we review evidence that experiences associated with childhood SES affect not only the outcome but also the pace of brain development. We argue that higher childhood SES is associated with protracted structural brain development and a prolonged trajectory of functional network segregation, ultimately leading to more efficient cortical networks in adulthood. We hypothesize that greater exposure to chronic stress accelerates brain maturation, whereas greater access to novel positive experiences decelerates maturation. We discuss the impact of variation in the pace of brain development on plasticity and learning. We provide a generative theoretical framework to catalyse future basic science and translational research on environmental influences on brain development.

Children's early experiences are associated with important later-life outcomes, including their earnings, educational attainment, physical well-being and mental health. How are children's experiences embedded in their developing brains to broaden, or constrain, their opportunities to live happy and healthy lives? Much of what we know about links between early experiences and adult outcomes has come from research on socio-economic status (SES). A multidimensional construct, SES is typically measured at the household level (for example, parental income, education or occupation) or the neighbourhood level (for instance, neighbourhood crime rate, poverty levels or median income). Higher SES is associated with lower exposure to stress, and with greater access to cognitive enrichment, such as high-quality education, child-directed language, books and toys. Variation in childhood SES has been associated with variation in measures of brain structure and function. However, surprisingly little is known about whether and how experiences associated with childhood SES affect the trajectory of brain maturation.

Here, we synthesize evidence that experiences associated with childhood SES affect not only the outcome, but also the pace of brain development, and consider the implications of early brain development for plasticity in childhood. We focus on whole-brain cortical measures of structure and function because, as a broad and multidimensional construct, SES probably exerts effects on a complex constellation of brain regions and their connections. We highlight the few longitudinal studies on SES and brain development but, because these studies are rare, we also draw on cross-sectional studies of relationships between SES and brain structure and function across development. We consider how experiences, including stress, cognitive enrichment and environmental variability, influence brain maturation and plasticity. We close by outlining promising future directions for research on how children's early experiences lead to disparities in later-life outcomes.

Structural brain development
Cortical thickness. Cortical thickness increases in the prenatal and immediate postnatal period, driven by dendritic and axonal growth as well as synaptogenesis. Peak synaptic density and peak cortical thickness are reached at different times across the brain, with sensory regions showing faster development and earlier peaks, and association regions showing slower developmental trajectories. The cortex thickens before 2 years of age, before undergoing widespread thinning across a protracted period starting between 2 and 5 years of age, and continuing through adolescence and early adulthood. Thinning is attributed to both regressive (synaptic pruning) and progressive (myelination) processes. In adulthood, a thicker cortex is associated with larger, more complex pyramidal neurons. Cortical surface area increases during childhood and into early adolescence, with the greatest increases occurring first in sensory areas, and later in association areas.

Children and adolescents from higher-SES environments generally have thicker cortex than those from lower-SES environments, but there is evidence that relationships between SES and cortical thickness vary with age. In the first postnatal year, when the cortex rapidly thickens, higher paternal education is associated with thinner cortex, particularly in the frontal lobes. This pattern is suggestive of more prolonged maturational processes in infants from higher-SES backgrounds. Later in development, in youth aged 3–20 years, SES moderates the negative relationship between age and cortical thickness such that youth from lower-SES backgrounds show a steeper curvilinear decrease in cortical thickness at a younger age than do youth from higher-SES backgrounds. Adolescents aged 12–18 years in low-income households show a steeper curvilinear relationship between age and cortical thickness than do adolescents in high-income households. For females, but not males, in low-income households, living in high-inequality neighbourhoods is again associated with a steeper negative relationship between age and cortical thickness. This evidence is consistent with the hypothesis that lower SES is associated with accelerated cortical thinning throughout childhood and adolescence. However, not all findings align with this hypothesis. Two recent studies examined youth aged 5–25 years and 14–19 years and did not find that SES moderated relationships between age and cortical thickness, although the former study reported positive correlations between SES
and cortical thickness. However, examining a large age range such as 5–25 years might obscure interaction effects that vary over the course of development, and SES-related variability in the rate of cortical thinning during late adolescence when thinning has slowed may be minimal (Fig. 1). In addition, neither study examined non-linear relationships between age and cortical thickness moderated by SES.

**Surface area.** Fewer studies have examined associations between SES and cortical surface area development. In infancy, surface area is not related to parental education or income. In late childhood and adolescence, however, higher SES is associated with greater surface area. In an analysis of the Pediatric Imaging, Neurocognition, and Genetics (PING) dataset, researchers applied sample weights to structural brain imaging data collected from children aged 3–18 years to create a 'weighted sample' approximating the distribution of SES, race/ethnicity and sex in the US population. When the researchers used the weighted sample to examine associations between surface area and age, the surface area peak shifted earlier as compared with the unweighted sample.
consistent with an interpretation of earlier or faster brain maturation in children from lower-SES backgrounds, who were under-represented in the original sample\textsuperscript{28}. In a recent longitudinal study of adolescents, higher SES was associated with a smaller decline in total surface area between 14 and 19 years of age\textsuperscript{26}.

**Cellular underpinnings.** The cellular processes that underlie cortical thickness and surface area measures obtained with MRI are still under active investigation. As noted already, cortical thickness is positively associated with synaptic density, and is negatively associated with myelination\textsuperscript{14,15}. One possibility is that experiences associated with low SES drive earlier curtailment of synaptic proliferation and a subsequently decreased range for optimal synaptic pruning and wiring of functional networks. Computational models of synaptic proliferation suggest that synaptic overgrowth and then pruning of weak synapses maximizes network performance, given the metabolic constraints of the brain\textsuperscript{29}. In biologically motivated models of network development, delaying synaptogenesis in higher-order layers of a network leads to greater energy efficiency and faster learning after development\textsuperscript{30}. Moreover, networks with more initial connections are better able to learn than networks with fewer initial connections\textsuperscript{31}. Computational models of synaptic proliferation and subsequent pruning early in development have identified a trade-off between rapid development, which enables earlier independence and less parental input, and optimal adult neural performance\textsuperscript{32}. SES-associated differences in early synaptic proliferation would affect the development of functional connectivity, which we examine in the following section.

**Functional network development**

A key goal of brain development is to establish efficient, specialized cortical systems. Functional activation of specific systems can be studied by imaging individuals performing well-designed tasks, but SES-associated differences in task accuracy and the interpretation of stimuli can affect conclusions about the underlying anatomy\textsuperscript{33}. By contrast, data collected when participants relax inside the scanner — that is, resting-state functional MRI (rs-fMRI) data — can be used to study all systems simultaneously without task confounds\textsuperscript{34}. Components of a functional system show statistically similar patterns of fluctuations in blood oxygenation, commonly referred to as functional connectivity\textsuperscript{35}. Resting-state analyses have generated conflicting answers to the question of whether higher SES is associated with faster functional maturation. One compelling study integrated grey and white matter structure with regional rs-fMRI measures to develop a model to classify individuals’ ages. It was found that individuals aged 8–22 years from lower-SES backgrounds were more likely to be classified as adults than their higher-SES counterparts\textsuperscript{36}. Other rs-fMRI studies also suggest that lower SES is associated with faster functional development: in youth aged 6–17 years, lower SES was associated with weaker connectivity in corticostratal connections that typically showed decreases in strength with age over development\textsuperscript{37,38}. However, some studies have found the opposite pattern: higher SES has been associated with greater functional connectivity between limbic regions that typically show age-related increases in functional connectivity over development\textsuperscript{39–41}. These studies largely examined patterns of regional metrics or connectivity between specific sets of regions rather than testing for broad effects of SES on the pace of network development throughout the brain. However, region-to-region connectivity can be strengthened by repeated co-activation, just as cells that fire together will wire together. Therefore, it is difficult to infer broad developmental processes from examining links between specific regions\textsuperscript{42}.

Newer approaches to analysing rs-fMRI data are computationally better suited to test the hypothesis that higher childhood SES is associated with protracted development of functional networks across the entire cortex. A network science approach, in particular, represents the brain as a collection of nodes (regions) and edges (connections), enabling us to address the whole-brain pattern of connectivity\textsuperscript{43,44}. The resulting network architecture can then be quantitatively characterized with use of tools from graph theory to identify key properties relevant to maturation\textsuperscript{45}. Two such properties are segregation and integration, both of which change during development\textsuperscript{46}. Segregation quantifies the presence of groups or subnetworks of densely interconnected nodes in a network, whereas integration assesses the extent to which information can be rapidly combined from distributed regions\textsuperscript{47}. Integration has a distinct meaning when one is interpreting diffusion data compared with when one is interpreting functional data\textsuperscript{11} (Box 1). Together, integration and segregation constitute the unique property of small-worldness found in adult brain networks: the perhaps counterintuitive presence of high levels of both segregation and integration at many different scales (see Ref.\textsuperscript{48} for a recent review). Given the associations between functional network segregation at rest and cognitive abilities\textsuperscript{49–51}, and that most research on SES and functional network development has examined segregation rather than integration, we focus specifically here on measures of functional network segregation.

Segregation in brain networks changes markedly over development, and can be measured at several scales. One measure of segregation at the nodal level is the clustering coefficient, which quantifies the connectivity in a node’s immediate neighbourhood. At the mesoscale and global levels, modularity captures the extent to which a network can be divided into distinct subnetworks or modules, and system segregation captures the extent to which systems within a functional network are distinctly partitioned\textsuperscript{52}. A coarse proxy for system segregation is within-system connectivity.

Studies of prenatal development show that a segregated network structure is present even in utero, with modular subnetworks that coarsely resemble those found in adults\textsuperscript{53–56}. Inter-regional variation in the width of time windows of synaptogenesis during prenatal and early postnatal development (for example, as seen in Ref.\textsuperscript{57}) gives rise to the highly connected hub nodes and modular structure seen in adult brain networks\textsuperscript{52–55}. Similarly to structural brain development\textsuperscript{56–58}, functional subnetworks underlying sensory systems become established at an earlier age than do the subnetworks underlying association systems\textsuperscript{59–61}. Mesoscale segregation increases with age later in childhood and adolescence, probably reflecting the refinement of network architecture; higher-order association systems in particular become more segregated with development\textsuperscript{61,62} (although some studies do not find positive associations between age and segregation during adolescence, perhaps owing to differences in age range and node or edge definitions; see Ref.\textsuperscript{63}). Maturation at the cellular level probably gives rise to these macro-scale developmental changes. Inhibitory interneurons have a role in limiting resting-state functional connectivity and establishing the boundaries between brain regions that are necessary for network segregation\textsuperscript{64}. In addition, connection strength is associated with microscale properties of connected brain regions, including the size and complexity of layer III pyramidal neurons\textsuperscript{65,66}, cytoarchitectonic similarity\textsuperscript{67} and excitatory–inhibitory receptor balance\textsuperscript{68}.
Only a few studies have examined associations between SES and functional brain development using a network science approach (Fig. 2), and these studies have used different measures of segregation. Although the use of different measures of segregation at different scales makes an overarching pattern difficult to interpret, here we draw upon existing studies to sketch a theoretical model for future work to detail. One study of infants less than 1-year-old found marginally significant associations between higher SES and both similarity to adult systems and within-system connectivity, a proxy for system segregation. The study’s authors interpret these observations as indicative that greater maturation is associated with higher SES. However, the significant associations were found only at 6 months of age and not at the other time points examined (1, 3, 9 or 12 months). In another study, youth aged 8–22 years from high-SES neighbourhoods show a stronger association between age and local segregation — clustering — than did youth from low-SES neighbourhoods. Although the study authors also examined a mesoscale measure of segregation, namely modularity, the moderating effect of SES on associations between age and modularity was accounted for by local segregation, suggesting that the fundamental driver was variation in local network topology. Specifically, during late childhood, youth from high-SES neighbourhoods showed lower local cortical functional segregation than did youth from low-SES neighbourhoods. However, youth from high-SES neighbourhoods showed a steeper positive relationship between segregation and age during adolescence, such that by their early 20s, they showed greater functional network segregation than youth from low-SES neighbourhoods. Another study of individuals in a similar age range (6–17 years) revealed an interaction between household and neighbourhood SES, such that among youth in low-SES neighbourhoods, higher household SES is associated with greater local functional network segregation (assessed by the clustering coefficient) in the prefrontal cortex. The available evidence is consistent with the hypothesis that higher SES is associated with more protracted functional network development, with youth from high-SES backgrounds showing more widespread connectivity and thus lower segregation early in development, before the rapid development of a more segregated network architecture that continues into adulthood.

In sum, these studies suggest that the effects of SES on structural development may be reflected in functional development, such that the extended period of structural development associated with high SES gives rise to a longer, slower trajectory of functional network segregation during development, leading to greater segregation. Although longitudinal studies with consistent measures of functional network organization necessary to strictly test these hypotheses do not yet exist, we draw upon existing work to sketch a theoretical model for future work. Lower SES is associated with faster thinning and blunted functional remodelling during childhood and adolescence. In late adolescence and young adulthood, individuals from higher-SES backgrounds show greater cortical thickness and greater segregation than do individuals from lower-SES backgrounds, perhaps as a result of differences in maturation rate. The findings described above also suggest that associations between SES and functional network segregation might follow a progression from local to global across the lifespan, with associations in childhood and early adolescence evident at the local level, and associations at the mesoscale and global level visible later in life. However, more work is needed to understand whether there are truly differing associations at different scales, as few studies thus far have examined multiple measures of segregation in conjunction.

We now turn to two of the most well-studied putative mechanisms underlying SES-associated differences in brain development: stress and cognitive enrichment. Previous conceptual models have organized variation in early experiences along dimensions of threat (similar to stress) and deprivation (the opposite of cognitive enrichment). We review these factors as possible contributors to the effects of SES on the pace of brain development.

**Stress**

Lower SES is consistently associated with greater chronic stress, and prior work extensively reviewed the links between SES and multiple conceptualizations...
of stress. There are at least three mechanisms by which chronic stress exposure could accelerate brain development. The first is that repeated use of stress-detection and stress-regulation circuitry, including the amygdala and medial prefrontal cortex, could lead to faster maturation of that circuitry. The second is that stress could cause faster ageing of the entire body by increasing glucocorticoid levels and allostatic load (physiological wear and tear) and by promoting activation of inflammatory processes. These same physiological processes can be activated by other experiences associated with lower SES, including exposure to environmental toxins (such as lead or air pollution), poorer sleep quality and less opportunity for physical activity. Stress is associated with accelerated cellular ageing, marked by changes in epigenetic processes such as methylation, which are detectable in childhood. Individuals from lower-SES backgrounds tend to enter puberty earlier, and this effect is driven most strongly by experiences of threat. Earlier puberty in turn might also accelerate brain maturation. One study found that the expression of the genes encoding the glucocorticoid receptor and the androgen receptor explained the most variance in cortical thinning in low-income female adolescents living in high-inequality neighbourhoods, suggestive of links between stress and both accelerated puberty and cortical thinning. A third possible mechanism by which chronic stress may accelerate brain development is that young individuals process threat as an overall signal of lack of protection and support — that is, they receive cues that the environment requires maturity — and this triggers adaptive top-down processes that cause development to proceed more quickly. This was recently termed the ‘developmental support hypothesis’ (see Ref. 93), and aligns with much evolutionary life-history research, including cross-species findings that parental investment is associated with slower maturation. Understanding which, if any, of these mechanisms affect the pace of brain development is essential for determining when and how it might be possible to intervene.

Animal models of early-life stress allow us to address issues of causality that cannot be examined in humans. The animal paradigm most analogous to the economic...
deprivation and stress associated with SES is the limited bedding and nesting model in rodents, which involves limiting the dam's access to sufficient bedding and nesting material. Although the limited bedding paradigm fails to capture many of the social, emotional and cognitive aspects of being raised in a low-SES environment, this constraint does result in fragmented and unpredictable nurturing behaviours and increased glucocorticoid release in the pups\textsuperscript{96,97}. Offspring of the dams exposed to this paradigm show earlier declines in the levels of markers of postnatal neurogenesis in the hippocampus, earlier increases in the levels of markers of synaptic maturity, earlier increases in the level of myelin basic protein and impairments in cognitive function\textsuperscript{98–100}. They also show an initial increase in neuronal proliferation in the hippocampus in early life, but at later times show reduced numbers of neurons and reduced hippocampal volume, suggestive of an earlier peak in neurogenesis\textsuperscript{101}. Prefrontal areas and the hippocampus show reduced spine density following exposure to this paradigm in the early postnatal period. These changes are associated with impairments in cognitive function\textsuperscript{102,103} that are prevented by blocking hormone, a stress-linked neuropeptide, immediately following exposure to this paradigm. This finding is consistent with a large body of work showing that some effects of the early environment are modulated by glucocorticoids\textsuperscript{104,105}. We now turn to the question of whether SES differences in cognitive enrichment or deprivation also drive differences in the pace of brain development.

**Cognitive enrichment**

Exposure to a complex environment with a variety of experiences and diverse learning materials is known as cognitive enrichment. The absence of cognitive enrichment is considered deprivation\textsuperscript{106,107}. Children growing up in higher-SES homes tend to be exposed to more complex and cognitively stimulating environments\textsuperscript{107,108} and cognitive enrichment is associated with improved cognition in youth independent of stress exposures\textsuperscript{99,106–108}. In one study, cognitive stimulation also mediated associations between SES and cortical thickness in prefrontal areas\textsuperscript{109}, highlighting its potential role as a mechanism of the influence of SES on brain development in childhood. Recapitulating these findings, SES-associated differences in children's cognitive function have been reported to be mediated by cognitive enrichment in the home\textsuperscript{110}.

Some models suggest that the absence of cognitive enrichment in specific domains leads to accelerated synaptic pruning in brain regions that process complex cognitive and social stimuli\textsuperscript{109,111}. The converse of this argument is that specific cognitive inputs might delay synaptic pruning in relevant brain circuitry. As in studies of stress, animal models allow us to investigate the causal influence of cognitive enrichment on brain development. Environmental enrichment paradigms typically have two main components: novel objects and novel social partners. Environmental enrichment in both juvenile and adult animals has been shown to lead to increased cortical thickness\textsuperscript{110,111}, driven by increases in dendritic volume and branching\textsuperscript{112,113}, dendritic spine count\textsuperscript{112,114}, synaptogenesis and glial proliferation\textsuperscript{115,116} (reviewed in Ref.\textsuperscript{117}). As little as 4 days of enrichment produces measurable changes in cortical thickness in rodents\textsuperscript{116,119,120} and longer exposure is associated with longer retention of increased thickness after return to a standard environment\textsuperscript{120}. Enrichment may also affect cortical surface area, but it is not commonly measured\textsuperscript{120}. Increased synaptogenesis, glial proliferation and dendritic plasticity could indicate a prolonged period of maturation leading to more complex brain circuitry, as computational models that suggest early synaptic overgrowth and overall slower development are advantageous for adult network abilities\textsuperscript{120,121}. In sum, there is some evidence that children's early experiences of stress and cognitive enrichment influence the pace of brain development.

**Consequences for plasticity**

Understanding how children's experiences affect the pace of brain maturation has consequences for understanding brain plasticity. Brain plasticity can be conceptualized in two ways: as a process and as a potential. The process of brain plasticity, including long-term potentiation and other structural and functional changes in response to experience, occurs throughout life. However, the brain's plasticity as potential for change varies with age. Developmental processes, including myelination, inhibition and the formation of perineuronal nets (PNNs; lattice-like extracellular structures that enwrap neurons and act as a physical brake on plasticity) decrease the brain's ability to change as children get older\textsuperscript{121,122} (BOX 2). If brain development proceeds more quickly in children from low-SES backgrounds, windows of high plasticity could also close.

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**Box 2 | Cellular and molecular mechanisms of plasticity**

In animal models, the study of critical or sensitive periods, windows of heightened plasticity when brain development depends on specific expected environmental inputs, has yielded insight into the mechanisms of the regulation of plasticity, summarized in the table along with neuroimaging measures well suited to track these mechanisms\textsuperscript{123–127}. Excitatory–inhibitory circuit balance, driven by the maturation of parvalbumin-positive (PV) inhibitory interneurons, leads to periods of heightened plasticity, and molecular ‘brake’-like regulators limit plasticity later in development\textsuperscript{122}. Accumulation of regulators such as the homeobox protein OTX2 and brain-derived neurotrophic factor (BDNF) trigger the maturation of PV+ neurons and opening of periods of heightened plasticity\textsuperscript{124}. Subsequently, brake-like factors such as perineuronal nets and myelin maintain the closure of periods of heightened plasticity, stabilizing neural circuitry to limit rewiring during adulthood. In humans, these brake-like factors accumulate during development in parallel with the progression of structural changes such as cortical thinning, first in primary sensory and motor areas and later in higher-order association areas\textsuperscript{125–127}. Neuromodulators such as dopamine, acetylcholine and serotonin can upregulate plasticity even once structural brakes are in place\textsuperscript{125–127,128,129}.
more quickly in these children, reducing the brain’s sensitivity to future experiences. In this section, we review evidence from animal models that experiences of stress and cognitive enrichment affect plasticity. Most of this research was done in adult animals, but the results suggest that these experiences would affect plasticity during development as well.

Studies in animal models have broadly shown that early-life stress decreases synaptic plasticity and promotes the developmental processes that reduce plasticity (such as inhibition and myelination). Offspring of dams exposed to the limited-bedding paradigm show earlier increases in the levels of markers of synaptic maturity, earlier increases in the level of myelin basic protein, an increased number of PNNs and reductions in adult synaptic plasticity, accompanied by impairments in cognitive function, compared with control offspring. The limited-bedding paradigm also causes reduced spine plasticity in the offspring’s prefrontal cortex and hippocampus. Increased myelination is not always observed following early-life stress: one study found that early social isolation leads to a decrease in myelination in the prefrontal cortex. Therefore, the impact of stress on myelination may depend on the type of stressor and the brain area examined. There are also indirect links between early-life stress and plasticity: early-life stress accelerates pubertal timing (age of onset of pubertal development or age at menarche), and ovarian hormones increase cortical inhibition. Studies of stress on plasticity in humans are rare. One study of post-mortem brains found that individuals who were exposed to child abuse had increased numbers of mature myelinating oligodendrocytes in the ventral medial prefrontal cortex. Another study used neuroimaging to show that veterans with post-traumatic stress disorder had higher T1-weighted/T2-weighted MRI signal, a marker of myelination, in the hippocampus. Both studies are consistent with the hypothesis that stress increases myelination, and may thereby limit plasticity.

Environmental-enrichment paradigms prolong and enhance plasticity. Enrichment during the juvenile period decreases the number of PNNs, enhances synaptic plasticity in the form of long-term potentiation and depression and influences parvalbumin-positive neuron expression. In adulthood, enrichment keeps inhibition at juvenile levels, prolonging early periods of plasticity.

Enrichment paradigms can also enhance plasticity in adults long past juvenile critical periods by reducing inhibition, decreasing PNN stability or increasing myelin remodelling, all potent contributors to plasticity. Environmental enrichment increases neuronal secretion of the cytokine interleukin-33 (IL-33), which signals to microglia to engulf PNNs, increasing synaptic plasticity. Environmental enrichment also enhances levels of neurotransmitters, including noradrenaline, dopamine and serotonin, which increase cortical plasticity and facilitate cortical remodelling. Mice lacking the dopamine D2 receptor or the dopamine D4 receptor fail to benefit in longevity from enriched environments. The social interaction component of an enriched environment increases release of oxytocin, which enhances plasticity and protects against stress-related changes in plasticity. To our knowledge, studies examining the impact of cognitive enrichment on plasticity in humans do not yet exist.

Stress and cognitive enrichment broadly capture the valence of experiences: stressful experiences are negative and should be avoided, whereas environmental enrichment paradigms are designed to be positive and rewarding. However, valence is not the only salient property of such experiences. The timing of experiences also has implications for plasticity (Fig. 3). Repeated exposure to the same experience should signal that the experience is more likely to occur consistently in the future, and that the brain should optimize to respond to it, even at a cost to plasticity. Experience-dependent myelination and PNN formation are two potential mechanisms by which repeated activation of brain circuitry might lead to reduced plasticity.

Empirical evidence in humans supports the theory that rote practice accelerates maturation of specific brain circuits. In adults, after several weeks of repetitive task practice, functional systems involved in the task become more segregated from each other, mimicking network segregation during development. Similarly, working memory training in young children aged 4–6 years results in changes in attention-related brain activity that resemble those that occur with maturation. Thus, some brain systems may mature more quickly in high-SES environments if they process experiences that are more common in these environments. For example, repetitive use of language systems will lead to stronger connections between language-processing regions. By contrast, rare experiences should signal that the environment is still changing and that plasticity is beneficial. Gopnik has argued that humans have extended childhoods to allow there to be a “turbo-powered super sensitive period” to accommodate our unpredictable environments. Computational evolutionary models suggest that children with more
variable experiences, regardless of the valence of these experiences, reduce their estimate of uncertainty about the environment later, and hence lose plasticity later than do children who experience less-variable environments. Environmental variability may also be intrinsically rewarding, increasing dopamine levels, thereby boosting plasticity.

We expect the valence and timing of experiences to interact. We suggest a model that predicts that experiences that are both negative and chronic or repeated are the most likely to accelerate brain development and reduce plasticity. Repeated exposure to negative experiences would lead to maturation of the networks that process these experiences, and would augment glucocorticoid levels, allostatic load and inflammatory processes that age the entire body. By contrast, experiences that are positive and rare are predicted by our model to be the most likely to decelerate brain development and enhance plasticity. The hormonal and neurochemical sequelae of positive experiences are not as well studied as those of negative experiences, but awe and surprise have been associated with the release of neurotransmitters associated with enhanced plasticity, including dopamine and acetylcholine. Positive social interactions lead to oxytocin release, which has also shown to enhance plasticity.

We expect that experiences that are negative and rare, such as acute traumas, may not necessarily have major impacts on the rate of global maturation, but that specific aspects of those experiences, such as their developmental timing, severity and broader context, may be important in determining their impact on development and plasticity. Similarly, experiences that are positive and repeated may not necessarily broadly impact the rate of global maturation. Indeed, some evidence suggests that in humans cognitive enrichment (or its converse, deprivation) has little effect on the pace of cellular ageing or pubertal timing. Future empirical work will help us refine a model of how specific aspects of early experiences alter the pace of brain development, with consequences for cognition and learning.

**Future directions and conclusions**

In this Perspective, we have considered evidence that experiences associated with childhood SES affect not only the outcome but also the pace of brain development, with potential influences on brain plasticity throughout life. We argue that low exposure to stress and high exposure to novel positive experiences promote protracted structural brain development, which gives rise to a later, longer trajectory of functional network segregation, ultimately leading to more efficient cortical networks in adulthood.

However, this model is based on incomplete data. Studies to date have not been fully representative of human diversity, focusing primarily on Western populations with nutritional excess. Studies have also been limited by methodological challenges, cross-sectional samples, lack of connection to adult research and correlational designs. Below, we discuss promising approaches to overcome these limitations and directly test our hypotheses in future research.

Methodological advances are necessary to fully understand how early experiences affect the pace of brain development. The application of network methods to developmental data is still in its infancy, as researchers take on the challenge of describing nodes and edges of brain networks in a biologically accurate and meaningful way. Studies have used many different measures of segregation to characterize functional brain networks, and it will be crucial for future research to examine how different measures relate to each other and to SES over development. The field has also become increasingly aware of how methodological decisions, including correcting for head motion and physiological artefacts, affect study conclusions, and thus affect our ability to make inferences across sets of studies. New methods are also needed for integrating structural and functional brain data. Few articles have examined both functional and structural brain development in the context of SES, and little is known about the relative ordering of trajectories of cortical thinning, white matter development and functional network segregation. Recent work has attempted to link changes in structure to changes in function, but the sequence of developmental progression, let alone environmental influences on that sequence, remains murky. Another area for future work involves linking histology and electrophysiology data to structural and functional MRI findings in animal models to facilitate translation to human work. Such an effort would enable us to test how early-life experiences influence cellular developmental processes, including myelination and inhibition, that give rise to macro-level measures, including cortical thickness, surface area and network segregation.

Many of the studies reviewed herein are cross-sectional. Cross-sectional data have inherent limitations when developmental processes are being examined, foremost among them the inability to infer the shape of developmental trajectories. Cross-sectional studies cannot establish temporal precedence and, if sampling is non-random, associations with age may be driven by the characteristics of the sample rather than by age. Longitudinal studies, such as the Adolescent Brain Cognitive Development (ABCD) study and the upcoming HEALTHy Brain and Child Development (HBd) study, will be necessary to fully understand how early environments influence trajectories of functional and structural brain development. Data from these longitudinal studies will enable us to examine whether changes in brain structure correspond to changes in functional network segregation, and whether measures of the early environment predict earlier or later peaks in these trajectories.

An important future direction is determining whether SES effects on early brain maturation set the stage for early brain ageing. There is initial evidence from a prospective study that traces of childhood SES are still present in the brain structure of young adults aged 23–25 years, even when adulthood SES is controlled for. We do not yet know whether this is also true of older adults, but studies suggest that cognitive enrichment might be important: cognitive stimulation in childhood is associated with larger brain volumes and better cognition in old age when adulthood SES is controlled for. Furthermore, a longitudinal study showed that higher levels of early cognitive stimulation are associated with slower cognitive decline and less neuropathology with ageing. Studies examining adulthood SES and brain structure and function find results that are broadly consistent with the theoretical framework we outline in this Perspective. In one study, adults from higher-SES backgrounds showed a weaker negative association between segregation and age than did adults from lower-SES backgrounds, consistent with an interpretation of a slower decline in functional network organization in higher-SES adults. Associations with adulthood SES were stronger than associations with childhood SES; however, because adulthood SES and childhood SES are correlated, these factors can be difficult to disentangle. Childhood SES is difficult to measure in an ageing sample because of recall biases. Relationships between parental education and childhood experiences may also have been different.
when today’s 80-year-olds were children from how they are for today’s 6-year-olds, making retrospective report of SES in adults difficult to map to current developmental research. In addition, low-SES populations may be poorly represented in ageing research, owing to lower-life expectancy and higher prevalence of other diseases and health issues that would exclude these populations from studies of healthy ageing. Ideally, future studies will follow individuals from birth to old age, although this may be more feasible in animal models (for example, as in Ref. 21).

Although longitudinal observational studies are useful, intervention studies are necessary to directly test whether children’s early experiences cause slower or faster brain development. Future work should test whether cognitive enrichment in humans leads to changes in the pace of brain development, and whether the timing of enrichment influences these effects. Although we cannot evaluate the impact of creating early stressful experiences for children, we can learn from the effect of naturally occurring stressors. The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a global public health crisis has resulted in an unforeseen natural experiment on how the timing — that is, the age of children when it occurred — and the severity of a stressor affect the pace of children’s maturation. However, the effect of the stress has been non-random, as the crisis has disproportionately affected lower-income communities and people from minority racial or ethnic groups and other marginalized populations.

Following the brain development of children who lived through this period will yield insight into the importance of stress timing on the rate of maturation.

It is possible to investigate causal effects of cognitive enrichment by studying educational interventions. Education is broadly beneficial for children’s development, leading to increased cognitive ability, and better health and wellness throughout life. Both the type and the timing of education could influence brain plasticity. Rote practice is likely to drive faster maturation of the brain systems involved, which would be beneficial for the task practised (for example, reading and writing), but it could compromise the ability to learn novel tasks. By contrast, rich and varied experiences that capture children’s attention and enhance their motivation, boosting levels of acetylcholine and dopamine, could decelerate the rate of brain maturation. Our model also predicts that educational experiences earlier in childhood will have a bigger effect on brain development and plasticity than experiences later in childhood, by changing the trajectory of maturation. Evidence for the efficacy of early interventions, such as from the Abecedarian Project and the Perry Preschool Program, is broadly consistent with this hypothesis; however, direct comparisons of the same curricula at different ages are rare, and thus the neural outcomes of changing the timing of such interventions are not yet known. Determining the consequences of educational strategies for the pace of brain maturation is an important area of future research.

In conclusion, disparate strands of evidence from neuroscience, psychology and medicine are consistent with a model in which the early environment affects not only the outcome but also the pace of human brain development. We propose that high stress and low cognitive enrichment accelerate developmental changes in cortical thickness and surface area, and shift the trajectory and amplitude of functional network segregation across development. We argue that changes in the pace of brain development also affect plasticity during development. Our work provides a generative theoretical framework for research on links between childhood experiences and brain changes over the lifespan, and reinforces the pressing need to elucidate changes in early development that lead to disparities in later-life outcomes. If we can develop new screening tools to detect accelerated development, we will be better able to implement educational and other interventions earlier, and prevent cascading consequences of early maturation for mental and physical health.

Citation diversity statement
Recent work in neuroscience and other fields has identified a bias in citation practices such that articles authored by women and scholars from minority racial or ethnic groups are undercited relative to the number of such articles in the field. The expected gender proportions in reference lists of five top neuroscience journals as reported by Dworkin et al. were 6.7% for woman (first author)/woman (last author), 9.4% for man/woman, 25.5% for woman/man and 58.4% for man/man. Inclusion of citation diversity statements has been proposed as a way of increasing transparency surrounding citation practice. We obtained the predicted gender of the first and last authors of each reference by using databases that store the probability of a name belonging to a woman or man, and classifying as unknown any names with under 70% predicted accuracy. Excluding self-citations of the authors of the current Perspective, for our references the proportions are 26% woman (first author)/woman (last author), 20% man/woman, 21% woman/man and 33% man/man. This method is limited in that the databases used may not, in every case, be indicative of gender identity, and in that it does not account for intersex, non-binary or transgender people. In addition, the expected proportions above were calculated across all neuroscience subfields, and may differ for particular subfields, such as developmental neuroscience. We look forward to future work to better understand how to support equitable practices in science.

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U.A.T. and A.P.M. researched data for the article and contributed substantially to discussion of the content. All authors wrote the article and reviewed and/or edited the manuscript before submission.

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