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Socioeconomic status and the brain: mechanistic insights from human and animal research

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Socioeconomic status and the brain: mechanistic insights from human and animal research

Daniel A. Hackman, Martha J. Farah and Michael J. Meaney

Abstract | Human brain development occurs within a socioeconomic context and childhood socioeconomic status (SES) influences neural development — particularly of the systems that subserve language and executive function. Research in humans and in animal models has implicated prenatal factors, parent–child interactions and cognitive stimulation in the home environment in the effects of SES on neural development. These findings provide a unique opportunity for understanding how environmental factors can lead to individual differences in brain development, and for improving the programmes and policies that are designed to alleviate SES-related disparities in mental health and academic achievement.

As the field of human neuroscience has matured, it has progressed from describing the 'typical' or 'average' human brain to characterizing individual differences in brain structure and function, and identifying their determinants. Socioeconomic status (SES), a measure of one's overall status and position in society, strongly influences an individual's experiences from childhood and through adult life. Research is beginning to shed light on the mechanisms through which experiences in the social world during early childhood affect the structure and function of the brain.

Growing up in a family with low SES is associated with substantially worse health and impaired psychological well-being, and impaired cognitive and emotional development throughout the lifespan[1–6]. In contrast to sociological and epidemiological approaches, neuroscience can identify the underlying cognitive and affective systems that are influenced by SES (BOX 1). In addition, neuroscience research — in animals and in humans — has provided candidate mechanisms for the cause–effect relationships between SES and neural development. This research has also demonstrated that at least some of these effects are reversible. Such a mechanistic understanding will enable the design of more specific and powerful interventions to prevent and remediate the effects of low childhood SES[7–9].

Other recent reviews have discussed research on SES-related differences in neurocognitive development[7–9]. In this Perspective, we focus on the candidate mechanisms by which SES influences brain development, drawing from research in humans and in animal models. We first describe studies in humans that show that SES influences cognitive and affective function in children, adolescents and young adults. We then discuss studies in human populations that have identified possible mediators of the effects of SES, and review research in animals in which these factors were directly manipulated to assess their effect on offspring outcomes.

SES effects on emotional and cognitive development [Au: please reduce to 1 line]

SES is a complex construct that is based on household income, material resources, education and occupation, as well as related neighbourhood and family characteristics, such as exposure to violence and toxins, parental care and provision of a cognitively stimulating environment[2,5,10,11] (for controversies regarding the measurement and the defining levels of SES see REFS 1,10,11). Not only the lowest stratum but all levels of SES affect emotional and cognitive development to varying degrees[1,12–14]. This implies that the effects of SES that are reviewed here are relevant to the entire population, although it should be noted that the strongest effects are often seen in people with the lowest levels of SES.

Compared with children and adolescents from higher-SES backgrounds, children and adolescents from low-SES backgrounds show higher rates of depression, anxiety, attention problems and conduct disorders[12,15–18], and a higher prevalence of internalizing (that is, depression- or anxiety-like) and externalizing (that is, aggressive and impulsive) behaviours [Au:OK?] [6,19–21], all of which increase with the duration of impoverishment[12,21]. In addition, childhood SES influences cognitive development; it is positively correlated with intelligence and academic achievement from early childhood and through adolescence [Au:OK?][2,3,6,14,19,22,23].

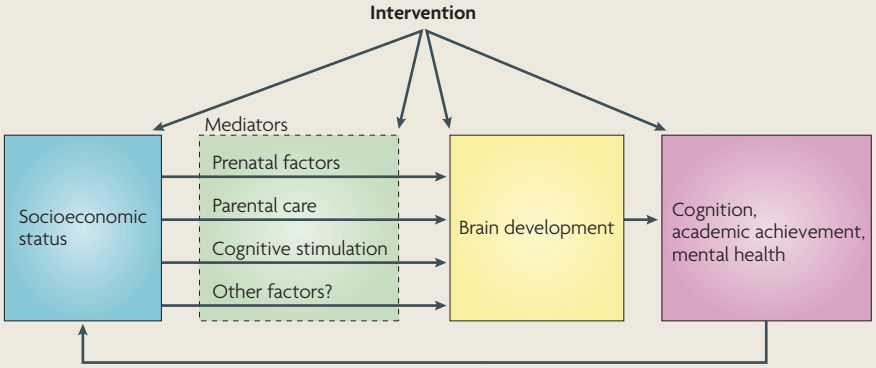
These effects are likely to account, at least in part, for the persistence of poverty across generations[24]: individuals of low childhood SES face various social and economic barriers to success and well-being, and do so with the added disadvantage of worse health, reduced emotional resilience and impaired cognitive skills.

SES and neurocognitive systems

It is difficult to discern the mechanisms that underlie the link between SES and intelligence, academic performance and mental health because each of the outcome variables — IQ, school achievement and diagnostic classifications — reflect the functioning of multiple underlying cognitive and socioemotional systems. Therefore, a promising approach for understanding how SES affects these outcome variables is to identify SES-related differences in the underlying cognitive and affective neural systems (BOX 1).

Childhood SES affects some neurocognitive systems more than others. Studies that assessed multiple neurocognitive systems

Box 1 | **The role of neuroscience in addressing socioeconomic status-related disparities**



Socioeconomic status (SES) has effects on cognition, academic achievement and mental health. These effects reflect the combined functioning of multiple underlying brain systems and are mediated by factors that influence the development of these systems (see the figure). [Au:OK?] Research on brain development enables us to identify the differences in the cognitive and affective neural systems that underlie the effects of SES on cognition, academic achievement and mental health. In addition, neuroscience research in animals and humans can provide biologically plausible candidate mediators for explaining the cause–effect relationships between SES and neural development. These mediators include prenatal factors, parental care and cognitive stimulation, as well as other possible mechanisms (BOX 2). It is also likely that the effects of SES during early childhood on cognition, academic achievement and mental health will influence adult socioeconomic advancement. Each aspect of this schematic (see the figure) is also a potential target for intervention and prevention programmes. These programmes could seek to influence, firstly, SES directly; secondly, the candidate mediators of SES effects; thirdly, aspects of brain development through strategies that include the training of specific neurocognitive functions; and finally, school achievement or psychopathology through changes in curricula or therapeutic treatment. By identifying novel targets for intervention and by providing a more complete explanation of the mechanisms that cause SES-related disparities, neuroscience research will enable the design of specific and theory-driven interventions to prevent and remediate the effects of low childhood SES.

found that the largest effects of SES are on language processing, with more moderate effects on executive function — particularly on working memory and cognitive control[13,25–27]. Additionally, some studies found moderate effects of SES on declarative memory and spatial cognition[13,25,28,29].

Studies that focus on language development have shown an effect of SES on vocabulary, phonological awareness (the ability to reflect on the sound and structure of language; an important ability for learning to read) and syntax[30]. For example, an early, influential study estimated that the vocabulary of American 3-year-olds from professional families is twice as large as that of children in families on welfare[31]. Structural differences in temporal and parietal brain areas that are involved in language have not been found across SES levels in children[32]. However, SES was positively correlated with the degree to which the left (relative to the right) inferior frontal gyrus is activated during a language task in young children[33], indicative of decreased specialization of language function in the left hemisphere in children with low SES. Moreover, left fusiform activity during reading was positively correlated with phonological awareness in lower-SES children, but not in higher-SES children[34].

SES-related differences in the executive functions of working memory and inhibitory control have been noted in children as young as 6–14 months of age[35]. SES-related differences in executive attentional systems have been reported in 6-year-old children[36], and SES-related disparities in various tasks of executive function have been described at multiple developmental stages through early adolescence[13,25,26,37–39]. Likewise, SES influences verbal and spatial working memory in children and adolescents[13,25–26,40], and spatial working memory in late adolescence[41]. Some studies do not find SES differences in all tasks of executive function[40,42–44], although this lack of effect may be explained in part by rigorous exclusion criteria, resulting in samples with particularly healthy and able low-SES children. Studies in adults show similar SES-related disparities in tasks measuring cognitive flexibility, immediate verbal learning and memory, and verbal fluency[45].

There are also SES-related differences in the degree to which specific neural systems are recruited during executive function tasks, even when task performance does not differ between SES groups. For example, event-related potentials (ERPs) reveal that low-SES children exhibit larger responses to unattended stimuli, which is indicative of difficulty in suppressing distraction early in the processing stream and thus, of reduced selective attention[46–47]. In addition, as measured with ERPs, low-SES children do not recruit prefrontal attention circuits in response to novel distracter stimuli to the same degree as higher-SES children[27]. Moreover, in a functional MRI-based task that requires the subject to shift between applying familiar stimulus–response rules and learning new rules, low-SES children preferentially recruit the right dorsolateral prefrontal cortex (DLPFC) when shifting to novel rules[48]. (The DLPFC is a region in which activation is inversely related to accuracy in applying the new rule.)[48].

There is also evidence of SES-related differences in the neural processing of emotion. Lower-SES adolescents exhibit lower left-sided brain activity at rest, as measured by resting alpha-asymmetry at frontal sites, a pattern that is typically seen in patients with depression[49]. Among college students, lower subjective social status is associated with an increased amygdala response to angry faces[50]. In adults, lower subjective social status is related to a smaller volume of the perigenual anterior cingulate cortex[51], a region that is functionally connected with the amygdala and that is implicated in the regulation of emotional states and the risk of affective disorders[52–53].

In summary, there is evidence of robust SES differences in language and executive function, as well as emerging evidence for differences in other cognitive and affective processes. Executive function seems to be particularly important in achieving positive life outcomes despite adversity in low-SES children and adolescents[54,55]. Impairments in executive function are also implicated in various affective and behavioural disorders, and language development in childhood is important for successful school performance[56–60]. Individual differences in these neurocognitive systems are determined in part by SES and these systems therefore emerge as candidate pathways by which SES might compromise academic achievement and increase the risk of mental illness.

Box 2 | **The ecology of socioeconomic status**

In addition to parenting quality and the *in utero* and home environments, there are other factors that may mediate the effects of socioeconomic status (SES) on neural development. These factors include:

- Toxin exposure: low-SES children show increased levels of lead in the blood[5]. Lead is a neurotoxin that affects IQ[144] and school achievement, particularly affecting reading ability[145].
- Nutrition: nutrients and caloric intake influence the neural mechanisms that subserve cognition and emotion[146]. Lower-SES families have less access to healthy foods and are more likely to experience food insufficiency and nutritional deficiency[5].
- Prenatal drug exposure: there is little evidence that prenatal drug exposure is a major contributor to the SES disparities noted in this article. Although alcohol and drug use during pregnancy is related to SES, the direction of the relationship varies by substance, and alcohol use in particular is less common in pregnant women of low SES[147–148]. Furthermore, the effects of prenatal cocaine exposure seem to be relatively small when the effects of other factors, such as the home environment, are controlled for[149].
- Stress: stress affects family relationships, including relationships with children. Low-SES families experience increased stress related to social rank, difficulties in providing for the family's needs, living in dangerous neighbourhoods and other factors. This can lead to chronic stress and thereby affect child development[5,96,150,151]. There is some evidence from research in animals and humans that stress specifically impairs attentional control[152,153], and that indicators of chronic stress exposure mediate the relationship between childhood SES and working memory[41].

Disentangling cause and effect

The association between SES and human brain functioning could indicate that the experiences that are typical of different levels of SES affect brain development ('social causation'). Alternatively, it could indicate that differences in brain functioning predispose people to a particular level of socioeconomic success and, therefore, to a particular SES ('social selection'). The two possibilities are not mutually exclusive and may operate at different times across development such that, for example, social causation may explain SES-related effects on neurocognitive development in childhood and adolescence, which over time may inhibit socioeconomic achievement and thus, SES in adulthood. In addition, it is possible that genomic variation in concert with environmental context may influence both family SES and child development, and that genetic variation may interact with SES to influence neurodevelopmental outcomes. Nevertheless, the current evidence indicates that SES-related differences in neural development, at least in part, reflect social causes.

In the realm of mental health, evidence for the social causation hypothesis of SES-related differences in the prevalence of depression and anxiety is strong (although social selection may also [Au:OK?] operate in schizophrenia, as the SES of people with schizophrenia is likely to decline as a consequence of their illness and illness-related impairments)[18,20,61,62]. Moreover, a natural 'experiment' in which one subset of a population received a sudden income supplement revealed that even small changes in income for impoverished families leads to decreased rates of childhood mental health problems, particularly for clinically significant externalizing behaviours[63]. This not only supports the 'social causation' hypothesis but also indicates that the excess mental health burden of low-SES families may be at least partly reversible by changes in income. In addition, findings from a study of twins indicate that the heritability of internalizing problems can be modified by SES. Here, the environment accounted for a greater percentage of the variation in internalization between twins at low-SES levels[64].

In the realm of cognitive functioning there is considerable evidence that environmental contexts exert causal influence[65]. Cross-fostering studies that compared children who were adopted within or between SES levels also found a strong environmental component to SES-related differences in IQ, again supporting the social causation hypothesis[66]. This approach may in fact have underestimated environmental effects, as the implicit assumption is that prenatal environmental factors are genetic rather than environmental. In addition, the impact of poverty is greater if poverty is experienced in early rather than late childhood[3,12] and this is difficult to explain in terms of heritability alone. Studies comparing mono- and di-zygotic twins also indicate that the magnitude of genetic effects on IQ depends on SES, such that cognitive ability is almost entirely predicted by environmental factors at lower-SES levels[67]. Thus, in addition to the known effects of genomic variation on executive function[68], it is likely that the development of executive function is influenced by the environment, especially at lower-SES levels. It is also worth noting that estimates of environmental effects in studies of twins depend on the variance in environment across the sample, so if there is insufficient variation in SES then overall environmental effects are likely to be underestimated. Moreover, the effects of SES and of genotype interact to produce phenotypes such as serotonin responsivity to fenfluramine [Au:OK?] and attention ability[69,70]. Lastly, some aspects of neural development that are influenced by SES, such as executive function, are also responsive to intervention. This is consistent with the 'social causation' hypothesis and demonstrates that differences may be at least partly reversible[60,71,72].

No single environmental factor is likely to explain all SES effects, and it is probable that specific factors mediate specific aspects of neurodevelopment. Two environmental factors that could mediate SES-related differences in neurocognitive development are healthcare access and education, both of which are better for children in higher levels of SES. Yet, they cannot entirely explain SES effects. For example, gradients of SES effects on health persist in countries with universal health care[1], and SES effects on cognition and neurodevelopment emerge early in childhood, before children have extensive, formal education[13,14,19,26,31,33,35–39,47].

Candidate mechanisms of SES effects

SES influences the quality of the physical and psychosocial environment throughout development[5]. Factors in the environment, such as exposure to cognitive stimulation in the home, toxins, nutrition, prenatal drug exposure and stress — including parental stress and its associated effects on parenting practices and parent-child interactions — might mediate the effects of SES on the brain (BOX 2). Consequently, the challenge is to identify the underlying mechanisms by which SES influences brain development. Hypotheses concerning these mechanisms can be formed and tested by integrating data from studies in humans and from animal models, each of which have different and complementary strengths and weaknesses (BOX 3). We focus on the three potential mechanisms underlying the effects of SES on neurocognitive development that have the broadest empirical support: prenatal factors, parental care and cognitive stimulation (see below).

Prenatal influences. Low SES in pregnant women increases the likelihood of premature birth and impaired fetal growth[73], both of which are predictive of increased rates of

Box 3 | **Animal and human research**

Animal models provide important insights into the effects of socioeconomic status (SES) on brain development, despite the fact that animals do not have SES *per se*. Nevertheless, animal models are able to capture many of the components and correlates of SES — including prenatal factors, postnatal parental behaviour and cognitive stimulation — and allow for a level of experimental control over these factors that is neither possible nor desirable in studies with humans. In addition, in humans these putative environmental mediators of SES effects are correlated with one another. Animal research enables their effects to be isolated and can reveal synergistic interactions among them. Of course, there are limits to the adequacy of animal models for human development, particularly when social and cultural phenomena are of interest. Stress that is induced experimentally in a rat, such as by physical restraint, may not reflect [Au:OK?] the psychosocial aspects of stress that are experienced by a human who is struggling economically. Furthermore, the extent to which parental care or cognitive stimulation correspond between animals and humans is undoubtedly low. Likewise, although efforts can be made to employ parallel outcome measures of certain executive function tasks in human and animal research, animal models of language performance or certain aspects of executive function, such as verbal working memory, are lacking. In humans these factors are nested within larger contexts that may be influential for SES [Au:OK?], for example, there are differences between rural and urban poverty[5]. [Au:OK?] It is therefore crucial to test hypotheses concerning the underlying causes of SES effects directly, by means other than experimental manipulation of the key candidate mechanisms in animal models. This can be accomplished using statistical mediation analysis, natural experiments, intervention studies[71,142] and strategies such as repeated, time-lagged measurements, structural equation modelling and propensity scores[1] to help to strengthen causal inferences. Using neuroimaging and molecular measures as well as the more conventional behavioural measures, this approach could in principle investigate specific neural mechanisms that research in animals has suggested may underlie the effects of SES on cognition and mental health. [Au:OK?]

childhood mental illness and poor school performance[74–78]. Low SES is also associated with higher levels of stress, higher infection rates and poor nutrition during pregnancy. All of these increase plasma levels of corticotropin-releasing factor (CRF) and glucocorticoids in both the mother and the fetus[76,79–81] and can thereby restrain fetal growth[76,79] and trigger prematurity[80]. Glucocorticoid administration during pregnancy is associated with increased externalizing behaviour, shyness, distractibility and inattention, as well as lower IQ in children[82]. Moreover, even modestly low birthweight is linked to smaller hippocampal volume in adults[83]. These findings suggest that conditions that are associated with low SES compromise fetal growth and neurodevelopment, with subsequent effects on neural function that persist into adulthood.

In rodents, pre- or peri-natal glucocorticoid administration to pregnant females reduces brain weight at birth, inhibits neurogenesis and delays neuronal maturation, myelination, gliogenesis and synapse formation[79]. Moreover, maternal stress during pregnancy decreases spine density in multiple brain areas that are related to emotion regulation, including the hippocampus, anterior cingulate and orbitofrontal cortex[84], and increases behavioural and hormonal responses to stress in the offspring in adulthood[76,79,85–87]. The effects on stress responsiveness in adulthood are abolished by normalization of glucocorticoid levels during pregnancy[88]. In Rhesus monkeys, fetal exposure to elevated glucocorticoid levels reduces hippocampal volume in adulthood[89]. The offspring of female Rhesus monkeys that were stressed during pregnancy exhibit decreased birthweight, impaired neuromotor development, attention deficits and emotional dysregulation across the lifespan[90]. Moreover, there is evidence in rodents that prenatal influences on hypothalamus–pituitary–adrenal (HPA) axis activity can be transmitted across generations in an epigenetic manner[91] (see below). Together, these findings suggest that in pregnant women, stressors that are associated with low SES predict birth outcomes that mimic the effects of increased fetal glucocorticoid exposure on neurodevelopment and that may persist across generations. Consequently, it is likely that SES effects might emerge during fetal development.

Parental care. Prenatal factors are unlikely to explain all of the effects of SES on neurodevelopment, particularly as SES effects are often still apparent even after controlling for birthweight[92]. Postnatal parental stress influences child development by decreasing parental involvement and care, as described by the family stress model[4]. In humans, low SES is associated with greater irritability and depressed and anxious moods in parents, which compromise parent–child interactions[93,94]. Parental stress leads to harsh and inconsistent discipline, less sensitivity to the needs of the child, reduced verbal communication and, in the children, insecure attachment to the primary care-giver[6,31,93–96]. Familial conflict and problematic parental behaviour — including (but not limited to) harsh and inconsistent discipline, neglect and abuse — are associated across all levels of SES with emotional and behavioural problems in children. These problems are not only observed when measured concurrently, such that parenting quality [Au:OK?] correlates with emotional and behavioural patterns in the child, but also when measured prospectively, as the quality of [Au:OK?] earlier parenting predicts children's emotional and behavioural patterns years later[94–95,97–99].

Parental care, and in particular parental discipline, parent–child verbal communication and sensitivity to the emotional needs of the child, at least partially mediates the effects of SES on emotional and cognitive function in children[6,19,92,100]. High-quality parent–child interactions are associated with resilience among children who live in stressful, impoverished environments[101]. Moreover, clinical programmes that aim to improve parenting practices in poor, high-risk families improve behavioural and cognitive outcomes in children[102–104], providing experimental evidence that is consistent with the role of parenting as a mediator for the effects of SES. The quality of parental care in early childhood predicts, in a longitudinal study of a low-SES sample, better declarative memory and smaller hippocampal volume in low-SES adolescents, and these associations are independent of cognitive stimulation (see below) and maternal intelligence[105,106].

Studies in rodents and non-human primates have revealed evidence for direct effects of stress on the quality of mother–infant interactions and on gene expression and neurodevelopment. In Bonnet macaques, restricted access to food is a stressor that greatly impairs mother–infant interactions, which in turn increases stress reactivity in the adolescent offspring, reflecting an enduring effect of parental care[107]. Likewise, in rodents, the frequency of licking and grooming of pups by the mother is diminished by chronic stress imposed during pregnancy[108,109]. Variations in the frequency of licking and grooming of rat pups are associated with changes in the neural systems that regulate behavioural and HPA responses to stress in adulthood (FIG. 1). The HPA response to

stress in mammals is largely mediated by the release of CRF from the hypothalamus, which is under negative feedback control from glucocorticoids, in part through the activation of glucocorticoid receptors in the hippocampus. The adult offspring of dams that exhibit high licking and grooming of pups show increased hippocampal glucocorticoid receptor expression, decreased hypothalamic CRF levels and more modest HPA responses to stress compared with the offspring of dams that exhibit low licking and grooming[110–114]. Adult offspring of mothers that exhibit high licking and grooming also have enhanced expression of genes for $GABA_A$ (γ-aminobutyric acid type A) receptor subunits in the amygdala that regulate inhibitory influences over stress responses, rendering the animals less fearful[110,111]. Cross-fostering studies in rats have revealed direct effects of postnatal maternal care (that is, independent of genomic influences) on hippocampal physiology and on the response to stress in the adult offspring[111,113]. Importantly, in rats, chronic stress during pregnancy alters the quality of mother–infant interactions[107,108], reducing the frequency of pup-licking in the dam and increasing stress reactivity in the offspring[113], and these effects can be transmitted across generations[115]. These findings recapitulate the theme that is apparent in studies of SES and human parenting, namely that stressful environments alter the quality of parenting and thus, the developmental outcomes.

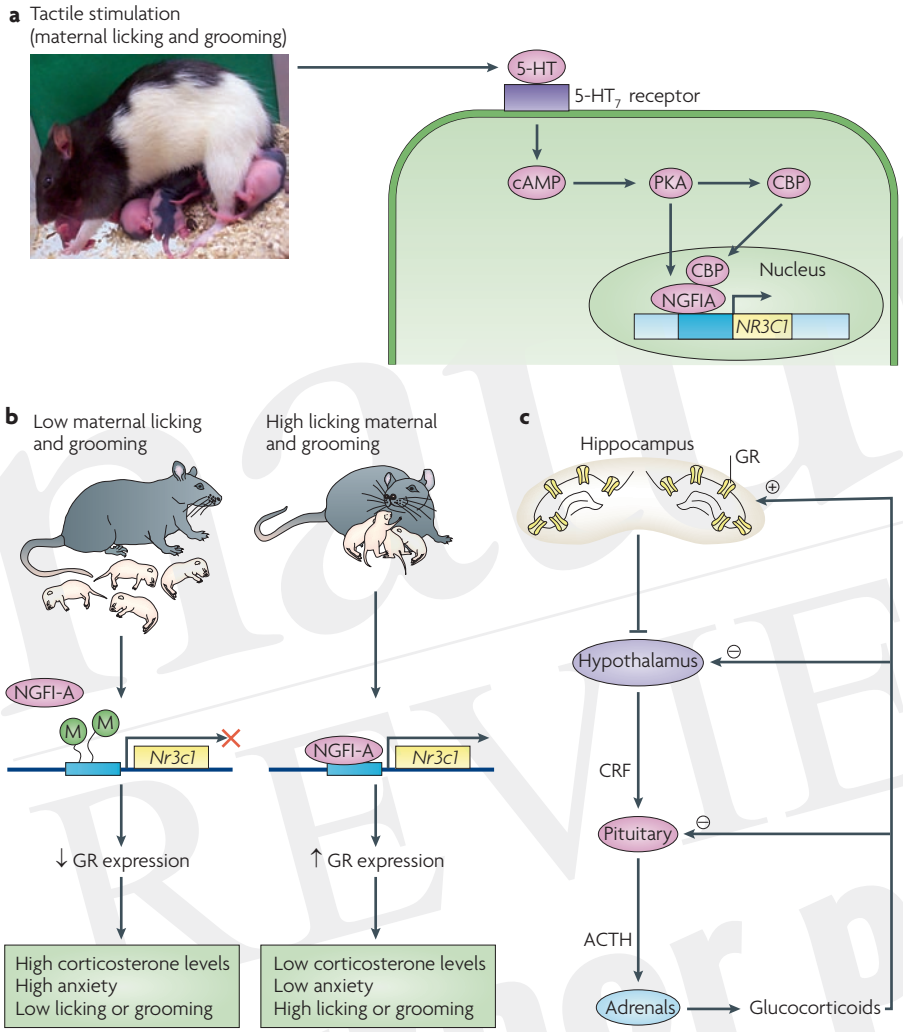


Figure 1 | **Parental regulation of the hypothalamic–pituitary–adrenal axis. a** | The current working model for the effect of maternal care (specifically, of licking and grooming pups) on the epigenetic regulation of the expression of *Nr3c1*, the gene that encodes the glucocorticoid receptor (GR). Licking and grooming of pups activates thyroid hormone-dependent increases in hippocampal serotonin (5-hydroxytryptamine or 5-HT) levels and 5-HT binding to the 5-HT_7 receptor. Activation of the 5-HT_7 receptor leads to the activation of a cyclic AMP–protein kinase A (PKA) cascade that induces the expression of the transcription factor nerve growth factor-inducible A (NGFIA) and cyclic AMP response element-binding (CREB) protein (CBP) expression and their association with the neuron-specific exon 1_7 GR gene promoter. **[Au:OK?] b** | In neonates, high levels of licking increases NGFIA and CBP association with the exon 1_7 promoter by triggering demethylation of a dinucleotide sequence (CpG) that is located within the NGFIA binding region of the exon. This subsequently increases the ability of NGFIA to activate GR gene expression. M, methylation. **c** | A schematic of the hypothalamic–pituitary–adrenal axis, the pivot **[Au:OK?]** of which are the corticotropin-releasing factor (CRF) neurons of the paraventricular nucleus of the hypothalamus. CRF is released into the portal system of the anterior pituitary, stimulating the synthesis and release of adrenocorticotropin (ACTH), which then stimulates adrenal glucocorticoid release. Glucocorticoids act on GRs in multiple brain regions, including the hippocampus, to inhibit the synthesis and release of CRF (that is, glucocorticoid negative feedback takes place). The adult offspring of mothers that exhibit high licking and grooming, by comparison to those of low licking and grooming dams, show increased GR expression, enhanced negative-feedback sensitivity to glucocorticoids, reduced CRF expression in the hypothalamus and more modest pituitary–adrenal responses to stress.

Studies in rats have suggested that epigenetic mechanisms mediate the effect of maternal care on hippocampal glucocorticoid receptor expression. This mechanism involves DNA methylation, which affects chromatin structure and thereby regulates transcription factor binding and subsequently, gene transcription[116]. As adults, the offspring of mothers that exhibit high licking and grooming show decreased cytosine methylation of the binding site for the transcription factor nerve growth factor-inducible A (NGFIA, also known as EGR1) that lies within the exon 1_7 promoter of *N1r3c1* (the gene that encodes the glucocorticoid receptor in the hippocampus; this results in increased NGFIA binding to this promoter, increased hippocampal glucocorticoid receptor expression and more modest HPA responses to stress[114,117,118]. In humans, child abuse is associated with increased methylation of the exon 1_F glucocorticoid receptor gene promoter (the homologue of exon 1_7 in rats) in the hippocampus[119]. These findings suggest that the effects of parental care may be mediated through a similar epigenetic mechanism in humans, although it remains to be investigated whether differences in childhood SES are associated with differences in DNA methylation and gene expression.

Variations in maternal care in rats also influence synaptic development in brain regions that regulate cognitive function. Licking and grooming of pups increases NMDA (*N*-methyl-D-aspartate) receptor

levels in the hippocampus and hippocampal expression of growth factors (brain-derived neurotrophic factor and basic fibroblast growth factor), which promote neuronal activation and synaptogenesis, respectively[120,121]. The adult offspring of mothers that exhibit high licking and grooming show increased synaptic density[120,122] and a greater capacity for synaptic plasticity in the hippocampus and prefrontal cortex (*in vivo*[123] or *in vitro*[122]), and improved performance in hippocampal and prefrontal cortex-dependent forms of learning and memory[120,123]. The effects on synaptic development and cognitive performance are reversed with cross-fostering[120], indicating that parental care has direct effects on neuronal development that are consistent with those reported in studies of cognitive development in children.

It should be noted that although the majority of the research described above focuses on maternal care, particularly in animal models, it is not necessarily the case that in humans only mother–child interactions influence the cognitive and emotional development of offspring. It is likely that nurturing and supportive care-giving by parents of either gender or by other members of the community is important for child development[124]. The important point is that broader social and economic context can influence the quality of parental care, which then influences the activity of the neural systems that regulate stress reactivity and cognition in offspring through the epigenetic regulation of gene expression.

The home environment: cognitive stimulation. SES influences the level of cognitive stimulation in the home, as described by the family investment model[4,6]. The quality of cognitive stimulation in the home includes, but is not limited to, factors such as the availability of books (and other literacy resources), computers, trips and parental communication. Together, these factors can explain the effects of SES on cognitive ability in children (for example, on reading and mathematics skills[12,19,21,23,92,125,126]) even when maternal IQ has been controlled for. The effect may be fairly specific as, in a longitudinal study, the level of cognitive stimulation in early childhood predicts language-related skills in low-SES adolescents independently of the quality of parental care and maternal intelligence[105].

Additional evidence for these effects emerges from studies of intervention programmes that enhance cognitive stimulation. Such programmes buffer **[Au:OK?]** the effects of low SES on cognitive development[6], boost school readiness[127] and promote academic achievement[128], even in studies in which baseline cognitive functioning and maternal education have been controlled for[129]. Such interventions also increase self-esteem and social competence[129], and reduce aggression[130], particularly among the most deprived children[131]. The key point is that the effects of poverty on specific cognitive outcomes can be reversed, in part, through enhanced cognitive stimulation. Long-term follow-up observations of the effects of early intervention, including randomized controlled trials, come from programmes such as the Perry Preschool Program (Michigan, USA), the Abecedarian Project (North Carolina, USA) and the Chicago Child–Parent Centers, USA. These include increased cognitive stimulation as part of more comprehensive intervention programmes. Intervention programmes caused higher scores on achievement tests, higher levels of education and income, and lower rates of incarceration decades after the completion of the programmes, despite the fact that in some studies the initial gains in IQ disappeared[132–135]. Such effects suggest that although experience at any age affects later outcomes, early cognitive stimulation is a particularly important determinant of later psychological functioning.

Animal models also provide a strong rationale for cognitive stimulation as a mediator of SES effects on neural development. Hebb observed that environmental complexity during development alters a wide range of neural functions[136]. Studies of environmental enrichment in which animals are housed under conditions that provide increased sensory, cognitive and motor stimulation (usually accompanied by increased social complexity) show that enrichment upregulates the expression of cellular signals that are involved in activity-dependent synapse formation. This includes factors that are involved in glutamatergic signalling[137], neurotrophins (including insulin-like growth factor 1, nerve growth factor, brain-derived neurotrophic factor and glial-derived neurotrophic factor), and synaptic proteins that are involved in synaptic proliferation and function[138]. Enrichment therefore increases dendritic branching, gliogenesis and synaptic density in the hippocampus and cortex, and promotes hippocampal neurogenesis and the integration of newly generated neurons into functional circuits[138–140]. These enrichment effects are associated with improved performance in tests of spatial learning and memory[138]. Rodents that were exposed to adversity in early life are more sensitive to environmental enrichment in adolescence[120,137,140]. Thus, basic neuroscience research shows how neurodevelopment is affected by variations in cognitive stimulation, a characteristic that often relates to SES.

Conclusions and policy implications

SES influences cognitive and emotional development. Nevertheless, the concept of SES has long been ignored in neuroscience, perhaps because of the complexity of the construct and the difficulty of experimentally controlling its many components. The research discussed here suggests that SES can be understood within the framework of neuroscience research. Childhood SES influences the development of specific neural systems. The biological nature of these SES-related differences may be easily misinterpreted as more 'essential', innate or immutable than SES-related differences in behaviour. However, as reviewed here, there is little evidence for such a claim. Instead, studies in humans suggest that prenatal factors, parent–offspring interactions and cognitive stimulation at least partly underlie the effects of SES on brain development. These effects are somewhat specific, with the level of cognitive stimulation in the home environment best predicting a child's cognitive development and the quality of parental care more closely related to its emotional development. Studies in non-human animals support the biological plausibility of these explanations. However, future research is required to confirm that these factors indeed account for SES effects on neural development and to apply this work to the development of more effective interventions.

Although these are early days for the study of SES and brain development, the integration of social and neural approaches to SES has a number of policy implications. First, it highlights brain development as a new target for intervention and prevention programmes (BOX 1). Until now, interventions have been targeted at changing SES directly by increasing family income[63,141], influencing the putative mediators of SES effects, such as parenting style, and influencing academic achievement and psychopathology through direct interventions, including educational or treatment programmes targeted at low-SES communities. The targeting of brain development has involved familiar approaches, such as improving children's access to medical care or nutritional supplementation. More recently, it has included programmes aimed at training particular neurocognitive systems directly, for example by using

computerized, game-based strategies for training executive functions or school curricula that employ specific exercises as well as overarching strategies to promote executive functions throughout the school day[60,71,72]. Such approaches seem to be promising from the perspective of basic neuroscience research, but future studies must empirically determine if such programmes reduce SES-related disparities.

Second, our emerging understanding of SES-related differences in neurocognitive systems places these disparities into a broad public health perspective. Converging evidence that differences in levels of parental care and cognitive stimulation in the home underlie SES-related differences in brain development highlight the importance of policies that shape the broader environments to which families are exposed. This evidence extends the discussion of child development beyond traditional policy arenas such as education and child-care. Precedence should be given to improving care for children and to providing enriching environments during pre- and post-natal development. [Au:OK?] Therefore, policies and programmes that reduce parental stress, enhance parental emotional well-being and provide adequate resources for parents and communities should be prioritized. [Au:OK?] Moreover, as women are often a child's primary caregiver, the effects reviewed here emphasize the significance of women's health, emotional well-being, material resources and education for child development[142].

The incorporation of SES into neuroscience research will become increasingly important as neuroscience is brought to bear in educational, marketing and forensic contexts. The applications of neuroscience in these contexts are often developed on the basis of findings in [Au:OK?] largely middle-SES subjects and therefore may not be broadly applicable to the population[143]. Neuroscience research has a unique role in synthesizing approaches from multiple disciplines that include sociology, medicine, public health, psychology and psychiatry to characterize SES-related differences in neural development and to chart the mechanisms through which childhood experience affects neural function. First, a neuroscience approach permits us to identify the neural phenotypes related to SES that underlie cognitive performance and mental health, and the potential targets for intervention. Second, an understanding of brain development in humans and animal models can be leveraged to define the causal relationship between 'SES-related exposures' and neural development. The investigation of SES and neural development is a promising area of study that, by delineating environmental influences on individual differences in neural development, can refine strategies to address SES-related disparities.

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Competing interests statement

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Socioeconomic status and the brain: mechanistic insights from human and animal research

Daniel A. Hackman, Martha J. Farah and Michael J. Meaney

Socioeconomic status (SES) influences brain development. Farah and colleagues show that prenatal factors, parent–child interactions and cognitive stimulation mediate this effect, and show that intervention at these levels can alleviate SES-related disparities in mental health and academic achievement. **[Au:ok? Word limit is 40 words.]**