Neurobiology of Stress 17 (2022) 100426

Contents lists available at ScienceDirect

Neurobiology of Stress

journal homepage: www.elsevier.com/locate/ynstr

Connecting the biology of stress, allostatic load and epigenetics to social structures and processes

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ARTICLE INFO

Keywords:
Toxic stress
Allostatic load
Early childhood
Poverty
Social determinants of health

ABSTRACT

How do sociology and stress biology connect in efforts to understand the impact of early childhood adversity on health and life chances? This memorial article describes the collaboration between Bruce and Craig McEwen in bringing stress neurobiology to sociologists. It attempts, in turn, to bring sociology to stress neurobiologists, the second goal of this collaboration. It frames the social sources of human stress in terms of the social determinants of health as well as more proximal childhood adversities. It also underlines the importance of supportive adult and community relationships in preventing toxic stress. Bruce was hopeful that stress biology research could inform public health efforts aimed at improving population health and more equitable life trajectories. To strengthen our understanding of stress and to contribute to that goal, stress neurobiologists can help tease out the complex social causes of stress by expanding the range of variables employed to identify its sources as well as the protections against it in human populations.

How do stress neurobiology and sociology connect? This article tells the story of what may seem to be an unlikely collaboration, helped along by close brotherly ties between Bruce and me and by our shared interest in understanding and addressing social inequalities. Our collaboration led to an attempt to bring the neurobiology of stress to skeptical sociologists. Another goal was to enlist stress neurobiologists in an effort to tease out the complicated social sources of toxic stress as well as the relational factors that protect against it. This article takes on that latter challenge.

1. An unlikely collaboration

For almost fifty years, Bruce's career and mine were entirely separate. Bruce's path led him from chemistry to cell biology to neuroscience and behavior and then to epidemiology and public health while running a laboratory with graduate students and post-docs. At the core of his evolving research was the epigenetics of stress hormone action on the brain and both the resultant damage to brain architecture and the adaptive plasticity of the brain in responding to the damage. A key element of this work built on the recognition that social experience shapes the brain and body epigenetically. Bruce's sociological awakening was encouraged and supported by participation in two MacArthur Networks, one on Health and Behavior and the second on Socioeconomic Status and Health. Further awakening occurred through his ongoing engagement with the National Scientific Council on the Developing Child. And the fact that I am a sociologist and that we talked regularly about our work during the last 20 years provided an important impetus to Bruce's growing self-identity as a molecular sociologist.

My trajectory as a sociologist took me from research about youth training schools and community-based alternatives for adjudged delinquents to studies of mediation, alternative dispute resolution, courts and lawyers, while teaching undergraduates. Along the way I drank from the sociological cup of suspicion about biological explanations of human behavior which seemed from the sociologist's perspective to be imperialistic – biology, especially genes, as destiny.

But Bruce and I shared an upbringing by socially conscious parents and Oberlin College educations where our social consciences were nurtured. Through my volunteer work with the United Way of Mid Coast Maine, which placed a priority on strengthening supports for early childhood development, I began to learn more about childhood adversity and talk with Bruce about his research, and he was eager to know about work on the ground with Maine families. Bits and pieces of stress neurobiology entered my teaching. Then, Bruce and I were invited to give the keynote at the May 2011 Annual Meeting of the United Way on "Early Childhood Experiences: What's at Stake for our Community's Health and Education." This extended my biology awakening, and I began to deepen my understanding of how social processes and structures help shape human neurobiology, which in turn influences behavior

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https://doi.org/10.1016/j.ynstr.2022.100426
Received 1 November 2021; Received in revised form 29 December 2021; Accepted 2 January 2022
Available online 4 January 2022

and life trajectories.

That United Way event provided the impetus for me to commit as my retirement project to learning about the neurobiology of stress as it relates to early childhood development and to the social contexts of families. For Bruce, who was engaged as a member of the National Scientific Council on the Developing Child, this was already comfortable territory, and he was happy to connect me with resources and contacts and to further strengthen his identity as a molecular sociologist.

So began our quest to bring the biology and neuroscience of stress to sociology and to imbue biology and neuroscience with deepened social context. Our co-authored article for the *Annual Review of Sociology* took on the former challenge (McEwen and McEwen 2017). It aimed at widening the theoretical perspectives and empirical frameworks of sociologists to include the potential impact of social processes, structures and relationships on human biology generally and stress neurobiology in particular. In doing so, it turned on its head the biological (genetic) determinism that sociologists fiercely resist and encouraged the inclusion of toxic stress as an intervening variable in empirical and theoretical work explaining how the social conditions of households influence the health and life trajectories of children.

Our 2019 joint lecture at the University of Pennsylvania on "Inequality and Early Childhood Adversity: Toxic Stress and Its Epigenetic Effects," only six weeks before Bruce's untimely death, furthered our collaboration and spoke to biologists and neuroscientists as well as to social scientists. This article builds on that lecture.

2. Bringing stress neurobiology into sociology

The problem that engaged our joint attention was the reality of intergenerational poverty in the United States, notwithstanding our national self-perception as a country of open, upward mobility. Early childhood poverty significantly increases the odds that children will not be ready for school at age 5, will not complete high school, and will be poor as adults. For example, Wagmiller and Adelman (2009) reported that of 35-year-olds who spent no time in poverty as children, less than 1% were poor as adults, but 8% of those who had spent less than 50% of that time in poverty were poor at 35, as were 45.3% of those spending over half their childhood in poverty. Identifying the forces that explain these differentials is a central issue for sociologists. The mechanisms that we typically attend to for that explanation include lack of pre-schooling, poorly funded and ineffective schools, economic barriers to higher education, challenging neighborhoods, and limited parental resources to promote child development.

Bruce helped me bring the stress neurobiology of early childhood adversity into the sociological conversation about inequality. The early childhood embodiment of inequality resulting from toxic stress appears to be another important mechanism shaping these odds. Joining the perspectives of neuroscience and sociology focuses us on toxic stress emerging from early-childhood adversities that themselves often result from social inequality, as well as from troubled relationships in the household and beyond. Toxic stress can have profound impacts on the ways that the brain and body develop and thus on life trajectories.

The approach Bruce and I developed provides comfort to sociologists by giving social forces preeminence in shaping aspects of biological processes of growth and development. It then points to the reciprocal role of biology for individual life trajectories and for social disparities in health, wealth and well-being. Fig. 1, reprinted here with permission from the Annual Review article, represents this approach (McEwen and McEwen 2017:449) and provides the major section headings of this article.

Although not its focus, Bruce's 2012 paper "Brain on stress: how the social environment gets under the skin" provided the sociological frame

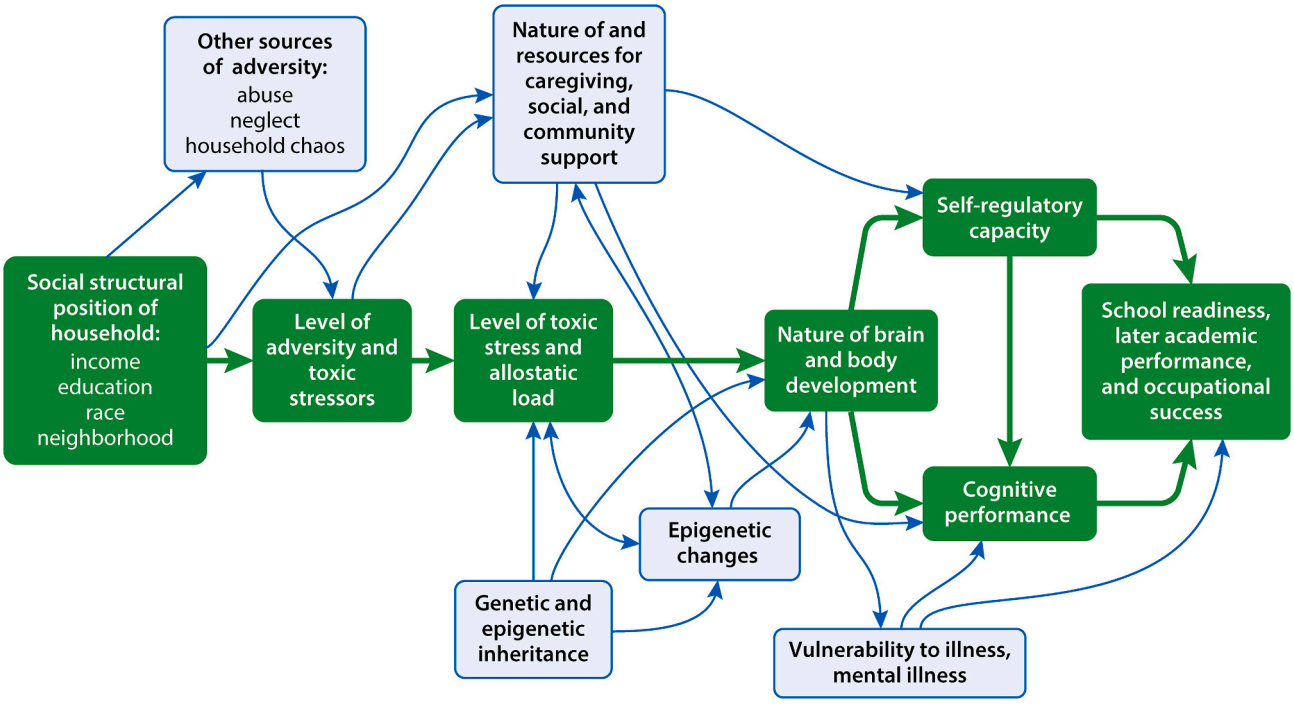

Fig. 1. A model of social structure, social supports, adversity, toxic stress and brain/body development in early childhood. Social circumstances (economic, neighborhood, household, and other) affect levels of adversity, which in turn cause toxic stress that results in allostatic load if strong, positive social supports are unavailable. Toxic stress and resulting allostatic load affect brain and body development and function in childhood, partially through epigenetic changes mediated in part by the neuroendocrine system. Genetic and epigenetic factors also affect the degree of individual sensitivity to toxic stress. The effects on brain and body development diminish emerging self-regulatory capacity and cognitive performance and increase vulnerability to physical and mental illness. Together, these effects reduce school readiness and later academic performance. Given the plasticity of the developing brain, many of these effects are reversible through social intervention.

for examining toxic stress and the biological pathways it follows to have an impact on child development as well as health and school success (McEwen, 2012). The boxes in Fig. 1 labeled *Social Structural Position* and *Other Sources of Adversity* were anticipated in that paper. He noted that "low socioeconomic status (SES) increases the likelihood of stressors in the home and neighborhood" (McEwen, 2012: 17182). He also underlined the important role of other sources of adversity, including adverse childhood experiences and chaos in the home. That paper recognized as well the importance of what he called "nurturing environments" – here in Fig. 1 labeled *Nature of Resources for Caregiving, Social and Community* Support – as potential moderators of the impact of adversity and as resources for rebuilding brain architecture.

Stress neurobiologists understand that such experiences epigenetically shape the brain, body and behavior in ways that, fortunately, are amenable to positive intervention. The green boxes in Fig. 1 represent the rough causal path we imagined for early childhood adversities created by social inequalities and by household dysfunction, recognizing that all of these are modulated by the availability of positive and supportive relationships with adults. Those adversities may result in levels of toxic stress manifested as allostatic overload (McEwen and Gianaros 2011). The extent of toxic stress, in turn, can affect epigenetically the path of brain development through what the genetic endowment will allow. As a result, toxic stress affects not only long-term health issues such as depression, substance abuse, diabetes and cardiovascular disease (Felitti et al., 1998) but also cognitive performance and self-regulatory capacity which impact school readiness and achievement and later occupational success (Evans and Schamberg 2009; Kim et al., 2013; Wagner et al., 2016; Farah 2017; Evans et al., 2021).

The Annual Review article emphasized the neurobiology of stress and encouraged sociologists to move beyond suspicion of biological explanations and incorporate the biology of stress into multi-dimensional and multi-disciplinary examinations of social inequality. That was the first mission of our collaboration. This article attempts to achieve the second mission that Bruce and I envisioned but were unable to complete together – one focused on encouraging neurobiologists to become more sociologically attentive in helping untangle the social sources of toxic stress and of the protections against it.

3. Social Structural Position of household and social determinants of health

The neurobiology of stress with human subjects has repeatedly looked to poverty or socioeconomic status (SES) as a predictor of health and as a source of stress. The MacArthur Network on Socioeconomic Status and Health (1996–2009), in which Bruce participated, focused attention on SES and led to an issue in the Annals of the New York Academy of Sciences on *The Biology of Disadvantage: Socioeconomic Status and Health* (Adler and Stewart 2010). Bruce's article with Peter Gianaros (McEwen and Gianaros, 2010) in that issue focused on stress-related pathways to health induced by financial hardship, feelings of marginalization, and subjective social status. Thus, Bruce was among the stress biologists and neuroscientists who gave much attention to income and the more complex construct of socioeconomic status in research (Farah 2017). Teresa Seeman et al. (2010) and others, including Bruce, linked lower SES to higher allostatic load over the life course. Strong evidence points to correlations between early childhood poverty and neurocognitive development (Farah et al., 2006; Noble et al. 2007), leading Martha Farah (2017) to review the "The Neuroscience of Socioeconomic Status" in *Neuron* in 2017.

However, this focus on SES and poverty only suggests the broader social context shaping health and life trajectories that Richard identified, first for the World Health Organization in 1998 and expanded in their edited book, Social Determinants of Health (Marmot and Wilkinson 1999). According to the World Health Organization (WHO), these social determinants of health (SDOH) are: the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies, and political systems (WHO 2021).

The goal of the highly influential SDOH framework was to help explain the vast disparities in health across and within nations. Marmot was an early member of the MacArthur Network with Bruce. Their exchanges must have moved Bruce further toward his identity as a molecular sociologist. They also, apparently, cemented Marmot's emphasis on stress neurobiology and allostatic load as central mechanisms through which the social determinants impacted health; Brunner and Marmot (1999) cited Bruce's 1998 paper (McEwen, 1998) in the book on SDOH. Awareness of this broader SDOH perspective on the social conditions affecting health was evident in the Network's collection on The Biology of Disadvantage with its chapters on neighborhood, work, and the social construct of race[1] as well as on social class (Adler and Stewart 2010).

Marmot and Wilkinson recognized that the many unique combinations of social conditions as well as genetic variation would modulate the effects of the social determinants across individuals. These were not determinative at an individual level. But as social epidemiologists they were concerned with population health – "the health outcomes of a group of individuals, including the distribution of such outcomes within the group" (Kindig and Stoddard 2003:380). Thus, the social determinants of health operate at the population level and have important implications for public health and social policies designed to improve population health and health equity.

As Bruce and I saw it, these social determinants shaped not only population health, but also the probabilities of differing life trajectories. For example, research evidence makes clear that school performance, behavioral problems, educational attainment, and adult earnings and work hours have a graded relationship to the social class of origin (Garcia and Weiss 2016; Duncan et al., 2010; Hackman and Farah 2009; McLeod and Kaiser 2004; McLoyd 1998). School readiness and school performance gaps by race/ethnicity and income in the United States widened between 1998 and 2010 and then declined, but they remain substantial (Reardon 2011; Reardon and Portilla, 2016). Although many social mechanisms help explain these differential patterns, biological pathways with stress as a central link add to the explanation. The SDOH frame enlarges the scope of the social forces at work beyond income and social class that can create toxic stress and affect those biological pathways.

3.1. Wealth

Differentials in wealth have independent impact on health, behavioral and academic outcomes for children, even while controlling for income (Miller et al., 2021; Conwell and Ye 2021). Wealth is often measured as net worth and provides an important indicator of how available assets – above and beyond current income – affect meeting basic needs and shaping life choices. The extent of household wealth affects the sense of economic security and well-being, capacity to invest in children, and the level of parental stress (Gibson-Davis and Hill, 2021). Availability of savings or of equity in house or investments provides a buffer against variations in income.

Inequalities in wealth are even more pronounced in the United States than income inequality. Profound wealth differentials are found by race and ethnicity where White children reside in households with assets that average 14 times the assets of households of Black children and six times the assets of Hispanic children (Gibson-Davis and Hill 2021). These inequalities affect child development (Shanks 2008) and school achievement, at least marginally (Conwell and Ye 2020). Even body-mass index relates inversely to household wealth (Boen et al. 2021).

[1] Throughout this article, race and ethnicity are referenced as social constructs, not biological categories. See Gannon, 2016, for example.

3.2. Race/ethnicity and racism

In a working paper dedicated to Bruce, the National Scientific Council on the Developing Child (2020:16) observed that "The long-standing designation of race as a risk factor for disparities in health outcomes diverts critical attention away from systemic racism and its deep historical roots as a pernicious cause of stress-related disease." A recent Policy Statement by the American Academy of Pediatrics asserts that "Racism is a core social determinant of health that is a driver of health inequities" (Trent et al., 2019). These effects presumably come from day-to-day stresses that affect caregivers and are compounded by the legacy of racism in laws and structured inequality in schooling, health care, housing, community and individual resources (National Scientific Council 2020). A substantial research literature documents inequities in health across racial and ethnic lines as well as gaps in educational outcomes, income and much else. For example, a review of research reports and meta-analyses of studies of self-reported experience with racial discrimination and health status concluded that such experiences relate both to mental health and many indicators of physical health (Williams et al., 2019). An earlier meta-analysis found not only links between perceived discrimination and physical and mental health but also with heightened stress responses (Pascoe and Richman 2009).

Biological processes play a role in creating these health disparities. The weathering hypothesis, for example, proposes that chronic exposure to disadvantage promotes acceleration of the normal aging process and earlier onset of poor health with allostatic load providing the key indicator of weathering (Geronimus et al., 2006). A recent review of relevant research showed that race/ethnicity relates to higher allostatic load, chronic stress, and greater evidence of inflammation (Forde et al., 2019). The research by Geronimus et al. (2006) found greater probability of high allostatic load scores for nonpoor Blacks than for poor Whites.

A decade ago Williams et al. (2010) pointed to the critical need for research that untangles the interconnected pathways through which race and racism shape health and well-being over the life course. Part of the challenge in doing so is to recognize the impact of multiple forms of racism – structural, institutional, individual and internalized (Smedley 2012). Experience of discrimination provides a measurable but arguably weak measure of the lived experience of racism. The less well seen but grinding daily reality of racism creates a background condition and daily micro-stressors that can make individuals hypervigilant and, as the stressors accumulate, contribute to toxic stress (Harrell 2000; Wyatt et al., 2003). A thorough review of downstream, midstream, and upstream causes of racial disparities in rates of premature births concludes that, "Racism is the only factor identified by this review that directly or indirectly could explain the racial distributions of all of the downstream and midstream causes, including [stress and] socioeconomic factors" (Braveman et al., 2021: 12).

3.3. Neighborhood

The nature of neighborhoods where children live has an independent effect on health and life trajectories but is interwoven with other social determinants such as segregation by SES and race/ethnicity (Williams and Collins 2001; Acevedo-Garcia et al., 2008). Average income in a neighborhood helps predict the reading and math scores of children (Sastry and Pebley 2010), and long-term residence in a disadvantaged neighborhood significantly reduces the chances of high school graduation (Wodtke et al., 2011). Being exposed to neighborhood poverty across generations diminishes children's cognitive capacity significantly (Sharkey and Elwert 2011). Linking these geographic patterns to biological processes, Schultz et al. (2012) found that indicators of allostatic load correlated with poverty level in a neighborhood, independent of household SES (Schultz et al., 2012). Other research found that both lower individual income and lower community socioeconomic status independent of individual income predicted attenuated brain serotonergic responsivity that is related to the metabolic syndrome and perhaps with behavioral problems (Manuck et al., 2005).

3.4. Other social determinants and public policy context

As noted earlier, the broad social frameworks of SES and wealth, race/ethnicity, and place frame more particular social determinants that structure people's lives. The World Health Organization includes these, for example: education, employment and job security, work-life conditions, housing access, food security, social inclusion and access to healthcare. The seminal Whitehall study of British civil servants that Bruce was exposed to through Michael Marmot exemplifies these. That research found the lower the civil service rank, the greater the probability of heart disease and, in a later study, that the degree of control over one's work showed an inverse relationship to vulnerability to heart disease (Marmot et al., 1984; Bosma et al., 1997).

Although the evidence is strong that the broad framework of social determinants operates similarly across nations, it is also clear that their effects are accentuated or buffered by variations in culture and social policy. Greater gaps by income in the early cognitive development of children in the United States compared to the United Kingdom, Australia and Canada appear to result from the differential distribution across nations of other parental resources (Bradbury et al., 2019). Social policy differences affect the burden of poverty in a society, for example, and particular social determinants of health such as unemployment, education, work-life conditions, supports for early childhood development, food and housing security, and many more. As a result, the nature or degree of relationship between the social determinants and stress as well as health and well-being are likely to be stronger or weaker in some nations (and states) than in others. For example, research about subjective sense of children's well-being concluded that it "is comparatively higher in those countries where family policies are more generous in the areas of preschool education, family services, family spending and duration of paid parental leave" (Mı'nguez 2017:1173). An examination of health disparities by SES over time and across nations leads to the conclusion that "current SES gradients in the United States are neither inevitable nor immutable," and a comparison of life expectancy trends with Canada suggests that a weaker safety net in the U. S. and other social policy differences are likely explanations of slower growth in life expectancy in the U. S. than in Canada (Dow and Rehkopf 2010:24).

4. Other sources of adversity – households

The social determinants of health provide a broad frame for looking at more proximal sources of stress-inducing adversity – labeled in Fig. 1 "Other sources of adversity: abuse, neglect, household chaos." The social structures in which people live and work help shape what happens in households, and what happens there matters for health and child well-being.

Research about Adverse Childhood Experiences (ACEs) developed in parallel to emergence of the neurobiology of SES and the identification of the social determinants of health. The path-breaking CDC-Kaiser Permanente study about ACEs first appeared in print in 1998 (Felitti et al., 1998). This social epidemiological research utilized a large sample of Kaiser Permanente patients in San Diego and examined the links between retrospectively reported child abuse/neglect as well as household dysfunction and the likelihood of adult physical and behavioral health issues.

The researchers developed an index of childhood adversity based on the nine most common childhood adversities reported by their largely white and middle-class adult sample: physical, sexual and verbal abuse, physical and emotional neglect, witnessing a mother being abused, the presence of a family member who was depressed or mentally ill or addicted to alcohol or another substance, and having a family member in prison. Losing a parent to separation or divorce was added later. They labeled these ten experiences Adverse Childhood Experiences (ACEs)

and came to utilize a 0–10 index that counted the number of kinds of adversity adults reported experiencing while growing up. Utilizing abstracted data from health evaluations and survey responses of those patients who agreed to participate, they found graded increases in likelihood of adult physical and behavioral health problems depending on the number of ACEs reported. These problems included ischemic heart disease, cancer, chronic lung disease, obesity, and depression and behavioral health issues such as drug abuse and alcoholism (Felitti et al., 1998).

The mechanism that Felitti and colleagues hypothesized to link childhood adversity and adult physical health was the use of smoking, drinking or drugs, and overeating to cope with the stress, anxiety and anger caused by adverse experiences. Although stress was a key psychological mechanism in their framework, it worked through these behaviors to cause later physical health issues. In the two decades since that publication, stress neurobiology has come to be seen as the key mechanism translating childhood adversity into adult health challenges.

A different approach to the impact of households on children points to chaotic household conditions – crowding and overstimulation from noise, lack of routines and structures – as a significant source of stress (Marsh et al., 2020; Evans et al., 2005; Garrett-Peters et al., 2016). Household chaos reduces predictability and diminishes the chance to develop stable, nurturing relationships. Household chaos appears to mediate some of the adverse effects of poverty and may also mediate some of the effects of the adversities described by Felitti and colleagues (Garrett-Peters et al., 2016). On the other hand, a childhood environment that is consistent, predictable, controllable and regular may itself provide a cushion against the effects of early childhood adversities, including those coming from the social determinants of health.

Social determinants call attention to the differential risks of household adversity. For example, analysis of data from 214,000 respondents to the Behavioral Risk Factor Surveillance System (BRFSS) survey of adults[2] showed average ACE scores 55% higher for the lowest income households compared to those with incomes of $50,000 or greater and 60% higher for respondents with less than high school education compared to those with college degrees. Unemployed respondents had ACE scores 46% greater than employed respondents. Blacks had scores 11% greater than Whites and the scores of multiracial respondents were 66% higher (Merrick et al., 2018).

Data about childhood adversity from the National Survey of Children's Health (NSCH) portray similar patterns (Bethell et al., 2017). Unlike the retrospective ACE study by Felitti and colleagues, the NSCH survey questions parents about a child's health and circumstances. Its measure of ACEs drops from the original ACE survey indicators of abuse or neglect but adds being treated unfairly because of one's race or ethnic group, witnessing or experiencing neighborhood violence, and living with economic insecurity. Importantly, this measure is not retrospective but rather based on self-reports of parents of children through age 18. My own analysis of data from that survey[3] shows a 56% greater likelihood that Black children experienced two or more ACEs compared to non-Hispanic White children. Children residing in the households with lowest income were almost three times more likely than children living in the highest income households to have two or more ACEs. A child in a household where the adults have not completed high school are almost twice as likely to experience two or more ACEs as children from households with college-educated parents. The experience of adversity also varies significantly across neighborhoods and geographic regions. For example, the likelihood that children will have experienced two or more adversities as measured by the National Survey of Children's Health was 28% in Oklahoma and 12% in New Jersey (Annie E. Casey Foundation 2021).

Because the social determinants themselves interrelate as well as being correlated with the varied household adversities, teasing out causal patterns presents enormous challenges. For example, a scoping review of research about household chaos reports that the relationship between low SES and measures of children's socioemotional adjustment, academic achievement and daily cortisol was mediated by indicators of chaos (Marsh et al., 2020). Other researchers found that poverty appeared to act through household disorganization in its relationship to low academic achievement (Garrett-Peters et al., 2016).

Sorting out causality among multiple risk factors is a statistical challenge even with relatively large samples. Evans and Kim (2010) focus instead on the potential of cumulative risk measures such as the limited ACE index to capture the interrelated set of adversities that can produce toxic stress and influence health outcomes. For example, a multiple risk score taking account of family environment and social circumstances served as a strong predictor of children's socio-emotional and cognitive development (Sameroff et al., 1987). Using an index of cumulative risk that included noise, crowding, housing problems, single parent, low income, and family turmoil, Evans (2003) reported significant relationships between it and indicators of allostatic load as well as a measure of psychological distress. In another study, Evans and Kim (2012) found that the length of time in poverty as a child related to elevated allostatic load, but that relationship was mediated by cumulative risk exposure. Stress biologists thus can enlarge the frame for examining stress in human populations by creating and testing measures of cumulative risk employing indicators of more distant and proximal social determinants.

5. Nature of and resources for care-giving, social and community support

The social determinants and childhood adversity tell only one part of the story of health and well-being over the life course. Warm and caring adult relationships and positive childhood experiences, as Bruce noted in 2012 (McEwen 2012), can protect against a prolonged stress response to adverse social conditions. Although primary caregivers are important, supports from child-care staff, teachers, coaches, mentors, ministers, and others play a significant role in helping children feel valued, cared for and protected.

The strength of positive supports helps account for the substantial individual variation in responses to the social determinants, including household adversity. For example, research in Wales using parts of the Children and Youth Resilience Measure (Ungar and Liebenberg 2011) documented a decline of 64% in the likelihood of poor health among children with four or more CDC-Kaiser ACEs when they reported being treated fairly, having supportive friends, having the chance to use their abilities, and being connected to a trusted adult they could look up to (Bellis et al., 2018). An analysis of data from the National Survey of Children's Health developed a measure using binary scoring of positive parenting practices – reading stories with a child; going on family outings; eating meals, singing and storytelling together; watching TV less than 2 hours a day. The data analysis showed that the risks of developmental delay and socio-emotional deficits were significantly greater for the absence of positive parenting than for the presence of four or more ACEs (Yamaoka and Bard 2019). Further a study of adult flourishing using data from the surveys of Midlife in the United States study found a step-wise relationship between scores on a scale gauging parental affection, attention and communication during childhood and an adult flourishing score. This relationship held for different levels of ACEs and childhood SES (Whitaker et al. 2021).

Of course, genetic and epigenetic variation play an extremely important role as well in understanding differing individual responses to

[2] This survey is sponsored but the United States Centers for Disease Control and Prevention along with other federal agencies and is administered in all 50 states. It employs an ACE measure closely adapted from the CDC-Kaiser research described earlier.

[3] Data extracted from the 2018-19 NSCH surveys using the interactive data search tool prepared by the Data Resource Center for Child & Adolescent Health (2021).

adversity (Boyce and Ellis, 2005a; Ellis et al., 2005; Boyce, 2019; Boyce et al., 2021). Genes may predispose a small subset of children to be highly sensitive to their environments, both positive and aversive, while others remain relatively unperturbed by environmental challenges. Epigenetic factors shaped by early experience, beginning in the womb, also appear to operate in creating a spectrum of differential sensitivity to social contexts. Such differences in susceptibility work two ways – for those who are most sensitive, adversity has strongly negative effects on health and behavior, but they are also especially responsive to supportive, nurturing relationships and to thrive in these relationships (Boyce 2019).

Taking a cue from research about positive childhood experiences, the American Academy of Pediatrics (AAP) issued in 2021 a Policy Statement on Preventing Childhood Toxic Stress that focuses on creating "safe, stable, and nurturing relationships (SSNRs) that buffer adversity and build resilience" (Garner and Yogman, 2021). The policy builds on a bioecological view of resilience (Bronfenbrenner and Evans 2000) that centers the ways in which nurturing and adverse experiences in early life become imbedded biologically, with implications for health and life trajectories. The AAP statement attempts to redirect emphasis from the deficit approach associated with the problem of toxic stress toward one that examines assets and strengthens them in order to build relational health that both protects against toxic stress and supports remaking brain architecture in its aftermath.

The bioecological approach the AAP adopted emphasizes that child development takes place through interaction with immediate and more distant social environments. The resulting view of resilience focuses on systems not individual traits. According to Masten et al. (2019:525), "Resilience of a person or a family extends beyond the individual or family system level to encompass the capacity and resources that can be mobilized in response to challenges through processes connecting that person or family to additional capacity and resources."

The social determinants also shape resilience in this multi-level system by making it more or less likely that supportive parenting and positive childhood experiences are present. They tend to be least available to those most vulnerable to potentially toxic social circumstances. Employing data from the National Survey of Children's Health, Crouse et al. (2021:7) established that, "Children of minority race or ethnicity were less likely to have a mentor for advice or guidance, live in a safe neighborhood, or live in a supportive neighborhood, and less likely to experience three or more PCEs [positive childhood experiences]." Similarly, children from the lowest income households had a significantly lower chance of three PCEs than children from households earning more than 200% of the federal poverty level (Crouse et al., 2021).

6. Advancing understanding of the social sources of stress and protection through stress neurobiology

Clearly, there is much still to learn. The dual challenge for neurobiologists and social scientists is to elaborate the emerging understanding of the impacts of stress on body and brain and to tease apart the complex interrelationships among the environmental forces that contribute to stress. In particular, expanded understanding of the multidimensionality and interrelationships of childhood adversities in the home, community, and society and their interaction with protective factors should be a major research priority, ideally in cross-disciplinary collaborations. Investing in that research is vitally important because the neurobiology and sociology of stress add significantly to the ways we think about inequality and suggest points of primary prevention and intervention to improve population health and diminish intergenerational transmission of inequality.

Measuring positive parenting or positive childhood experiences poses as many problems as appraising childhood adversity or capturing a wide array of social determinants. There is no agreed upon list of either adverse or positive childhood experiences or of the characteristics of positive parenting. The CDC-Kaiser index of adverse childhood experiences is widely used, but it leaves out elements of household chaos and neglects the broader social determinants that can directly affect the likelihood of toxic stress (McEwen and Gregerson 2019). Constructs of positive experiences and parenting are largely ad hoc and have drawn on survey items in the data sets under analysis. The Children and Youth Resilience Measure (Ungar and Liebenberg 2011) has been widely used for assessing resilience – understood broadly in terms of individual qualities and community supports – but a review of research (Renbarger et al., 2020) concludes that context-specific research is needed to understand better the nature of resilience in varied communities. Making all this more complex is the recognition that many positive childhood experiences or evidence of positive parenting turn out to be at one end of continua with adverse childhood experiences at the opposite pole.

What then are stress neurobiologists to do? No single research project with humans can tackle the multiplicity of variables at work in complex chains of causation. But research that looks beyond single sources of stress and accounts for protective factors will, as it accumulates, help with unravelling these complexities.

7. Conclusion: plasticity, change and hope

Bruce was an optimist and saw the developing understanding of stress neurobiology both as vitally important science and as a vehicle for improving the lives of individuals and of the societies we live in. He entered the study of stress neurobiology through animal research and with important insights about the regulation of gene expression and built on his developing understanding of hormonal influences on the brain and its plasticity. But relatively early in his career, he asked, "How do we apply what we learn from animals to the human condition?"[4]

These perspectives show through in the conclusion to a chapter Bruce wrote providing "A life-course, epigenetic perspective on resilience in brain and body" (2020) that was published after his death. In the conclusion of that chapter, he wrote hopefully about finding ways to open up windows of plasticity and to overcome a major challenge throughout the life course – that of redirecting future "behavior and physiology in more positive and healthy directions (Halfon et al., 2014). In keeping with the original definition of epigenetics (Waddington, 1942) as the emergence of characteristics not previously evident or even predictable from an earlier developmental stage …, we do not mean 'reversibility' as in 'rolling back the developmental clock' but rather 'redirection' as well as 'resilience,' which can be defined as 'achieving a successful outcome in the face of adversity'" (2020:15).

Bruce's search for ways to achieve those successful outcomes seemed almost boundless. For example, it included connecting his work to the world of meditation training and research through interactions with Dr. Jon Kabat-Zinn or participating with the Dalai Lama in a Mind & Life Institute dialogue at Rockefeller University in 2012. It involved playing a key role in convening the Hope for Depression Research Foundation Task Force and supervising research that translated findings about rodents into research on depressed adults. The animal model showed acetyl-L-carnitine (LAC) promoted anti-depressant responses, and the human research found lowest LAC level in patients with treatment-resistant depression (Nasca et al., 2018); Bruce hoped this work might lead to better diagnosis and treatment for depression. He and his lab collaborated on research suggesting the drug riluzole could slow the development of Alzheimer's disease (Matthews et al., 2021). He served on the Boards of the Society for Women's Health Research and the EveryDay Wellness Health Advisory Board among many others. The list could go on.

But, as we have seen, Bruce also nourished his identity as a molecular

[4] Rockefeller University, Oral history with Bruce McEwen, 2017 at https://www.rockefeller.edu/about/history/oral-history-project/interview-bruce-mcewen/.

sociologist through engagement with the MacArthur networks and participation in the National Scientific Council on the Developing Child. In his Rockefeller oral history, Bruce noted that "We know that environmental complexity changes the brain and now that, of course, comes to haunt us in terms of socioeconomic status, poverty, things of that sort. We are the products of the many influences we have including the culture, the experiences we have growing up. They shape the body and brain in different ways."

His science was committed to understanding the impact of the social determinants on body and brain and to finding ways to treat the consequences. But Bruce also wanted to reduce adversity and diminish inequities in health and life chances. Just as stronger understanding of the neuroendocrine system and stress may lead to cures of debilitating diseases, deeper understanding of the interplay of social mechanisms that work for and against health and well-being may lead to policy initiatives that reallocate resources and lead to the reduction of adversity and toxic stress. He hoped, as do I, that the research of stress neurobiologists could help in unravelling those complex social mechanisms.

Declarations

There are no conflicts of interest.

CRediT authorship contribution statement

Craig A. McEwen: Conceptualization, Data curation, no original data, Formal analysis, Funding acquisition, Unfunded writing, Investigation, No reporting of original research, Methodology, Review article—no original research, Project administration, no research project administered, Writing, Writing and editing.

References

Acevedo-Garcia, D., Osypuk, T.L., McArdle, N., Williams, D.R., 2008. Toward a policy-relevant analysis of geographic and racial/ethnic disparities in child health. Health Aff. 27 (2), 321–333. https://doi.org/10.1377/hlthaff.27.2.321.

Adler, N.E., Stewart, J. (Eds.), 2010a. The Biology of Disadvantage: Socioeconomic Status and Health, 1186, pp. 1–275. Ann N Y Acad Sci. (1).

Adler, N.E., Stewart, J., 2010b. Health disparities across the lifespan: meaning, methods, and mechanisms. Ann. N. Y. Acad. Sci. 1186, 5–23. https://doi.org/10.1111/j.1749-6632.2009.05337.

Annie E. Casey Foundation, Kids Count Data Center, 2021. Children who have experienced two or more adverse experiences in the United States. https://datacenter.kidscount.org/data/bar/9709-children-who-have-experienced-two-or-more-adverse-experiences?loc=1&loct=1#2/2-11/false/1648/any/18962, 16 October 2021.

Bellis, M.A., Hughes, K., Ford, K., Hardcastle, K.A., Sharp, C.A., Wood, S., Homolova, L., Davies, A., 2018. Adverse childhood experiences and sources of childhood resilience: a retrospective study of their combined relationships with child health and educational attendance. BMC Publ. Health 18, 792. https://doi.org/10.1186/s12889-018-5699-8.

Bethell, C., Carle, A., Hudziak, J., Powers, K., Wade, R., Braveman, P., 2017. Methods to assess adverse childhood experiences of children and families: toward approaches to promote child well-being in policy and practice. Acad Pediatr 17 (7 Suppl. l), S51–S69. https://doi.org/10.1016/j.acap.2017.04.161.

Boen, C., Keister, L.A., Graetz, N., 2021. Household wealth and child body mass index: patterns and mechanisms. RSF 7 (3), 80–100. https://doi.org/10.7758/RSF.2021.7.3.04.

Bosma, H., Marmot, M.G., Hemingway, H., Nicholson, A.C., Brunner, E., Stansfeld, S.A., 1997. Low job control and risk of coronary heart disease in Whitehall II (prospective cohort) study. BMJ 314, 558–565. https://doi.org/10.1136/bmj.314.7080.558.

Boyce, W.T., 2019. The Orchid and the Dandelion: Why Some Children Struggle and How All Can Thrive. Vintage, New York.

Boyce, W.T., Ellis, B.J., 2005. Biological sensitivity to context: I. An evolutionary-developmental theory of the origins and functions of stress reactivity. Dev. Psychopathol. 17, 271–301. https://doi.org/10.1017/S0954579405050145.

Boyce, W.T., Levitt, P., Martinez, F.D., McEwen, B.S., Shonkoff, J.P., 2021. Genes, Environments, and Time: The Biology of Adversity and Resilience. Pediatrics. https://doi.org/10.1542/peds.2020-1651.

Bradbury, B., Waldfogel, J., Washbrook, E., 2019. Income-related gaps in early child cognitive development: why are they larger in the United States than in the United Kingdom, Australia, and Canada? Demography 56 (1), 367–390. https://doi.org/10.1007/s13524-018-0738-8.

Braveman, P., Gottlieb, L., 2014. The social determinants of health: it's time to consider the causes of the causes. Publ. Health Rep. 129 (Suppl. 2), 19–31. https://doi.org/10.1177/00333549141291S206.

Bronfenbrenner, U., Evans, G.W., 2000. Developmental science in the 21st century: emerging questions, theoretical models, research designs and empirical findings. Soc. Dev. 9, 115–125. https://doi.org/10.1111/1467-9507.00114.

Brunner, E., Marmot, M., 1999. Social organization, stress, and health. In: Marmot, M., Wilkinson, R. (Eds.), Social Determinants of Health. Oxford, New York, pp. 6–30.

Conwell, J.A., Zi Ye, L., 2021. All wealth is not created equal: race, parental net worth, and children's achievement, RSF. The Russell Sage Foundation Journal of the Social Sciences 7 (3), 101–121. https://doi.org/10.7758/RSF.2021.7.3.05. RSF.

Crouse, E., Radcliff, E., Merrell, M.A., Brown, M.J., Ingram, L.A., Probst, J., 2021. Racial/ethnic differences in positive childhood experiences across a national sample. Child Abuse Negl. 115 https://doi.org/10.1016/j.chiabu.2021.105012.

Data Resource Center for Child & Adolescent Health, 2021. National survey of children's health (2016-present). https://www.childhealthdata.org/browse/survey, 14 October 2021.

Dow, W.H., Rehkopf, D.H., 2010. Socioeconomic gradients in health in international and historical context. Ann. N. Y. Acad. Sci. 1186, 24–36. https://doi.org/10.1111/j.1749-6632.2009.05384.x.

Duncan, G.J., Ziol-Guest, K.M., Kalil, A., 2010. Early-childhood poverty and adult attainment, behavior, and health. Child Dev. 81, 306–325. https://doi.org/10.1111/j.1467-8624.2009.01396.x.

Ellis, B.J., Essex, M.J., Boyce, W.T., 2005. Biological sensitivity to context: II. Empirical explorations of an evolutionary-developmental theory. Dev. Psychopathol. 17 (2), 303–328. https://doi.org/10.1017/S0954579405050157.

Evans, G.W., 2003. A multimethodological analysis of cumulative risk and allostatic load among rural children. Dev. Psychol. 39, 924–933. https://doi.org/10.1037/0012-1649.39.5.924.

Evans, G.W., Kim, P., 2010. Multiple risk exposure as a potential explanatory mechanism for the socioeconomic status–health gradient. Ann. N. Y. Acad. Sci. 1186, 174–189. https://doi.org/10.1111/j.1749-6632.2009.05336.x.

Evans, G.W., Kim, P., 2012. Childhood poverty and young adult allostatic load: the mediating role of childhood cumulative risk exposure. Psychol. Sci. 23, 979–983. https://doi.org/10.1177/0956797612441218.

Evans, G.W., Schamberg, M.A., 2009. Childhood poverty, chronic stress, and adult working memory. Proc. Natl. Acad. Sci. U. S. A. 106 (16), 6545–6549. https://doi.org/10.1073/pnas.0811910106.

Evans, G.W., Gonnella, C., Marcynyszyn, L.A., Gentile, L., Salpekar, N., 2005. The role of chaos in poverty and children's socioemotional adjustment. Psychol. Sci. 16 (7), 560–565. https://doi.org/10.1111/j.0956-7976.2005.01575.x.

Evans, G.W., Farah, M.J., Hackman, D.A., 2021. Early childhood poverty and adult executive functioning: distinct, mediating pathways for different domains of executive functioning. Dev. Sci. 24, e13084 https://doi.org/10.1111/desc.13084.

Farah, M.J., 2017. The neuroscience of socioeconomic status: correlates, causes, and consequences. Neuron 96, 56–71. https://doi.org/10.1016/j.neuron.2017.08.034.

Farah, M., Shera, D.M., Savage, J.H., Betancourt, L., Gianenetta, J.M., Brodsky, N.L., Malmud, E.K., Hurt, H., 2006. Childhood poverty: specific associations with neurocognitive development. Brain Res. 1110 (1), 166–174. https://doi.org/10.1016/j.brainres.2006.06.072.

Felitti, V.J., Anda, R.F., Nordenberg, D., Williamson, D.F., Spitz, A.M., Edwards, V., Koss, M.P., Marks, J.S., 1998. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: the adverse childhood experiences (ACE) study. Am. J. Prev. Med. 14 (4), 245–258. https://doi.org/10.1016/s0749-3797(98)00017-8.

Forde, A.T., Crookes, D.M., Suglia, S.F., Demmer, R.T., 2019. The weathering hypothesis as an explanation for racial disparities in health: a systematic review. Ann. Epidemiol. 33, 1–18. https://doi.org/10.1016/j.annepidem.2019.02.011.

Gannon, M, 2016. Race is a social construct, scientists argue. Scientific American, Live Science. https://www.scientificamerican.com/article/race-is-a-social-construct-scientists-argue/.

Garcia, E., Weiss, E., 2016. Education Inequalities at the School Starting Gate: Gaps, Trends, and Strategies to Address Them. Economic Policy Institute. https://files.eric.ed.gov/fulltext/ED588751.pdf. (Accessed 14 October 2021).

Garner, A., Yogman, M., Committee on psychosocial aspects of child and family health, developmental and behavioral pediatrics, Council on early childhood, 2021. Preventing childhood toxic stress: partnering with families and communities to promote relational health. JAMA Pediatr. 148 (2) https://doi.org/10.1542/peds.2021-052582.

Garrett-Peters, P.T., Mokrova, I., Vernon-Feagans, L., Willoughby, M., Pan, Y., et al., 2016. The role of household chaos in understanding relations between early poverty and children's academic achievement. Early Child. Res. Q. 37, 16–25. https://doi.org/10.1016/j.ecresq.2016.02.004.

Geronimus, A.T., Hicken, M., Keene, D., Bound, J., 2006. "Weathering" and age patterns of allostatic load scores among blacks and whites in the United States. Am. J. Publ. Health 96 (5), 826–833. https://doi.org/10.2105/AJPH.2004.060749.

Gibson-Davis, C., Hill, H.D., 2021. Childhood wealth inequality in the United States: implications for social stratification and well-being. RSF 7 (3), 1–26. https://doi.org/10.7758/RSF.2021.7.3.01.

Hackman, D.A., Farah, M.J., 2009. Socioeconomic status and the developing brain. Trends Cognit. Sci. 13, 65–73. https://doi.org/10.1016/j.tics.2008.11.003.

Halfon, N., Larson, K., Lu, M., Tullis, E., Russ, S., 2014. Lifecourse health development: past, present and future. Matern. Child Health J. 18 (2), 344–365. https://doi.org/10.1007/s10995-013-1346-2.

Harrell, S.P., 2000. A multidimensional conceptualization of racism-related stress: implications for the well-being of people of color. Am. J. Orthopsychiatry 70 (1), 42–57. https://doi.org/10.1037/h0087722.

Kim, P., Evans, G.W., Angstadt, M., Ho, S.S., Sripada, C.S., et al., 2013. Effects of childhood poverty and chronic stress on emotion regulatory brain function. Proc.

Natl. Acad. Sci. U. S. A. 110, 18442–18447. https://doi.org/10.1073/pnas.1308240110.
Kindig, D., Stoddart, G., 2003. What is population health? Am. J. Publ. Health 93 (3), 380–383. https://doi.org/10.2105/ajph.93.3.380.
Manuck, S.B., Bleil, M.E., Petersen, K.L., Flory, J.D., Mann, J.J., Ferrell, R.E., Muldoon, M.F., 2005. The socio-economic status of communities predicts variation in brain serotonergic responsivity. Psychol. Med. 35, 519–528. https://doi.org/10.1017/s0033291704003757.
Marmot, M., Wilkinson, R.G. (Eds.), 1999. Social Determinants of Health. Oxford University Press, New York.
Marmot, M.G., Shipley, M.J., Rose, G., 1984. Inequalities in death–specific explanations of a general pattern? Lancet 323 (8384), 1003–1006. https://doi.org/10.1016/s0140-6736(84)92337-7.
Marsh, S., Dobson, R., Maddison, R., 2020. The relationship between household chaos and child, parent, and family outcomes: a systematic scoping review. BMC Publ. Health 20, 513. https://doi.org/10.1186/s12889-020-08587-8.
Masten, A.S., Lucke, C.M., Nelson, K.M., Stallworthy, I.C., 2021. Resilience in development and psychopathology: multisystem perspectives. Annu. Rev. Clin. Psychol. 17, 521–549. https://doi.org/10.1146/annurev-clinpsy-081219-120307.
Matthews, D.C., Mao, X., Dowd, K., Tsakanikas, D., Jiang, C.S., et al., 2021. Riluzole, a glutamate modulator, slows cerebral glucose metabolism decline in patients with Alzheimer's disease. Brain. https://doi.org/10.1093/brain/awab222.
McEwen, B.S., 1998. Protective and damaging effects of stress mediators. N. Engl. J. Med. 338 (3), 171–179. https://doi.org/10.1056/NEJM199801153380307. Jan 15.
McEwen, B.S., 2012. Brain on stress: how the social environment gets under the skin. Proc. Natl. Acad. Sci. U. S. A. 109 (Suppl. 2), 17180–17185. https://doi.org/10.1073/pnas.1121254109.
McEwen, B., 2020. A life-course, epigenetic perspective on resilience in brain and body. In: Chen, A. (Ed.), Stress Resilience: Molecular and Behavioral Aspects. Elsevier, Cambridge MA, pp. 1–21.
McEwen, B.S., Gianaros, P.J., 2010. Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. Ann. N. Y. Acad. Sci. 1186, 190–222. https://doi.org/10.1111/j.1749-6632.2009.05331.x.
McEwen, B.S., Gianaros, P.J., 2011. Stress- and allostasis-induced brain plasticity. Annu. Rev. Med. 62, 431–445. https://doi.org/10.1146/annurev-med-052209-100430.
McEwen, C.A., Gregerson, S., 2019. A critical assessment of the adverse childhood experiences study at 20 years. Am. J. Prev. Med. 56 (6), 790–794. https://doi.org/10.1016/j.amepre.2018.10.016.
McEwen, C.A., McEwen, B.S., 2017. Social structure, adversity, toxic stress, and intergenerational poverty: an early childhood model. Annu. Rev. Sociol. 43, 445–472. https://doi.org/10.1146/annurev-soc-060116-053252.
McLeod, J.D., Kaiser, K., 2004. Childhood emotional and behavioral problems and educational attainment. Am. Socio. Rev. 69, 636–658. https://doi.org/10.1177/000312240406900502.
McLoyd, V.C., 1998. Socioeconomic disadvantages and child development. Am. Psychol. 53, 185–204. https://doi.org/10.1037//0003-066x.53.2.185.
Merrick, M.T., Ford, D.C., Ports, K.A., 2018. Prevalence of adverse childhood experiences from the 2011-2014 behavioral risk factor surveillance system in 23 states. JAMA Pediatr. 172, 1038–1044. https://doi.org/10.1001/jamapediatrics.2018.2537.
Miller, P., Podvysotska, T., Betancur, L., Votruba-Drzal, E., 2021. Wealth and child development: differences in associations by family income and developmental stage. RSF 7, 154–174. https://doi.org/10.7758/RSF.2021.7.3.07.
Mínguez, A.M., 2017. The role of family policy in explaining the international variation in child subjective well-being. Soc. Indicat. Res. 134, 1173–1194. https://doi.org/10.1007/s11205-016-1456-5.
Nasca, C., Bigio, B., Lee, F.S., Young, S.P., Kautz, M.M., Albright, A., et al., 2018. Acetyl-l-carnitine deficiency in patients with major depressive disorder. Proc. Natl. Acad. Sci. U. S. A. 115 (34), 8627–8632. https://doi.org/10.1073/pnas.1801609115.
National Scientific Council on the Developing Child, 2020. Connecting the brain to the rest of the body: Early childhood development and lifelong health are deeply intertwined: Working paper 15. https://developingchild.harvard.edu/resources/connecting-the-brain-to-the-rest-of-the-body-early-childhood-development-and-lifelong-health-are-deeply-intertwined/, 13 October 2021.
Noble, K.G., McCandless, B.D., Farah, M.J., 2007. Socioeconomic gradients predict individual differences in neurocognitive abilities. Dev. Sci. 10, 464–480. https://doi.org/10.1111/j.1467-7687.2007.00600.x.
Pascoe, E.A., Richman, L.S., 2009. Perceived discrimination and health: a meta-analytic review. Psychol. Bull. 135 (4), 531–554. https://doi.org/10.1037/a0016059.
Reardon, S.F., 2011. The widening achievement gap between the rich and the poor: New evidence and possible explanations. In: Duncan, G.J., Murnane, R.J. (Eds.), Whither Opportunity: Rising Inequality, Schools, and Children's Life Chances. Russell Sage, New York, pp. 91–115.
Reardon, S.F., Portilla, X.A., 2016. Recent trends in income, racial, and ethnic school readiness gaps at kindergarten entry. AERA Open 2 (3), 1–18. https://doi.org/10.1177/2332858416657343.
Renbarger, R.L., Padgett, R.N., Cowden, R.G., Govender, K., Yilmaz, M.Z., Scott, L.M., et al., 2020. Culturally relevant resilience: a psychometric meta-analysis of the child and youth resilience measure (CYRM). J. Res. Adolesc. 30, 896–912. https://doi.org/10.1111/jora.12569.
Sameroff, A., Seifer, R., Zax, M., Barocas, R., 1987. Early indicators of developmental risk: Rochester longitudinal study. Schizophr. Bull. 13 (3), 383–394. https://doi.org/10.1093/schbul/13.3.383, 1987.
Sastry, N., Pebley, A.R., 2010. Family and neighborhood sources of socioeconomic inequality in childrens' achievement. Demography 47, 777–800. https://doi.org/10.1353/dem.0.0114.
Schultz, A.J., Mentz, G., Lachance, L., Johnson, J., Gaines, C., Israel, B., 2012. Associations between socioeconomic status and allostatic load: effects of neighborhood poverty and tests of mediating pathways. Am. J. Publ. Health 102, 1706–1714. https://doi.org/10.2105/AJPH.2011.300412.
Seeman, T., Epel, E., Gruenewald, T., Karlamangla, A., McEwen, B.S., 2010. Socio-economic differentials in peripheral biology: cumulative allostatic load. Ann. N. Y. Acad. Sci. 1186, 223–239. https://doi.org/10.1111/j.1749-6632.2009.05341.x.
Shanks, T.R.W., 2008. The impacts of household wealth on child development. J. Poverty 11 (2), 93–116. https://doi.org/10.1300/J134v11n02_05.
Sharkey, P., Elwert, F., 2011. The legacy of disadvantage: multigenerational neighborhood effects on cognitive ability. Am. J. Sociol. 116, 1934–1981. https://doi.org/10.1086/660009.
Smedley, B.D., 2012. The lived experience of race and its health consequences. Am. J. Publ. Health 102 (5), 933–935. https://doi.org/10.2105/AJPH.2011.300643.
Trent, M., Dooley, D.G., Dougé, J., 2019. The impact of racism on child and adolescent health. JAMA Pediatr. 144 (2) https://doi.org/10.1542/peds.2019-1765.
Ungar, M., Liebenberg, L., 2011. Assessing resilience across cultures using mixed methods: construction of the child and youth resilience measure. J. Mix. Methods Res. 16, 431–454. https://doi.org/10.1177/1558689811400607.
Waddington, C.H., 1942. The epigenotype. Int. J. Epidemiol. 41 (1), 10–13. https://doi.org/10.1093/ije/dyr184.
Wagmiller, R.L., Adelman, R.M., 2009. Childhood and Intergenerational Poverty: the Long-Term Consequences of Growing up Poor. National Center for Children in Poverty, New York. https://www.nccp.org/publication/childhood-and-intergenerational-poverty/. (Accessed 13 October 2021).
Wagner, S.L., Cepeda, I., Krieger, D., Maggi, S., D'Angiulli, A., Weinberg, J., Grunau, R. E., 2016. Higher cortisol is associated with poorer executive functioning in preschool children: the role of parenting stress, parent coping and quality of daycare. Child Neuropsychol. 22 (7), 853–869. https://doi.org/10.1080/09297049.2015.1080232.
Whitaker, R.C., Dearth-Wesley, T., Herman, A.N., 2021. Childhood family connection and adult flourishing: associations across levels of childhood adversity. Acad Pediatr. https://doi.org/10.1016/j.acap.2021.03.002.
Williams, D.R., Collins, C., 2001. Racial residential segregation: a fundamental cause of racial disparities in health. Publ. Health Rep. 116 (5), 404–416. https://doi.org/10.1093/phr/116.5.404.
Williams, D.R., Mohammed, S.A., Leavell, J., Collins, C., 2010. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. Ann. N. Y. Acad. Sci. 1186, 69–101. https://doi.org/10.1111/j.1749-6632.2009.05339.x.
Williams, D.R., Lawrence, J.A., Davis, B.A., 2019. Racism and health: evidence and needed research. Annu. Rev. Publ. Health 40, 105–125. https://doi.org/10.1146/annurev-publhealth-040218-043750.
Wodtke, G.T., Harding, D.J., Elwert, F., 2011. Neighborhood effects in temporal perspective: the impact of long-term exposure to concentrated disadvantage on high school graduation. Am. Socio. Rev. 76, 713–736. https://doi.org/10.1177/0003122411420816.
World Health Organization, 2021. Social determinants of health. https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1. (Accessed 13 October 2021).
Wyatt, S.B., Williams, D.R., Calvin, R., Henderson, F.C., Walker, E.R., Winters, K., 2003. Racism and cardiovascular disease in African Americans. Am. J. Med. Sci. 325 (6), 315–331. https://doi.org/10.1097/00000441-200306000-00003.
Yamaoka, Y., Bard, D.E., 2019. Positive parenting matters in the face of early adversity. Am. J. Prev. Med. 56 (4), 530–539. https://doi.org/10.1016/j.amepre.2018.11.018.