



## Understanding the link between early adversity and disease – Stress, immunity, and prevention



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Experiences of adversity, particularly in early life, are linked to long-term mental and physical health consequences (Cohen et al., 2007). The effects of adverse experiences are thought to accumulate with greater exposure to stress (Evans et al., 2013). However, even in cases in which children are removed from harm and therefore no longer exposed to significant adversity, the effect from early exposures typically lingers (Nelson et al., 2014). For those interested in promoting the long-term health and well-being of all humans, there are obvious reasons to target our efforts on the early years of life. The plasticity of the developing brain leaves infants and young children particularly vulnerable to the effects of adversity. Simply put, there is no time in a human life in which environmental events, both good and bad, can have such a dramatic impact on functioning. Furthermore, given that the brain builds from a bottom-up process, experiences of early adversity are most likely to affect foundational brain architecture that the rest of the brain builds upon.

The umbrella term “early adversity” includes types of events that are obviously directly harmful (e.g., physical abuse), as well as those experiences that are likely to be less direct in their impact (e.g., poverty). For example, it is clear that physical abuse can cause physical injury, activate the body’s threat response (e.g., the autonomic nervous system), and affect the feelings of safety and security in the child’s home environment. However, other forms of early adversity are more difficult to define, and thus it is more difficult to identify their impact. Namely, relatively lower socioeconomic status (SES) is associated with a wide range of negative outcomes (Duncan et al., 2017). Yet it is unclear how poverty affects humans directly. This is a critical question, as health disparities are well documented. It is essential to identify how early adversity can negatively affect health outcomes. In other words, what are the mechanisms of risk that lead to the onset of a disease or disorder?

Recently, my colleagues and I conducted a meta-analysis of 111,156 individuals (Muscatell et al., 2018). We found that lower SES was associated with higher levels of circulating C-reactive protein (CRP) and Interleukin-6 (IL-6), two inflammatory markers in which elevations are linked to cardiovascular disease, stroke, depression, and all-cause mortality. In other work, stress in early life has been linked to increased cortisol production, a hormone that while essential for normal

physiologic functions, may be neurotoxic in excess, as it is associated with reduced volume in the hippocampus, a critical brain region for emotion and memory (Davis et al., 2017; De Bellis et al., 1999; Humphreys et al., 2018). Our meta-analysis provides insight into potential drivers of the association between adversity and CRP and IL-6 levels, as the associations between SES and inflammation were attenuated when researchers accounted for the effects of cigarette smoking in their analyses. The same was true for considering body mass index. Thus, pathways from poverty to illness may be partially explained by smoking and obesity, health behaviors associated with changes in inflammation. Thus, early adversity may be undermining the body’s immune system both directly and indirectly. As readers of this journal are well aware, examining these biological mediators of behavioral outcomes, including inflammation and hormone production, are an extremely promising line of inquiry as they help to explain how stress gets “under the skin” and may also provide a more temporally sensitive yard-stick by which to measure intervention effects aimed to mitigate or prevent the effects of early adversity.

As an infant mental health psychologist, I am particularly encouraged by a growing interest in investing in early life. We are most likely to see a positive return from investment when targeting young children and families (see the Nurse-Family Partnership; Miller, 2015). Nevertheless, building evidence on the causal nature of poverty on development may be important for generating consensus that reducing exposure to early adversity is a worthy cause that may also deliver positive returns for individuals and society at large. For obvious ethical reasons, we cannot randomly assign children or families to be poor. We can, however, reduce experiences of poverty for children and test those effects, and this design, when conducted as a randomized controlled trial is a way for us to determine causality in humans. Currently, the first randomized clinical trial to test whether reducing poverty affects infants and young children’s cognitive, emotional, and brain development is underway at four sites (New York City, New Orleans, St. Paul/Minneapolis, and Omaha communities), in which one thousand low-income women and their newborns will receive unconditional cash gifts of either \$333/month or \$20/month for over 3 years (<https://www.babysfirstyears.com/>). Only time will tell, but such an effort, if found to improve children’s long-term mental and physical health, can provide a

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clear roadmap for how to improve the outcomes of those most at risk for experiencing early adversity and its negative consequences across the lifespan.

Adverse early experiences put children on a trajectory for subsequent illness and premature death. The effect of stressful experiences may alter our immune system and other related biological systems, and appear to persist even after the stressful experiences stop. Finding ways to reduce stress exposure in early life, through improvements in caregiving environments, are most likely to result in significant improvements in the well-being of at-risk individuals, and should be a public health imperative.

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