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2021 Klaus J. Jacobs Research Prize

“Studying the long-term impacts of adversity can enable more effective interventions”

Charles Nelson studies the effects of early childhood experience on brain and behavioral development, particularly the impact of early psychosocial adversity during the critical first 2 years of life and the possibility that critical periods can be reopened for therapeutic intervention.

How did you come to be interested in this work?

Early in my career my interest in experience-dependent development led me to explore the infant’s ability to “read” the information in faces, a critical ability throughout the lifespan but particularly prior to the onset of language. Nearly 30 years ago I proposed that the neural architecture that subserves face processing becomes specialized by exposure to faces during critical periods of development; indeed, this work has been cited thousands of times and has proven very influential in the field as a model system of how developmental timing guides human development.

Over the past two decades, however, I have increasingly turned my attention to a more insidious form of experience: the effects of adverse environments on human development. It is now well established that adverse childhood experiences can undermine many aspects of development and that these effects can become biologically embedded and persist across the lifespan. However, our research also shows that some of the deleterious impacts on the brain and on behavior can be reversed by screening and early interventions.

When are the most critical periods for a child’s development?

Growing evidence indicates that in the first three years of life, a host of biological (e.g., malnutrition) and psychosocial (e.g., extreme poverty) hazards can affect a child’s developmental trajectory and lead to increased risk of adverse physical and mental health outcomes. Such impacts can be observed across multiple systems, affecting cardiovascular, immune, metabolic, and brain health, and may extend far beyond childhood, affecting life course health. As my work and that of others have begun to describe, these effects may be mediated in various direct and indirect ways.

Illuminating these pathways creates opportunities for developing mitigation and intervention strategies.

What are some of the types of adversity a child might face?

Adversity might be best thought of as a violation of the expectable environment. It can take the form of exposure to biological hazards such as malnutrition, environmental toxins, or chronic illness or infection, as well as psychosocial hazards such as maltreatment, neighborhood or domestic violence, physical or emotional abuse, chronic neglect, family economic hardship, or caregiver substance abuse or mental illness. Not all adversities trigger the same response or produce the same impact—sexual abuse may have more serious or lasting consequences than parental divorce, for instance. The duration, timing, number, and interactions between adversities all can affect how these stresses impact a child.

What are the effects of adversity during these critical periods?

Researchers have uncovered several neurobiological, physical, and behavioral consequences of adversity experienced during these critical childhood periods. Prolonged activation of the body's stress response system during adversity is associated with reductions in white and gray matter volume in several areas of the brain, reduced brain electrical activity, and differences in brain development that are associated with decreasing executive function and educational achievement.

Exposure to adversities such as poverty can lead to growth failure and wasting. Children exposed to high levels of psychological stress have a greater risk of common childhood diseases including ear infections, asthma, viral infections, and intestinal and urinary tract infections, among others. Children experiencing trauma, such as witnessing the murder of a family member or experiencing sexual assault, are also at elevated risk of several other psychiatric disorders, including depression, post-traumatic stress disorder, substance abuse, self-harm, and suicidal thoughts and attempts. These effects can extend past childhood to increase the risk of adult chronic conditions including heart disease, some cancers, chronic obstructive pulmonary disease, depression, and diabetes.

Behaviorally, childhood exposure to adversity can increase risk taking, aggressive behavior, involvement in violence, and difficulty forming and maintaining relationships.

Are these effects permanent or can they be reversed?

This is an area where more research is needed, but our studies and others have shown that early intervention, before age 2, has the best chance of reversing some of these effects.

In the Budapest Early Intervention Project, for instance, we found that some of the deleterious behavioral and neurobiological effects of adversity in institutionalized children can be reversed if they are removed from the institutional environment before age 2. Although the first 3 years of life are emphasized in this field, older children can be remarkably resilient and plastic in terms of their personalities and behaviors. Even for children living in adverse circumstances, much can be done now to make a difference by preventing such disorders from developing and from intervening once they have surfaced. Screening children to refer them to early intervention services and providing intervention strategies to help children manage their toxic stress response and to support families coping with adversity are available in some places. Linking and optimizing preventive child health and education initiatives early in life are key to successful intervention and should be scaled up. Community, school, and after-school based interventions can reduce the effects of traumatic events among children and adolescents living in adverse circumstances. As we learn more about the impacts of adversity in childhood, it has become clear that there is not just one “critical” or “sensitive” period for development, but multiple and cascading periods and neural circuits involved for complex phenomena like caregiving or language learning. The more we learn about how and when these critical periods unfold during adversity, we may be able to leverage that knowledge to redirect development along a typical trajectory.

What did you learn from the groundbreaking Budapest Early Intervention Project with orphans in Hungary?

In the Bucharest Early Intervention Project (BEIP), my colleagues and I have demonstrated over the past 20 years that children experiencing early and prolonged psychosocial deprivation suffer permanent impairments and delays to neural, biological, and psychological development. We found children reared in institutions showed greatly diminished intellectual performance (borderline intellectual disability) relative to children reared in their families of origin. Second, as a group, children randomly assigned to foster care experienced significant gains in cognitive function. Our findings suggest that there may be a sensitive period spanning the first 2 years of life within which the onset of foster care exerts a maximal effect on cognitive development. We think that the younger a child is when placed in foster care, the better the outcome. Indeed, there was a continuing “cost” to children who remained in the institution over the course of our study.

What current studies are being worked on and what do you hope to achieve with them?

We are working with families in Boston, Massachusetts now who report low parental educational attainment (typically high school or less), low-income, and exposure to significant stressors, including chronic unemployment, financial insecurity, high rates of neighborhood poverty, and maternal depression. There are two groups that are virtually identical, but the second cohort additionally includes infants born prematurely who required stays in a Neonatal Intensive Care Unit (NICU).

Infants were recruited and tested for the first time at 2 months of age, then followed up at 6-, 9-, 12-, and 24-months, with a small subset followed until 36 months. We collected a wide variety of measures from these infants, including electroencephalograms (EEG), biological samples such as urine and saliva from the children and blood drawn from the mothers, a host of behavioral data, and detailed information about the child's home environment, including maternal perceived and actual stress exposure, and levels of maternal depression and anxiety.

In our first publication, we reported that the more stress mothers perceived, the greater the reduction in infant brain activity in higher frequency EEG bands. We demonstrated how neurodevelopmental tools could be used to identify children most susceptible to the adverse effects of early stress exposure. We also examined associations between maternal stress in the early language environment and neurodevelopment. We found that maternal reports of exposure to stressful life events, and perceived stress, were negatively correlated with child vocalizations and conversational turn-taking when infants were 6 and 12 months of age.

Taken together, these data suggest a strong linkage between the stress mothers experience or perceive soon after their child is born and deleterious neurodevelopmental outcomes in infants over the first year of life. This is an extraordinarily rich, informative study with potential for even greater contributions if we continue to follow these cohorts.

What are some of the broader impacts of your work on the wellbeing of children and the support of family structures?

The most obvious application of my work thus far has been to influence social policies towards young children. For example, UNICEF, the World Health Organization, and the European Union all use the work from BEIP as the strongest evidence to date to convince governments throughout the world to stop placing orphaned or abandoned children in institutions. (Note that between March-December 2020, 1 million children have been orphaned because of COVID-19.) More broadly, my work on early adversity has woven itself into the policies and practices of both educators and lawmakers such that both professions now pay careful attention to children's early environments.

In a variety of areas, this has led to shifts in policy that have benefited children. A recent example from the U.S. concerns policies the Biden administration has advanced to countermand the Trump administration policy of separating children from their parents at the U.S.-Mexican border.

How will the Klaus J. Jacobs Research Prize money be used?

I will use the funds to critically expand on the ongoing Boston-based study. As discussed, the study thus far has yielded a number of intriguing findings; however, my hope is to leverage our success with these cohorts by vastly expanding the scope of the current study. Doing so will yield truly novel findings with important implications for early intervention.

Over the next 5 years, I see myself attempting to understand several challenging theoretical issues. First, we know relatively little about the neural underpinnings of critical periods in human children and little about the nature, timing and duration of experiences that influence critical period development. Moreover, although there are intriguing animal data suggesting that critical periods can be reopened, thus far the (largely pharmacological) tools used to rescue critical periods impact the entire brain, not particular circuits. Understanding how to rescue a critical period has important implications for developing more effective treatment strategies for children who have been deprived of key experiences or have been exposed to adverse experiences in the first years of life. Lastly, of profound relevance to the development of early intervention strategies are two fundamental issues: First, how do we disaggregate and/or model the multiple forms of adversity that commonly affect children and second, how do we examine the impact adversity has across multiple, nested levels of development (neural, biological, psychological)? These are the questions to which I will devote much of my attention in the coming years.