COMMENTARY

Baboons, bonds, biology, and lessons about early life adversity

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Adverse childhood experiences (ACEs) have been defined as those that exhibit a dose–response relationship with health risk behaviors and chronic diseases known to increase mortality (1). ACEs are also associated with biomarkers related to inflammation, genetics, and endocrine functioning (e.g., cortisol) (2). The standard compendium of 10 ACEs includes abuse (physical, emotional, sexual), neglect (physical, emotional), and household dysfunction (mental illness, mother treated violently, divorce, incarcerated relative, substance abuse). ACEs are, unfortunately, an all-too-prevalent reality in the US population. In 2017 to 2018, about 33% of children aged 0 to 17 had experienced at least one ACE, and 14% had experienced two or more (3). The question that now occupies many researchers in this field is, "How do events that happen in childhood persist to affect adult physical and mental health?" Data that address life course questions such as this are rarely available in studies of humans. In PNAS, Rosenbaum et al. (4) take advantage of a rich longitudinal data resource in their long-standing field study of female savannah baboons to test the plausibility of a well-reasoned hypothesis: Early life adversity is associated with increased fecal glucocorticoid (fGC) concentrations in adulthood, and this effect is mediated by social bond strength in adulthood (Fig. 1*A*).

Rosenbaum et al. report that baboon females with early adverse experiences had fGC concentrations that were 9 to 14% higher compared to those among females with no such experiences. However, these effects were not mediated by having weak social bonds as adults; in fact, variation in social bonds was only a weak predictor of fGC concentrations, while the direct effect of adversity on fGC concentrations was about 11 times stronger. Glucocorticoids have been found to be important mediators of the relationship between individuals' experiences and health outcomes (5). In addition, because technical advances have enabled researchers to estimate glucocorticoid concentrations in a variety of matrices (saliva, hair, urine, and feces), such studies are now possible in field settings.

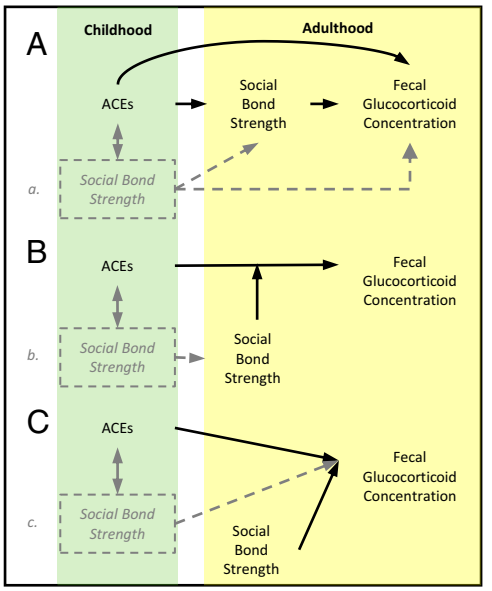

Fig. 1. Pathways linking early life adversity to adult fecal glucocorticoid (fGC) concentrations. Gray font and dashed arrows depict how childhood social bond strength could enter into explanations for adult fGC concentrations. (*A*) Mediation model: Adult social bond strength mediates the association between early life adversity and adult fGC concentrations. (*B*) Moderation model: Adult social bond strength moderates the association between early life adversity and adult fGC concentrations. (*C*) Independent effects model: Early life adversity and adult bond strength are independently associated with adult fGC concentrations. (*a*) Long-term (persistent) effects of childhood social bonds on adult fGC concentrations, possibly mediated by adult social bonds. (*b*) Moderating effect of childhood social bonds on the association between ACEs and adult fGC concentrations, mediated by adult social bonds. (*c*) Independent effects of ACEs, childhood social bonds, and adult social bonds on adult fGC concentrations.

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Author contributions: L.C.H. and J.P.C. wrote the paper.

The authors declare no competing interest.

See companion article, "Social bonds do not mediate the relationship between early adversity and adult glucocorticoids in wild baboons," 10.1073/pnas.2004524117.

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First published August 27, 2020.

Glucocorticoids are not the only measures that are sensitive to early life adversity, and although adult social bonds did not mediate the effect of early life adversity on adult fGC concentrations, social relationships may play an important role in mediating effects of early life adversity on other biological systems. For example, lymphoid tissue is innervated by fibers of the sympathetic nervous system (SNS), a second major physiological system that is responsive to animals' experiences. Evidence suggests innervation densities are highly plastic. Primate studies conducted in the laboratory, in which animals can be randomly assigned to treatment groups, have demonstrated that social conditions that inhibit the establishment of deep social bonds result in denser innervation patterns than is the case when animals are in more stable social environments (6). Increased SNS fiber density is associated with a reduction in the type I interferon response to viral infection and with increased viral replication. We do not yet know whether early adverse events have a lasting impact on innervation densities in lymphoid tissue, but they serve as another mechanism by which experience can impact processes related to health. These measures will be more difficult to obtain in a field setting, however, highlighting the value of multiple approaches to questions pertaining to life course processes.

A comparative approach adds value, especially when seeking to understand life course processes. Very few studies of humans are maintained over participants' life course, much less with repeated assessments in each domain of inquiry from childhood to adulthood. Without such data, causal attributions are virtually impossible. Animal models can help fill that gap. When people think of the phrase "animal model," however, they probably think of a handful of vertebrate species (mice, rats, rhesus monkeys), and almost certainly think of "the laboratory" as the location where the model is developed and studied. However, that view is too narrow, as is illustrated by Rosenbaum et al., who explore the relationships between early life adversity, adult social bond quality, and concentrations of glucocorticoids in adult female savannah baboons living in the Amboseli ecosystem in Kenya. It is the latest paper from a group whose field site dates back to the early 1970s, and incorporates data collected in the last 20 to 25 y. The Amboseli Baboon Research Project has had a profound impact in a variety of areas of animal biology and primatology. From early on in this project, there was a recognition of the importance of collecting physiological data in addition to behavioral data to understand the mechanisms by which aspects of the environment—abiotic, biotic, and conspecific—affect behavior, health, fitness, and longevity. This was a rare orientation for a field project in the 1970s but has led to a wealth of data that are relevant not only for understanding the behavioral biology of the baboons themselves, but also for understanding parallel questions in our own species. The longitudinal nature of the work at this site, combined with early decisions to collect biological samples on the animals, have produced a completely unique animal model of the life course that serves as an important complement to the similar work conducted on primates in the laboratory, as well as work conducted with humans.

Rosenbaum et al. posed some alternative mechanisms by which social bonds might affect the link between ACEs and fGC concentrations, one of which was the "social buffering" hypothesis. In humans, social support is often thought of as a buffer of stressful experiences; people with better support experience less of the negative impact of stressful life events. Although not tested by the authors, it seems reasonable to posit that strong social bonds will moderate, rather than mediate, the association between ACEs and fGC concentrations in female baboons (Fig. 1*B*). The "independent effects model" (Fig. 1*C*), that ACEs and adult social bonds would have unique and additive effects on fGC concentrations, was not supported by the data in Rosenbaum et al.'s study.

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Fig. 1 depicts multiple pathways that could explain the association between ACEs and fGC concentrations, some of which introduce childhood social bonds into the story. ACEs often occur in the context of toxic family relationships and poor parenting; indeed, these contexts define some ACEs. The correlation between ACEs and childhood social bonds leaves open the question of the relative strength of these two inputs on adult outcomes, or whether childhood social bonds mediate the effect of ACEs on adult outcomes. A rich literature documents the relationship between good parental bonds in childhood, including a secure attachment style, and the development of social competencies, social support, and stronger social bonds in adulthood. In Fig. 1*a*, childhood social bonds affect both adult social bonds and adult fGC concentrations. Adult social bonds may mediate the association between childhood bonds and adult fGC concentrations, but one could also posit that weak childhood bonds have an effect on fGC concentrations not through adult social relationships but through the early life reprogramming of biological systems that sets a trajectory for physiological dysregulation into adulthood (7). In Fig. 1*b*, social bonds are again depicted as moderating or buffering the impact of ACEs on adult fGC concentrations, but in this instance the buffering effect comes from childhood social bonds operating indirectly through adult social bonds. Finally, in Fig. 1*c*, ACEs, childhood bonds, and adult bonds contribute additively and independently to fGC concentrations. These models are just some examples of the range of possible relationships among early life adversity, social bonds, and glucocorticoids that are possible when the life course is taken into consideration. In addition, with data such as have been collected in the baboon study, these are testable models.

We acknowledge that, although life course data on humans are rare, novel approaches have been devised to circumvent this limitation. Yang et al. (8) harmonized data from four longitudinal studies to probe mechanisms for the association between low socioeconomic status (SES) in childhood and health in later life. Each study was based on a large, population-based sample followed longitudinally, but differed in the age of respondents at baseline. These included young adults (12 to 18 y) in the National Longitudinal Study of Adolescent to Adult Health, young to midlife adults (25 to 65 y) in the National Survey of Midlife Development in the United States, older adults (50+ y) in the Health and Retirement Study, and 57- to 85-y-olds in the National Social Life, Health, and Aging Project. Each study included at least one measure of systemic inflammation at each measurement occasion (e.g., C-reactive protein), multiple measures of metabolic status (e.g., high-density lipoprotein and total cholesterol, hemoglobin A1c), and multiple indicators of childhood and adulthood SES (e.g., parental and own education, income). By creating a standardized composite score for each of these measurement

domains in each study, the authors were able to test different models hypothesized to explain the relationship between early-life SES and later-life health.

Among the findings was evidence that early-life SES had an indirect effect on health in older adults through the association between early-life and later-life SES, reminiscent of the model proposed in Fig. 1*a*, where child social bonds operate through adult social bonds to affect glucocorticoid concentrations. Analyzing combined datasets is an efficient means of using of extant data but may be insufficient to infer causality. However, by leveraging multiple approaches and multiple species, consistent patterns of effects increase confidence in the plausibility of posited mechanisms.

We would be remiss if we did not circle round to fundamental reasons for research on adverse early life experiences in humans and nonhumans: to learn who is most susceptible, and how and when in the life course interventions should be targeted to reduce, first, the prevalence of ACEs, and, second, their impact on later-life health outcomes. Here again, animal models can provide valuable insights. In the case of interventions, for example, studies from the late 1960s showed that pairing adolescent isolate-reared rhesus monkeys (the extreme, perhaps of ACE) with nonthreatening infants normalizes somewhat the isolate's behavior (9). This work has led directly to ongoing studies aimed at whether such an intervention can ameliorate the endocrine and immune processes disrupted by poor social bond quality. In humans, ACEs dramatically increase risk for poor mental health, problematic substance use, and interpersonal violence in adulthood (10), and these very effects represent adverse early life contexts for the next generation. Policy is needed to encourage and support the development and implementation of national, state, and community-level programs to prevent the perpetuation of ACEs across generations. A supportive environment, including good quality neighborhoods, workplaces, and community organizations, can go a long way to enhance individuals' resilience to the long-term effects of exposure to ACEs (11).

Acknowledgments

L.C.H.'s research is supported by National Institutes of Health Grants R01AG048511 and R01AG050605. J.P.C.'s research is supported by National Institutes of Health Grant P51OD011107 to the California National Primate Research Center.

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