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Thinking Clearly About Biology and Childhood Adversity: Next Steps for Continued Progress

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Abstract
In a previous *Perspectives* article, we described conceptual problems that pose challenges for research on the effects of childhood adversity and offered promising directions for future research on this topic. In a commentary on that article, McLaughlin et al. disagree with some of these criticisms and defend the utility of their current approaches. Here, we briefly summarize where these perspectives overlap and diverge, using the exchange of views to highlight pressing gaps in knowledge that can be addressed through continued empirical research.

Keywords
early life stress, adversity, stress neurobiology, child maltreatment

In our recent *Perspectives on Psychological Science* contribution (Smith & Pollak, 2021), we offered a critique of current approaches frequently used to conceptualize childhood adversity, and advanced ideas with potential to accelerate progress in understanding these phenomena. The motivation for our 2021 article was the observation that research on child adversity relies almost exclusively on measuring discrete events that have (or have not) occurred in a child's life but fails to integrate variability in how an individual child understands, interprets, or experiences those events. This is despite an extensive literature in adults and nonhuman animals (dating back to Lazarus & Folkman in 1984) indicating that variability in individuals' perceptions of events is most likely to account for how adversity "gets under the skin," affecting long-term neural and behavioral outcomes. Part of this main point is that ignoring children's perceptions of events has reified taxonomies of adversity types that are modern social constructions at the expense of identifying classifications that carve nature at its joints and align with human biology. The difference in views between our original article and the associated commentary offers an opportunity to highlight pressing questions about the biobehavioral effects of childhood adversity, as well as critical appraisal of the approaches used to answer these questions.

The agreement on many issues across both Smith and Pollak (2021) and McLaughlin et al. (2021) provides a solid foundation for future research. Both sets of authors concur there is little to be gained by continuing to use scales and measures that consist of noting either the presence or the absence or the sum total of people's exposures to negative events (e.g., the adverse childhood experiences [ACEs] approach). These metrics were historically critical in establishing the now well-replicated, robust association between negative events in childhood and a broad range of negative outcomes later in development. But counting the presence of negative or adverse events alone has not generated data that address specific underlying mechanisms linking these event exposures to negative outcomes, and this approach has not explained individual variability in these outcomes. For this reason, we and McLaughlin et al. agree on the utility of applying the construct of dimensions, broadly construed as features of children's lives that vary continuously, as a more productive way to characterize adversity.

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However, we and McLaughlin et al. propose different ways of conceptualizing, identifying, and measuring potentially relevant dimensions. McLaughlin et al. advocate a particular focus on the dimensions of threat versus deprivation. They define these dimensions by identifying whether children have been exposed to an event, or set of events, believed to distinctly characterize each dimension: Threat-related event exposures include evidence of physical, sexual, and emotional abuse as well as domestic violence, whereas deprivation-related event exposures are indexed by physical neglect, emotional neglect, and food deprivation among others (these papers are summarized in Smith and Pollak, 2021, Table S1). More recently, McLaughlin and colleagues have recognized some of the limitations of this approach, and instead of grouping children by whether they have experienced threat events or deprivation events, they now advocate summing these event exposures within each dimension (Colich et al., 2020; Sheridan et al., 2020). They assess the relationship between an outcome variable and a child's total threat score while statistically controlling for the child's deprivation score. Then they do the same for the deprivation score while controlling for threat score. These authors maintain that this approach captures dimensions because it clusters different events and exposures together to generate continuous scores for each child. But we disagree with the premise of this approach. In our view, McLaughlin et al.'s grouping and summing of children's event exposures is not meaningfully different from traditional approaches and therefore suffers from the same limitations a dimensional approach is meant to address. This is because although different events and sources of information are clustered together and combined, the resulting data are merely an aggregate of cumulative scores. Despite calling these data by a new name, "dimensions," McLaughlin et al.'s approach yields essentially the same type of information as traditional cumulative approaches.

There is a second difference of opinion between these sets of authors concerning how to determine whether any particular dimension truly holds promise for understanding childhood adversity and biology. Until now, the dimensional approach has rarely been used outside of the threat/deprivation distinction and has thus become somewhat synonymous with this narrow approach. But there are many different types of dimensions that can be studied with regard to adversity-related outcomes, as we described (Smith and Pollak, 2021). While recognizing the initial intuitive appeal of "threat" and "deprivation," we expressed skepticism about whether these are valid and meaningful distinctions that can generate deep understanding about biological responses to an environment. To illustrate one problem with these constructs, imagine a child living with a parent who physically beats them. Features of this situation such as fear of injury, violence, and exposure to hostility would lead McLaughlin et al. to classify this event in the dimension of threat. But also inherent in this child's situation is concurrent deprivation (lack of security, comfort, protection, sensitivity, and parental support). Trying to separate such a real-life situation into distinct dimensions of threat versus deprivation is, to paraphrase the philosopher W. V. Quine (1976), like trying to pull apart a gray sweater in search of separate black threads and white threads. In addition, there are a host of other potentially relevant developmental factors (and perhaps more useful dimensions) in this example, such as a lack of caregiver predictability and high environmental uncertainty, that McLaughlin et al. agree are important dimensions of experiences. This type of conceptual problem, which we referred to as "fuzzy categories" (Smith & Pollak, 2021), likely accounts for the lack of robust neurobiological evidence for a threat-versus-deprivation distinction. Increased attention to measurement of such factors as the degree of predictability or of social support in children's environments may allow researchers to assess the probability that exposure to certain events will actually be perceived as threatening or adverse in contrast to assuming that all events are experienced by all children in similar ways (Brody et al., 2019; Brown et al., 2020; Granger et al., 2020).

One significant advantage of the approach used by McLaughlin et al. is that they rely upon traditional measures of adverse events that are easily accessible and already familiar to the scientific community. But this very advantage also carries a high cost of imprecision, which leads us to reason that cataloguing negative events in this way to measure "threat" is unlikely to be meaningfully and specifically tied to human neurophysiology. Our view is that biological responses to threat occur only if and when organisms perceive themselves as under threat—data not captured by measures that simply catalogue event exposures. In other words, activation of a biological response to adversity does not occur until individuals have interpreted their circumstances as being adverse (Brosschot et al., 2018; McEwen & Akil, 2020; Sapolsky, 2015). A situation that one person experiences as highly adverse may be construed as a challenge for another or neither adverse nor challenging for a third individual. This is why even administration of potent laboratory stressors, such the Trier Social Stress Test, consistently yield a significant proportion of participants who show no biological response to the stressor (Harnett et al., 2015; Pruessner et al., 2005; Seery, 2011). Yet the hurdle posed by our view is that more measurement tools that assess variation in children's perceptions and interpretations of their life

events are in need of development. Fortunately, some measures do exist (Williamson et al., 2003), and emerging research suggests that the creation of new methods to measure children's perceptions of adversity will capture variation in behavioral, health, and biological outcomes (Danese & Widom, 2020; Jepma et al., 2018; Rivenbark et al., 2020). Such an approach, which will need to include empirically derived rather than a priori dimensional constructs, can aid in elucidating which dimensions are biologically meaningful.

The question of how to best conceptualize the dimensions most relevant to understanding child adversity and brain development also highlights problems with the way "deprivation" is operationally defined. McLaughlin et al. interpreted our article as formulating an argument inconsistent with experience-dependent learning. However, we are not questioning the existence of neural plasticity or experience-dependent learning; the issue is how deprivation is operationally defined and measured in research on child adversity. The studies by Hubel and Wiesel (1962) are a classic example of how theory, mechanisms, and measurement of neural plasticity are aligned with regard to understanding deprivation: When an eye is sutured such that nerves do not receive sensory input, that lack of activity results in changes to the visual cortex. In this model, deprivation is measured in a way that maps onto the brain system being studied. Our concern is not whether sensory inputs affect the brain; rather, we question whether the types of variables currently used by many researchers in the field, including McLaughlin et al., are too broad and distal to uncover specific effects of experiences such as deprivation on neural development. We raise questions about whether commonly used predictor variables such as parental loss or the child's mother's level of education are too imprecise and distal to reveal consistent effects of experience on brain development.

In this regard, McLaughlin et al. claim that research linking language experience to neural development supports their argument for why deprivation (as they measure it) may have specific effects on the brain. But we see their analogy as unsound. First, cases in which human children are grossly deprived of linguistic input are so rare that there are no consistent data on these effects; the few instances that have been subject to study are also confounded by a host of other co-occurring social and neurological conditions that preempt conclusions about language deprivation and brain development. Second, the effects of linguistic experience on children's development are much more specific than what can be captured under a broad rubric of "deprivation." For example, scientists can measure with precision whether the phonetic categories to which infants are exposed will affect auditory perception later in development or how exposure to certain syntactic rules early in development influences subsequent success at learning additional languages. But there are no data supporting a general critical period for all aspects of language development or a model for language deprivation in general and brain development. Future research can consider more precise ways to measure social or emotional deprivation likely to map onto aspects of brain function.

There is certainly a need for more research aimed at defining and clarifying both the relevant dimensions for understanding outcomes associated with adversity, as well as greater precision and theoretical coherence about the mechanisms through which hypothesized dimensions effect the developing brain. In this respect, we concur with McLaughlin, Weissman, and Bitrán (2019) that the existing corpus of literature examining neurobiological effects of childhood adversity consists of too few studies, vast inconsistencies among methods and findings, and limitations due to small numbers of participants. Yet whereas McLaughlin et al. claim their model generates clear predictions and point to their own research as evidence that threat and deprivation are meaningful biological concepts, we view the extant literature as too inconsistent to support this distinction. For example, Dennison et al. (2017) conclude that poor performance on a monetary-incentive-delay task supports deprivation specific effects on behavioral approach motivation, whereas Kasparek et al. (2020) conclude that deficits in the same task are specific to threat. Although McLaughlin et al. state that their theory makes no predictions about specific effects of threat or deprivation on stress-response systems, they continue to cite their own empirical papers that do make such claims (Busso et al., 2017; Slopen et al., 2019) and interpret a variety of findings related to the effects of traumatic events on primary stress-response systems through the lens of threat versus deprivation (Heleniak et al., 2016; McLaughlin et al., 2014). Perhaps most important, research from independent laboratories has not cohered with respect to whether "threat" and "deprivation" represent biologically meaningful dimensions. For example, a recent, large longitudinal neuroimaging study of a population-representative birth cohort observed no consistent different effects on the brain of childhood threat versus deprivation (Gehred et al., 2021). Researchers will be able to reach their own conclusions about the weight of evidence in this regard as more data emerge that are completely independent of the authors involved in the present debate.

Our hope is that this exchange of views in *Perspectives* will help stimulate new ideas for research on the effects of childhood adversity, an issue of humanitarian and public-health significance. Despite the millions of

lives affected by childhood adversity, much of the research literature remains riddled with varied forms of measurement that are not only applied inconsistently but also often used without a clear conceptual foundation. This has resulted in a published literature that has yet to generate effective neuroscience-informed interventions for children in dire need. To progress, the field needs some basis for classifying adversity. But using unsound classifications will only obfuscate understanding of childhood experience and brain development. We see tremendous promise in the development of new approaches that de-emphasize eliciting events, and instead place emphasis on how children construe their experience and the dimensions of children's circumstances likely to influence those perceptions.

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