Neurodevelopmental mechanisms linking early experiences and mental health: Translating science to promote well-being among youth

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Abstract

Early experiences can have profound and lasting effects on mental health. Delineating neurodevelopmental pathways related to risk and resilience following adversity exposure is critical for promoting well-being and targeting interventions. A rapidly growing cross-species literature has facilitated advances in identifying neural and behavioral mechanisms linking early experiences with mental health, highlighting a central role of corticolimbic circuitry involved in learning and emotion regulation. Building upon knowledge of corticolimbic development related to stress and buffering factors, we describe the importance of the developmental timing and experiential elements of adversity in mental health outcomes. Finally, we discuss opportunities to translate knowledge of the developing brain and early experiences to optimize interventions for youth with psychopathology and to inform policy that promotes healthy development at the societal level.

Keywords: childhood; adolescence; psychopathology; adversity; brain development

Public Significance Statement

- Early experiences can have lasting effects on mental health, and stress exposure is one of the strongest risk factors for the development of psychopathology.
- Delineating the mechanisms that confer risk and resilience in the context of early-life stress can inform efforts to promote well-being.
- This paper discusses efforts to translate developmental neuroscience to optimize interventions and inform policy that enhances youth well-being.

Neurodevelopmental mechanisms linking early experiences and mental health: Translating science to promote well-being among youth

Early experiences can have a profound influence on the developing brain and behavior, with early environments shaping emotional behavior and mental health for years to come. The majority of mental health disorders emerge during childhood and adolescence (Kessler et al., 2005), and youth exposed to early adversity are at elevated risk (McLaughlin et al., 2012). At the same time, childhood and adolescence are periods of immense opportunity, with heightened plasticity conferring potential for resilience (i.e., favorable outcomes despite exposure to adversity; Masten et al., 2021). Delineating the neurobiological pathways by which early experiences relate to psychopathology is critical for targeted treatment approaches and informing policy that promotes youth well-being.

Mechanisms Linking Early Experiences with Mental Health

Cross-species evidence suggests that a significant pathway by which early experiences become biologically embedded to influence mental health is via alterations to stress response systems (Gunnar et al., 2009) and corticolimbic circuitry involved in learning about salient aspects of the environment and regulating emotion (D. G. Gee, 2016). Indeed, youth exposed to early adversity show alterations in hypothalamic-pituitary-adrenal (HPA) axis function (Gunnar et al., 2009; McLaughlin et al., 2015) and both the structure and function of the ventromedial prefrontal cortex (vmPFC), amygdala, and hippocampus and their connections (McLaughlin et al., 2019 for review). Meta-analytic evidence supports the idea that stress exposure affects corticolimbic circuitry in youth, with some distinct and some shared alterations in mental health conditions of pediatric posttraumatic stress disorder (PTSD), anxiety, and depression (Kribakaran et al., 2020). Connections between prefrontal and limbic regions may be especially

sensitive to adversity due to a high density of glucocorticoid receptors (Honkaniemi et al., 1992) and the developmental timing of circuit maturation (D. G. Gee & Casey, 2015; Lupien et al., 2009; Tottenham & Sheridan, 2009). Whereas prefrontal regions and their connections with limbic structures undergo protracted development, the amygdala matures relatively earlier and may be particularly sensitive to the early social environment (Hanson & Nacewicz, 2021). Environmental influences on corticolimbic circuitry in early life may play an active role in shaping longer-term neural and behavioral phenotypes (Gabard-Durnam et al., 2016), including future responding to adversity (Hanson et al., 2015; Weissman et al., 2020). Collectively, these studies highlight the central role of corticolimbic circuitry in mediating the effects of early adversity on risk for psychopathology.

Stress-related alterations in the timing of corticolimbic development

Building upon the large body of evidence that early experiences and adversity affect corticolimbic circuitry and stress physiology, a growing literature suggests that early-life stress affects the timing or pace of development itself (B. L. Callaghan & Tottenham, 2016; Colich et al., 2020; Tooley et al., 2021). In typical development, corticolimbic circuitry undergoes protracted maturation, with changes throughout infancy, childhood, and adolescence (Gee et al., 2018). The reciprocal connections between the amygdala and vmPFC that support effective emotion regulation and fear extinction in healthy adults show protracted development throughout childhood and adolescence both functionally and structurally (D. G. Gee et al., 2018 for review). As excessive fears decline and emotion regulation improves with age, frontoamygdala connectivity undergoes a developmental switch (D. G. Gee, Humphreys, et al., 2013) that may

reflect a transition from greater bottom-up to stronger top-down influences (D. G. Gee, Hanson, et al., 2022).

By contrast, early adversity has been associated with accelerated maturation of corticolimbic circuitry in both rodents and humans (Colich et al., 2020 for review). Though much remains unknown about the function and long-term correlates of shifts in developmental timing, accelerated development could be adaptive to prioritize opportunities for reproduction (Belsky et al., 1991) or to meet the demands for more independent regulation of stress and emotion (B. L. Callaghan & Tottenham, 2016) in the context of a harsh environment. Recent work demonstrating acceleration of frontoamygdala connectivity following early adversity found that the more mature pattern of connectivity was associated with slower telomere shortening and slower pubertal tempo (Miller et al., 2020), suggesting protective neural system effects in the context of accelerated cellular aging following early adversity. Paralleling these findings, children exposed to caregiver deprivation who showed a more mature pattern of vmPFC-amygdala connectivity displayed lower separation anxiety (D. G. Gee, Gabard-Durnam, et al., 2013), consistent with evidence that stronger inverse frontoamygdala connectivity is associated with lower internalizing symptoms among youth exposed to early adversity (Herringa et al., 2016). While much of the research on stress acceleration has been conducted in cross-sectional studies, recent longitudinal evidence showed that stressful events were associated with accelerated development of corticolimbic circuitry during adolescence (Brieant et al., 2021). In this study, those adolescents who displayed the pattern of accelerated development also showed lower internalizing symptoms at follow-up, consistent with the idea that earlier maturation may represent an ontogenetic adaptation (Ellis et al., 2017). At the same time, there are likely to be long-term consequences of precocious maturation, and some studies have found evidence of

delay or a lack of differences following adversity (Colich et al., 2020). Recent evidence suggests that acceleration may be specific to corticolimbic circuitry and not to other brain networks (Herzberg et al., 2021) and may vary as a function of adversity-related factors (Keding et al., 2021). Future research will be important to examine longer-term effects of accelerated development and to provide a more comprehensive understanding of the influences of early adversity on the timing of maturation.

Supporting caregiving and factors promoting resilience

A growing literature has provided increasing insight into the behavioral and neurobiological processes by which early experiences promote healthy development and resilience in the context of adversity. Stable, supportive caregiving is one of the strongest protective factors against psychopathology in the context of early adversity (Sapienza & Masten, 2011) and can buffer the effect of adversity on HPA axis function, corticolimbic networks, and epigenetic aging (Brody et al., 2016, 2019; Gunnar & Donzella, 2002). While longstanding evidence has shown that the affective quality and content of caregiver signals impact neurodevelopment across species (Moriceau & Sullivan, 2005), research has increasingly highlighted specific patterns of caregivers' behavior that relate to socioemotional development in humans (Cohodes, Preece, et al., 2021; Farber et al., 2020). One way that caregivers promote well-being is by helping to regulate children's emotions and stress reactivity in the context of adversity (Cohodes, McCauley, et al., 2021). Recent research provides insight into the neurobiological mechanisms that may underlie these effects. Paralleling evidence across species (Moriceau & Sullivan, 2006), caregiver presence can buffer children's responses to stress by dampening cortisol reactivity (Hostinar et al., 2015) and amygdala reactivity (D. G. Gee et al.,

2014). As corticolimbic circuitry matures, children's reliance on caregivers for external regulation may wane as regulatory abilities become internalized and other major attachment figures, such as close peers or romantic partners, take on an increasing role in social buffering (D. G. Gee, 2016; Hostinar et al., 2014).

Early biological embedding of safe and predictable caregiver-related cues during infancy may set the stage for caregivers, and eventually other attachment figures, to support regulation later in development (D. G. Gee & Cohodes, 2021; Hostinar et al., 2014). Consistent with the idea that early caregiving experiences may shape later experiences of social buffering, early caregiving adversity is associated with weaker caregiver buffering later in development across species (e.g., B. L. Callaghan et al., 2019). However, there is substantial variability in caregiver buffering following adversity. Approximately 40% of youth who experienced caregiving adversity show reduced amygdala reactivity to parental cues. These youth exhibit lower anxiety up to three years later (B. L. Callaghan et al., 2019), suggesting that caregiver buffering of amygdala reactivity may promote resilience among adversity-exposed youth at elevated risk of psychopathology.

Sensitive Periods and Developmental Timing

Typical brain development is marked by dynamic changes that have broad implications for how early experiences shape brain maturation and long-term behavioral outcomes. Given changes in neuroplasticity and that the neural circuitry sensitive to adversity undergoes dynamic changes from the prenatal period through young adulthood, the effects of adversity are likely to vary as a function of the developmental stage at which adversity occurs (D. G. Gee & Casey, 2015; Lupien et al., 2009; Tottenham & Sheridan, 2009). One important way in which the timing

of adversity relates to developmental trajectories is through sensitive periods of heightened neuroplasticity, during which a specific environmental input has an especially strong effect on specific brain circuit and later functioning (Werker & Hensch, 2015). Unlike experience-expectant plasticity, which tends to occur early in development and is thought to reflect neural preparation to encode species-expected environmental stimuli associated with sensitive periods, experience-dependent plasticity occurs in response to individual experiences and facilitates learning throughout development (Gabard-Durnam & McLaughlin, 2019).

While sensitive periods have been more commonly identified for sensory modalities such as visual or auditory systems, emerging evidence in non-human animals points to a sensitive period for socioemotional development involving stress and anxiety (e.g., Yang et al., 2012). In humans, findings from the Bucharest Early Intervention Project (Nelson et al., 2007) show that youth exposed to institutionalized care show more secure attachment, more normative stress responses, and more normative neurodevelopmental trajectories following placement into a foster care intervention prior to 24 months of age, relative to peers placed later (McLaughlin et al., 2011, 2015; Vanderwert et al., 2016), suggesting a potential sensitive period in the first two years of life. It remains unclear whether earlier placement is associated with more favorable outcomes due to a shorter duration of adversity exposure or due to interactions with plasticity, or both. Consistent evidence has shown that the absence of stable, nurturing caregiving during the postnatal period and infancy disrupts corticolimbic development across species (D. G. Gee, Gabard-Durnam, et al., 2013; Howell et al., 2019; Johnson et al., 2018; Yan et al., 2017). Future work will provide critical insight into precisely what becomes biologically embedded during this period and how the absence of specific caregiving inputs during this window could have cascading effects later in development (D. G. Gee & Cohodes, 2021).

Parsing Heterogeneity in the Nature of Early Experiences

Given vast heterogeneity in the nature of early adversity and in developmental outcomes, approaches that focus on specific timing-related and experiential elements of adversity exposure have the potential to identify key factors that moderate the effects of adversity and to more precisely parse variability in outcomes (Cohodes, Kitt, et al., 2021; Ellis et al., 2022; Manly et al., 2001; McLaughlin et al., 2021). To date, dimensional models of early adversity have highlighted factors such as threat and deprivation (McLaughlin & Sheridan, 2016) and unpredictability (Baram et al., 2012; Belsky et al., 2012; Ellis et al., 2009) as being associated with distinct neurobiological and behavioral trajectories. Parsing such variability may be essential for mechanistic insights and targeted intervention approaches (D. G. Gee, 2021b).

However, various challenges exist in modeling heterogeneity in early experiences. There is significant chronicity and co-occurrence of adversities during development (e.g., McLaughlin et al., 2012), and youth experience adversity in broader, dynamic contexts (Hyde et al., 2020; Ip et al., 2022; McCoy, 2013). Building upon foundational approaches that have been used to test predictions about a priori dimensions or timing of adversity, data-driven computational approaches may be particularly useful for identifying specific developmental windows associated with heightened risk or for examining variability in exposure or outcomes to empirically derive key features of adversity exposure (D. G. Gee, 2021b). As one example, a recent study applied similarity network fusion to decompose heterogeneous associations between brain structure and specific aspects of the childhood environment using large-scale environmental and brain imaging data from the Adolescent Brain Cognitive Development Study (Hong et al., 2021). Similarity network fusion was initially developed to integrate multimodal data in the genetics field and has

more recently been applied to integrate neuroimaging data with phenotypic data (Wang et al., 2014). Findings identified subgroups of youth with more homogenous brain-environment associations, and this subtyping enhanced prediction of mental health symptoms. These findings suggest that it is possible to meaningfully parse heterogeneity in associations between the early environment and brain features during development, and that doing so may enhance risk identification and facilitate mechanistic insights.

As conceptual models evolve, dimensional models of adversity may benefit from increased emphasis on a child's own perception of a given event (Danese & Widom, 2020; Pollak & Smith, 2021), and they can allow for the incorporation of additional dimensions (McLaughlin et al., 2021). As one example, building upon a robust literature on the developmental timing of adversity (D. G. Gee, 2021b for review), Cohodes and colleagues (2021) have emphasized the importance of interactions between key experiential elements of adversity (e.g., caregiver involvement, controllability) and the developmental timing of adversity exposure. Delineating when specific experiential elements of adversity differentially impact outcomes, and how those effects differ by developmental stage, could inform efforts to optimize risk identification based on developmental stage or the nature of adversity exposure (Cohodes, Kitt, et al., 2021).

Importantly, conceptual models of early adversity must consider the broader socio-ecological contexts in which youth develop. Understanding heterogeneity in early adversity and mental health requires considering cultural, geographic, racial, and ethnic differences in exposure to adversity—as well as distinct ways of experiencing and understanding these adversities (Biel & Coates, 2021). Early adversity is experienced at higher rates by minoritized communities (Merrick et al., 2018; Shonkoff et al., 2021), and structural racism has shaped social and

environmental conditions in ways that contribute to racial inequities in mental health (Anglin et al., 2021; G. C. Gee & Ford, 2011). As one example, Black and Latinx families are disproportionately exposed to environmental pollutants and discriminatory incarceration (Bailey et al., 2017; Wildeman & Wang, 2017). In line with recent theoretical and empirical advances in understanding the effects of race-based stress (e.g., discrimination, stereotype threat) and racism on biological processes and mental health (Carter et al., 2022; Fani et al., 2021; Levy et al., 2016), delineating mechanistic pathways, as well as buffering factors, will require interdisciplinary collaboration with scholars across fields such as social psychology and cross-cultural psychiatry.

Translating Developmental Neuroscience to Optimize Interventions

Translating research on trajectories of corticolimbic development and mechanisms linking early experiences with mental health can inform intervention strategies in several key ways. As one example, while evidence-based interventions for anxiety and PTSD can be highly effective, a substantial proportion of youth do not benefit sufficiently from current first-line treatments (Gillies et al., 2016; Walkup et al., 2008). Up to 50% of children and adolescents with anxiety disorders still meet criteria for an anxiety disorder or experience relapse following treatment (Ginsburg et al., 2018; Walkup et al., 2008), highlighting the need to optimize existing interventions. Although response rates for exposure-based cognitive behavioral therapy are similar across childhood, adolescence, and adulthood (Kendall & Peterman, 2015), the factors contributing to insufficient response rates, and thus optimal approaches to enhance treatment efficacy, may meaningfully differ across age (Odriozola & Gee, 2021). In youth, one hypothesis is that some children and adolescents do not benefit sufficiently from current treatments because

these interventions are largely based on principles that have been studied and implemented in adults (Lee et al., 2014). Applying knowledge of how mechanisms of fear reduction and stress responding vary across development may enhance efforts to optimize interventions for youth at specific developmental stages (Figure 1).

Targeting the biological state of the developing brain

Exposure-based therapies for anxiety and PTSD are based upon principles of fear extinction, which relies on connections between the vmPFC and amygdala. Corresponding to a time of protracted development of these regulatory connections (D. G. Gee et al., 2018), cross-species studies have found diminished fear extinction (Pattwell et al., 2012) and altered vmPFC-amygdala involvement in extinction (Morriss et al., 2019) during adolescence. Stress alters these same connections, and early-life stress may lead to a shift in frontoamygdala development that could predate the onset of anxiety disorders and constrain flexibility for coping with stress (D. G. Gee, Gabard-Durnam, et al., 2013). Youth with anxiety disorders or stress-related psychopathology may benefit from efforts to optimize fear reduction through mechanisms that target alternative neural circuitry, for example by bypassing prefrontally-mediated pathways or by targeting connections that are relatively stronger during adolescence (Lee et al., 2014).

Building upon prior research that aims to enhance fear reduction beyond traditional extinction (Lee et al., 2014), safety signal learning via conditioned inhibition may offer a promising approach to reduce excessive fear during adolescence. In safety signal learning, a cue that is overly trained to signal the absence of threat is used to reduce fear in the presence of a threatening cue. In contrast to extinction, where a previously threatening cue is presented repeatedly without the aversive outcome, this approach involves associating *distinct*

environmental stimuli (i.e., safety signals) with the non-occurrence of aversive events (Christianson et al., 2012). While the neural mechanisms supporting safety signal learning continue to be explored, particularly during development and in anxiety disorders (Harrewijn et al., 2021), cross-species evidence suggests that this approach does not rely primarily on vmPFC-amygdala connections and instead involves a pathway between the hippocampus and dorsal anterior cingulate cortex (prelimbic cortex in rodents) (Meyer et al., 2019). Given evidence of protracted vmPFC-amygdala development and augmented hippocampal-prelimbic cortex connectivity during the adolescent period in rodents (Pattwell et al., 2016), judicious application of safety signals to enhance fear reduction could be particularly useful during adolescence (Odriozola & Gee, 2021). Individual differences in experiences—such as current and prior exposure to trauma—are likely to contribute to variability in the extent to which adolescents benefit from safety learned via conditioned inhibition. Whereas stress disrupts extinction learning, evidence in rodents suggests that safety signals may robustly reduce anxiety-like behavior even following stress (Woon et al., 2020). Moreover, adolescence may be a unique stage when conditioned inhibition is robust to effects of stress experienced in childhood (Meyer et al., 2021). Taken together, safety signal learning could potentially target an alternative neural circuit to promote resilience beyond traditional extinction-based approaches during adolescence. Ongoing research in humans will be important for identifying particular stimuli that could signal safety, and such stimuli are likely to depend on developmental stage (Odriozola & Gee, 2021). Particularly given research on the buffering effects of close others (D. G. Gee et al., 2014; Hornstein et al., 2016), leveraging cues related to caregivers (e.g., childhood) or peers (e.g., adolescence) could provide a valuable starting point.

Leveraging developmental and individual differences to tailor interventions

Considering developmental and individual differences, and their interactions, can offer even stronger knowledge with which to guide targeted interventions (D. G. Gee, Sisk, et al., 2022). For example, interventions could be tailored for a given individual based on factors such as an individual's profile of adversity exposure (Cohodes, Kitt, et al., 2021) or patterns of parent-child interaction (Kitt et al., 2022). In addition, identifying sensitive periods and delineating developmental patterns of experience-driven plasticity are critical for optimizing interventions (McLaughlin & Gabard-Durnam, 2022). While periods of heightened plasticity can be associated with heightened vulnerability, they also present enhanced opportunities for positive change through intervention (D. G. Gee & Casey, 2015) and potential to reshape neurobiological systems that were disrupted by stress earlier in development (Sisk & Gee, 2022). Recent evidence points to opportunities for reshaping of the HPA axis during adolescence among youth exposed to early adversity who are later living in more favorable conditions (DePasquale et al., 2019; Gunnar et al., 2019). These findings suggest that puberty may confer greater plasticity in the HPA axis, facilitating recalibration to the current environment and the potential for heightened influences of supportive social environments during this time. At the same time, it is important to note that the role of pubertal recalibration in later socioemotional functioning remains unclear, with some longitudinal evidence that recalibration is associated with poorer adjustment (N. B. Perry et al., 2020, 2022). Taken together, identifying sensitive periods and effectively parsing heterogeneity across development and individuals has the potential to inform when and for whom interventions will be most effective (Cohodes, Kitt, et al., 2021; Sisk & Gee, 2022).

Considerations in cross-species translation

The ability to manipulate the type and timing of adversity exposure, as well as risk and protective factors, in animal models has provided critical opportunities to test key predictions about development and adversity exposure (Dettmer & Suomi, 2014; Kalin & Shelton, 2003; Sanchez & Pollak, 2009). In particular, research in rodents and non-human primates has advanced knowledge about sensitive periods of neuroplasticity and the neurobiological mechanisms that link adversity with developmental outcomes (Bath et al., 2016; Chen & Baram, 2016; Lupien et al., 2009; Malter Cohen et al., 2013; McEwen, 2008). In addition, cross-species research has been essential for delineating the complex interplay between environmental, genetic, and epigenetic factors (Champagne, 2010; Fogelman & Canli, 2019; McCrory et al., 2010). As one example, cross-species studies have provided novel insight into the role of epigenetic effects, such as regulation of gene expression, in linking early experiences with alterations in corticolimbic circuitry and behavior (McClelland et al., 2011; Roth et al., 2009; Short & Baram, 2019; Torres-Berrío et al., 2019; Weaver et al., 2004). Such mechanistic insights may help to identify novel treatment targets or to inform ways to enhance treatment efficacy for youth with stress-related psychopathology.

However, translating insights from research in non-human animals to inform interventions for humans is inherently challenging. Laboratory studies with animals can be highly controlled. By contrast, humans live in vastly complex and dynamic environments, within broader social and cultural contexts (Hyde et al., 2020; Kirmayer et al., 2010). We experience the world through the lens of our complex life histories, and we interpret our experiences and engage in meaning-making in ways that likely shape our responses to stress (Birk, 2021; Steger & Park, 2012; Tottenham, 2020). Another key challenge involves the degree to which anatomy in rodents

or macaques parallels that in humans, which varies across neural systems (Xu et al., 2020). While translational research on early adversity has benefited from a relatively high degree of cross-species conservation of neural circuitry that is sensitive to adversity (Birn et al., 2014; LeDoux & Pine, 2016; Phelps & LeDoux, 2005), meaningful differences in frontoamygdala circuitry exist (B. Callaghan et al., 2019; Meyer et al., 2022). Progress in translation will be greatly facilitated through direct collaborations (Davis et al., 2017; Dincheva et al., 2015; Malter Cohen et al., 2013; Meyer et al., 2019; R. E. Perry et al., 2020) and cross-talk between researchers studying early adversity in animals and humans (Brenhouse & Bath, 2019; Sanchez & Pollak, 2009), as well as with treatment developers and clinicians (Meyer et al., 2022). Such dialogues will be essential to facilitate the translation of insights from animal models to basic human neuroscience to clinical practice, and in the opposite direction. Grounding conceptual models in key social transitions (e.g., B. Callaghan et al., 2019) and collaborating across disciplines to meaningfully consider the impact of social and cultural contexts for interventions (Kirmayer & Ban, 2013; Levy et al., 2016) can help to bridge the gap between animal models and interventions for youth.

Informing Policy to Promote Well-Being among Youth

At a broader societal level, research on child and adolescent development and the neurobiological mechanisms linking early experiences with mental health can inform policy and guide structural change (D. G. Gee, 2021a). Public policy must prioritize the well-being of all youth and ensure that the burden of coping with adversity does not fall on youth and their families, particularly given disproportionate effects on families of lower-income and minoritized racial and ethnic backgrounds (Anderson et al., 2021; Condon et al., 2020; Shonkoff et al.,

2021). Consistent with the idea that resilience depends on multiple levels of interacting systems in society (Masten et al., 2021), evidence shows that intervening at the family, community, or broader societal level is often most effective for promoting favorable outcomes following adversity. Children and adolescents can show remarkable capacity for resilience following trauma, and mental health interventions can be highly effective in promoting recovery. At the same time, in addition to identifying mechanisms related to resilience and informing interventions, scientists have an obligation to contribute to efforts to dismantle systems that cause trauma in the first place (Cohodes, Kribakaran, et al., 2021; Wildeman & Wang, 2017). Clinical and developmental scientists can contribute to such change by conducting rigorous research that is relevant to pressing societal problems, broadly sharing that work in meaningful ways, and engaging in genuine collaborations—that honor the experiences and knowledge of affected communities—with scholars from other disciplines and policymakers. Embracing these responsibilities will ensure that our research extends beyond the laboratory to guide policy and practices that protect youth from harm, to promote the fundamental right to healthy development (Casey, 2019), and, ultimately, to contribute to a more equitable and humane society.

While there is much work to be done, developmental science has had notable impacts on policy. Among these, research on adolescent brain development has influenced numerous cases in the juvenile justice system (Casey et al., 2020; Cohen & Casey, 2014), and studies from the Bucharest Early Intervention Project (Nelson et al., 2007) have demonstrated the importance of early intervention and propelled societal shifts away from institutionalized care. Ongoing policy discussions about paid family leave (Brito et al., 2022) and poverty reduction (Noble et al., 2021) have centered research on child development. In recent years, developmental science has been critical for shaping policy related to the detention and separation of migrant families at the

U.S./Mexico border resulting from the U.S. Government's "Zero Tolerance Policy" on immigration. Guided by a wealth of evidence demonstrating the consequences of forced parent-child separation on brain development and mental health (Cohodes, Kribakaran, et al., 2021; Sidamon-Eristoff et al., 2022), and the stress-buffering effects of caregivers, developmental scientists significantly contributed to international discussion about this humanitarian crisis (D. G. Gee & Cohodes, 2019). Together with research on the importance of early intervention, these findings informed policy to guide reunification and were cited prominently in the judge's ruling that the U.S. government must provide access to mental health care for all separated families (Jordan, 2019). Despite persistent calls to action (Cohodes et al., 2020; Kribakaran & Gee, 2020; Pompa, 2019) and devastating reports of harm (Brabeck et al., 2014; Hampton et al., 2021; MacLean et al., 2019; Sidamon-Eristoff et al., 2022), migrant children and families continue to face separation, detention, and deportation at alarming rates in the United States (Montoya-Galvez, 2022). Developmental and clinical scientists have advocated for key policy recommendations to mitigate harm and increase mental healthcare access, and for systemic and structural changes that would eliminate the infliction of trauma against migrant children in the United States (Cohodes, Kribakaran, et al., 2021). We must continue to play a role in partnering across fields to enact change that promotes well-being for all youth.

Conclusions

Early experiences can have profound effects on the developing brain and behavior, and exposure to adversity is a potent risk factor for psychopathology among children and adolescents. Cross-species investigations have facilitated substantial progress in delineating neurodevelopmental mechanisms associated with risk and resilience following early adversity,

and in parsing heterogeneity in the developmental timing and nature of exposure to adversity. However, the multifaceted and dynamic nature of human experiences, embedded within rich social and cultural contexts, present translational challenges. Meaningful cross-species and interdisciplinary collaborations will be essential to future progress and translation to enhance the efficacy of interventions for youth with psychopathology and to inform policy that promotes well-being among youth on a broader societal level.

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Figure 1.

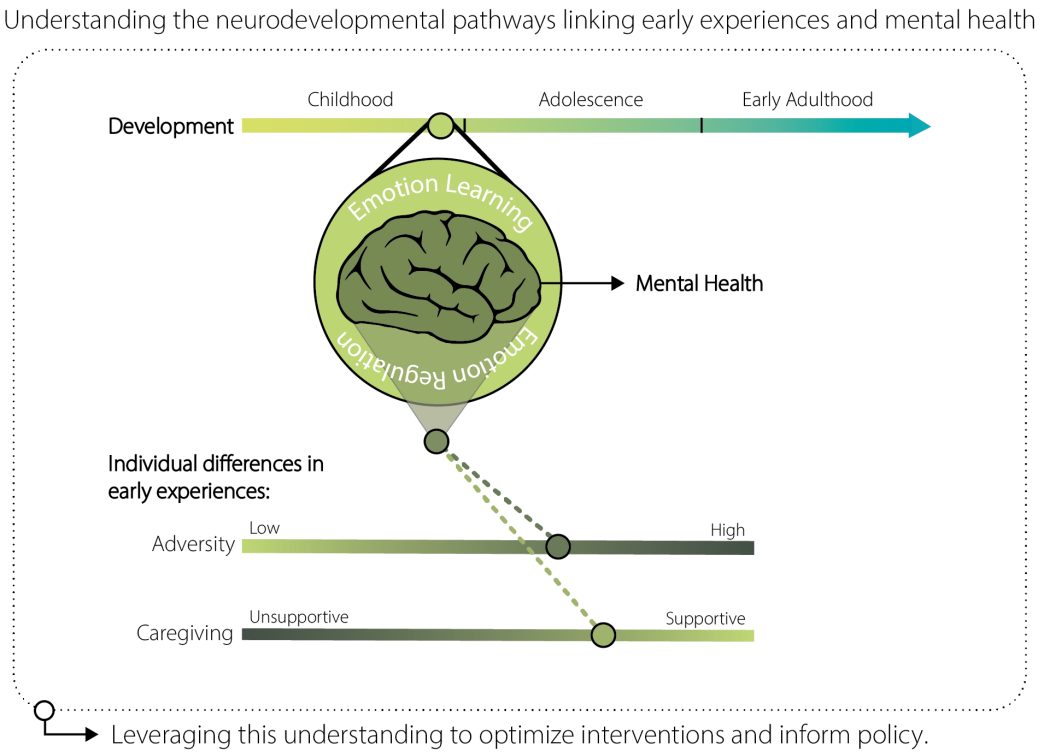

Figure 1. Translating knowledge of the neurodevelopmental pathways linking early experiences and mental health to inform interventions and policy.

Experiences that occur early in life can have profound effects on development and mental health. Cross-species research has demonstrated the role of corticolimbic neural circuitry supporting emotion learning and emotion regulation in linking early experiences with mental health. There is substantial heterogeneity in the nature and timing of adversity and in neural and behavioral development. Developmental stage and individual differences in exposure to adversity and buffering factors (e.g., caregiving support) relate to variability in neurodevelopmental pathways and mental health. Variability in a given factor that differs across individuals is depicted via a spectrum of shading. Translating findings from this research can inform efforts to optimize interventions for youth with psychopathology and to inform policy that supports well-being.

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