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Neurodevelopmental mechanisms linking ACEs with psychopathology

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Introduction

Exposure to childhood adversity is common, with more than half of children in the US experiencing at least one form of adversity by the time they reach adulthood (Green et al., 2010; McLaughlin et al., 2012). These experiences are strongly associated with risk for psychopathology and other negative outcomes in childhood, adolescence, and adulthood (Cicchetti & Toth, 1995; Green et al., 2010; McLaughlin et al., 2012). Exposure to childhood adversity increases risk for onset of both internalizing (Edwards, Holden, Felitti, & Anda, 2003) and externalizing psychopathology (Biederman, Petty, Clarke, Lomedico, & Faraone, 2011; De Sanctis, Nomura, Newcorn, & Halperin, 2012), with effects that persist into adulthood (Kessler et al., 2010). In studies that experimentally manipulate adversity exposure via early intervention that removes children from adverse rearing environments, causal evidence for an effect of adversity on psychopathology has been observed (e.g., Humphreys et al., 2015; Muennig, Schweinhart, Montie, & Neidell, 2009; Nelson et al., 2007). Given this robust evidence base, the field is well poised to move beyond questions of whether adversity influences psychopathology to those that focus on the pathways through which this impact occurs. Here we briefly review the history of how the developmental effects of childhood adversity have been conceptualized before presenting a new theory—the dimensional model of adversity and psychopathology (DMAP)—proposed by the authors of this chapter (McLaughlin, Sheridan, & Lambert, 2014; Sheridan & McLaughlin, 2014).

Cumulative risk model

Seminal work on childhood adversity focused on linking single types of adversity, such as poverty, abuse, and neglect (e.g., Brooks-Gunn & Duncan, 1997; Cicchetti & Toth, 1995) to health and developmental outcomes. This work was central to demonstrating the importance of these early adverse experiences for shaping psychopathology, but was largely abandoned after evidence for the strong co-occurrence of different adversity types emerged (e.g., Dong et al., 2004). Children are often exposed to multiple forms of maltreatment (e.g., Vachon, Krueger, Rogosch, & Cicchetti, 2015), and many kinds of adverse experiences, such as poverty and abuse co-occurr in the same children (Barnett, Manly, & Cicchetti, 1993). Importantly, this co-occurrence is greatest in nonrepresentative or clinical samples. For example, in the National Comorbidity Survey Replication—Adolescent Supplement (NCS-A; Merikangas, Avenevoli, Costello, Koretz, & Kessler, 2009), a nationally representative survey of adolescents, poverty and physical abuse were correlated at about $r = .20$ (McLaughlin et al., 2012). A more macroview of adversity examines associations between number of early adversities and psychopathology or other developmental outcomes (Edwards et al., 2003; Felitti et al., 1998). The resulting prevailing approach used to examine the consequences of adversity exposure for negative health outcomes is a cumulative risk model (Evans, Li, & Whipple, 2013; Felitti et al., 1998). At the core of this approach is a focus on the amount of exposure to adversity, but not the kind of exposure a child has experienced.

Evidence for this approach has been robust. The cumulative risk model has been useful in highlighting the strong links between adversity exposure and many negative health outcomes and has pushed the field toward reducing exposure to adversity and providing intervention to the most vulnerable. A robust set of studies taking a cumulative risk approach has shown a dose–response relationship between exposure of adversities with negative physical and mental health outcomes, such that increasing exposure is associated with elevated risk both physical and mental health problems (Chapman et al., 2004; Dube, Felitti, Dong, Giles, & Anda, 2003; Edwards et al., 2003; Felitti et al., 1998; Green et al., 2010; Hakulinen et al., 2016; McLaughlin et al., 2010, 2012; Vachon et al., 2015). This equifinality, whereby the multiple forms of adversity are associated with virtually all commonly occurring mental health outcomes in both childhood and adulthood, is well established (e.g., Green et al., 2010; Kessler et al., 2010; McLaughlin et al., 2012).

What we review now is evidence concerning the mechanisms through which this link is forged. The cumulative risk model points clearly to the fact that individuals with multiple forms of exposure are at highest risk for negative health outcomes; however, it also implicitly suggests that all forms of adversity function through the same underlying mechanisms.

This has a less well-developed evidence base. One mechanism that could account for this equifinality has been proposed; specifically, disruption of the physiological stress response system or increases in allostatic load. Evidence for the stress pathway is robust in rodents (Eiland & McEwen, 2010; Francis, Champagne, Liu, & Meaney, 1999; Liu, Diorio, Day, Francis, & Meaney, 2000). In humans, exposure to multiple forms of adversity in childhood is consistently linked with disruptions in stress physiology and related immune dysfunction, particularly when these outcomes are measured in adulthood (Danese et al., 2009; Danese & McEwen, 2012; Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010). When these mechanistic links are measured in childhood, disruption of the stress response is often observed, but less consistently and these associations do not closely mimic the work in rodents, even in well-controlled studies where the adversity exposure to rodents and humans is equated (e.g., McLaughlin, Sheridan, Tibu, Fox, Zeanah, & Nelson, 2015).

Most importantly, the single stress pathway is problematic because it ignores numerous other known developmental mechanisms through which early experience shapes brain development, which is experience-dependent and maximally plastic during early life (Fox, Levitt, & Nelson, 2010). Decades of work in human and animal models have established the presence of sensitive periods for sensory modalities (Collignon et al., 2013; de Haan, Johnson, & Halit, 2003; Hensch, 2004, 2005; Wiesel & Hubel, 1965). These periods of increased plasticity function to allow the developing brain to adapt to the environment in which it will grow, resulting in long-term change that shifts fundamental capacity and developmental trajectories lasting into adulthood. Developmental plasticity functions through basic learning mechanisms, where iterative experience, or a lack of experience, shapes the neural substrate, which supports functioning of a particular type. Although stress is one mechanism through which adversity impacts neural development, it is likely not the only mechanism, and we argue that learning processes supporting developmental plasticity should be considered as candidate mechanisms through which adversity comes to impact neural development and, subsequently, a range of negative health outcomes. The introduction of developmental plasticity as a mechanism through which adversity comes to impact health allows for more specific links between types of adversity exposures and developmental outcomes as we describe now.

Dimensional model of adversity and psychopathology

In recent work, we have examined developmental mechanisms related to early learning and specific forms of adversity. This complement to the cumulative risk model—the DMAP (McLaughlin et al., 2014; Sheridan &

McLaughlin, 2014, 2016)—is based on the principle that across the range of adverse childhood experiences (ACEs; e.g., maltreatment, community violence), different types of adversity share common features that can be conceptualized along specific dimensions of environmental experience. Two initial dimensions proposed in our model are threat, which encompasses experiences of interpersonal violence involving harm or threat of harm to the child, and deprivation, which involves an absence of expected caregiver inputs from the environment, resulting in a reduction in cognitive, social, and emotional stimulation. Although other core dimensions of environmental experience likely exist, we chose these two dimensions because they have been well studied in relation to childhood adversity. The history of research into the impact of maltreatment, as an example of threat, on psychopathology is extensive, wide ranging, and robust (e.g., Cicchetti & Toth, 1995; Vachon et al., 2015). A similarly robust literature with an equally long history has examined lack of cognitive stimulation as one pathway through which poverty impacts developmental outcomes (e.g., Bradley & Corwyn, 2002; Brooks-Gunn & Duncan, 1997). In addition, these dimensions reflect a core aspect of environmental experience for a number of commonly studied adversities (e.g., threat encompasses both experiences of violence in the community and violence occurring within the family, such as abuse and domestic violence), allowing us to rely on existing measures of adversity to investigate the dimensional model. A dimensional approach allows investigation of differences between distinct types of environmental experiences (i.e., threat and deprivation) without relying on overly specific comparisons of particular adversity types (e.g., comparing neglect and physical abuse), as was historically done prior to the development of the cumulative risk approach. Finally, ample evidence in both humans and animals already exists, which links threat and deprivation with neurobiology in a way that allows us to propose clear neural mechanisms that are likely to be influenced by these exposures.

In the following sections, we articulate the predictions of the DMAP with regard to the neurodevelopmental mechanisms that are likely to be differentially influenced by experiences of threat and deprivation. These predictions are also outlined in greater detail elsewhere (McLaughlin et al., 2014; McLaughlin & Sheridan, 2016; Sheridan & McLaughlin, 2014, 2016).

Threat

Exposure to threat is conceptualized within DMAP as the presence of a specific type of aversive learning experience that occurs during periods of peak developmental plasticity. Repeated exposure to threat (e.g., interpersonal violence) during childhood, when neural systems that support learning about threat and safety are maximally plastic, will alter these neural

systems in ways that facilitate the rapid identification of threat in the environment and mobilize strong emotional and behavioral responses to potential threats. This reflects an adaptive response to living in an environment characterized by danger, but may contribute to the emergence of psychopathology later in development. Consistent with these ideas, existing evidence demonstrates that exposure to threats early in development alters neural circuitry underlying fear learning in animals, including lasting changes in hippocampus and amygdala structure and function. In animal models, early-life exposure to stress has been associated with earlier development of fear learning (Callaghan & Richardson, 2012, 2013). For example, rodent pups who experience maltreatment by dams show avoidance of shock-associated odors earlier in development than standard-reared pups (Moriceau, Shionoya, Jakubs, & Sullivan, 2009). These findings in fear learning are related to changes in amygdala and ventromedial prefrontal cortex (vmPFC) function. The neural circuitry underlying fear learning is well characterized in animals (Johansen, Cain, Ostroff, & LeDoux, 2011; Kim & Jung, 2006). The amygdala underlies the acquisition and expression of conditioned fear (Phillips & LeDoux, 1992). In contrast, fear extinction, the process which allows the decrease of learned fear, relies on the hippocampus and vmPFC, the latter of which directly inhibits the amygdala (Bouton, Westbrook, Corcoran, & Maren, 2006). Thus, early threat exposure is linked with increased dendritic spines in the amygdala, elevated amygdala activity, and deficits in inhibitory pathways regulating the amygdala as well as dendritic atrophy in vmPFC and poor vmPFC-amygdala synaptic transmission (Eiland & McEwen, 2012).

Few studies in humans have examined early threat exposure to fear learning across development, due in part to challenges in developing paradigms that can be ethically used in children (Pine et al., 2001). However, in two studies, we have shown that children and adolescents with a history of trauma exposure demonstrate disrupted fear learning, reflecting difficulty discriminating between threat and safety cues (McLaughlin et al., 2016) and developmentally earlier fear acquisition (Machlin, Miller, Snyder, Mclaughlin, & Sheridan, 2019), findings that are remarkably consistent with the animal literature.

While few studies to date have examined the neural correlates of fear learning in children exposed to adversity, a robust literature has demonstrated that other processes, which rely on the same underlying neural circuitry, are disrupted in children with a history of threat exposure. For example, previous studies have linked violence exposure in childhood with altered patterns of information processing that prioritize threat-related information, including heightened perceptual sensitivity and attentional biases to negative emotional stimuli (Pollak & Sinha, 2002; Pollak & Tolley-Schell, 2003). In addition, multiple studies have demonstrated heightened amygdala reactivity to negative stimuli in children exposed

to threat (Heleniak, Jenness, Stoep, McCauley, & McLaughlin, 2016; McCrory et al., 2013, 2011; McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015), along with a wide range of difficulties with emotion regulation (Heleniak et al., 2016; Milojevich, Norwalk, & Sheridan, 2019; Weissman et al., 2019). Childhood threat exposure is associated with reduced volume of and thickness of the vmPFC (Gold et al., 2016; Hanson et al., 2010) and reduced resting-state amygdala-vmPFC connectivity (Burghy et al., 2012).

In sum, there is robust evidence in animal models and in human studies examining discrete adversity types (e.g., abuse, violence exposure) that threat exposure during childhood is associated with heightened emotional reactivity, poor emotion regulation, and disruptions in fear learning. In subsequent studies, we attempted to demonstrate that these effects are relatively isolated from the impact of deprivation, which we argue impacts health outcomes via different neurocognitive pathways.

Deprivation

Deprivation refers to an absence of social and cognitive stimulation and constrained opportunities for learning among children whose interactions with supportive caregivers are limited. Because most types of early learning occur in the context of interactions with caregivers, learning opportunities are constrained among children who experience less frequent and stable caregiving. The absence of consistent interactions with a caregiver deprives children of sensory, motoric, linguistic, and social experiences that caregivers provide as fodder for early learning. This kind of deprivation has frequently been observed among children who experience neglect and institutional rearing (Kaufman Kantor et al., 2004; Smyke et al., 2007). One of the primary drivers of experience dependent plasticity is the developmental process of synaptic pruning. Through pruning, the environment directly impacts neural structure such that the most efficient neural connections are preserved across development and the least efficient pathways are pruned away (Bourgeois, Goldman-Rakic, & Rakic, 1994; Huttenlocher, Levine, & Vevea, 1998). The neural system that emerges is designed to be maximally efficient within the environment in which it developed. If the environment in which a child develops is rich with complex cognitive stimulation from age-appropriate cognitive and social interactions, the emergent neural systems are likely to require many redundant and complex connections between neurons to navigate this environment. In contrast, if the environment is lacking in stimulation, the resulting neural system may be less redundant, the cortex would be thinner, and behavior relying on those redundant inputs would be impaired. The DMAP hypothesis suggests that reduced or low complexity inputs hijack the typical pruning process, resulting in early and extreme synaptic pruning in circuits that are not receiving complex input expected

from the environment, and ultimately producing a neural system adapted to a less complex environment. In support of this possibility, animal models demonstrate that global deprivation in rodent models leads to widespread decreases in cortical volume (Bennett, Diamond, Krech, & Rosenzweig, 1964). Similarly, institutional rearing in humans, which is associated with reduced social and cognitive inputs of numerous kinds, is associated with global decreases in gray matter volume (Sheridan, Fox, Zeanah, McLaughlin, & Nelson 3rd., 2012).

We argue that early deprivation in cognitive and social stimulation will have pronounced effects on children's cognitive development, particularly in the domains of language and executive functioning (Sheridan & McLaughlin, 2016). Poor performance on tasks of expressive and receptive language and executive functioning has been consistently observed among children who experience deprivation related to neglect (Allen & Oliver, 1982; Culp et al., 1991; Spratt et al., 2012) and these impacts are over and above the impact of other forms of maltreatment on cognitive function (Hildyard & Wolfe, 2002). Severe forms of deprivation, such as institutional rearing, are also consistently linked with deficits in linguistic and executive function (Albers, Johnson, Hostetter, Iverson, & Miller, 1997; Bos, Fox, Zeanah, & Nelson Iii, 2009; Colvert et al., 2008; Pollak et al., 2010; Tibu et al., 2016; Windsor et al., 2011) as have adversities associated with deprivation such as low family socioeconomic status (SES; Blair, 2002; Farah et al., 2006; Fernald, Marchman, & Weisleder, 2013; Noble, McCandliss, & Farah, 2007; Noble, Norman, & Farah, 2005; Raver, McCoy, & Lowenstein, 2013). Altered function in the neural networks that support language and executive functioning, particularly the lateral prefrontal cortex, has also been observed in children who have experienced deprived early environments, including institutional rearing (Mueller et al., 2010) and low SES (Kishiyama, Boyce, Jimenez, Perry, & Knight, 2009; Raizada, Richards, Meltzoff, & Kuhl, 2008; Sheridan, Sarsour, Jutte, D'Esposito, & Boyce, 2012). Lower SES is additionally associated with thinner cortex and reduced surface area broadly across numerous areas of association cortex (Mackey et al., 2015; Noble et al., 2015; Noble, Houston, Kan, & Sowell, 2012).

This variability in cognitive development related to neglect, institutionalization, and low SES is likely shaped by early learning opportunities and environmental stimulation. The degree of stimulation in the home and the amount and quality of maternal language predicts children's language skills (Farah et al., 2008; Hoff, 2003) and the degree of enrichment and stimulation in the early caregiving environment is associated with cognitive outcomes, including executive functioning and school achievement (Crosnoe et al., 2010; Duncan & National Institute of Child Health and Human Development Early Child Care Research Network, 2003; Sarsour et al., 2011). SES-related differences in both language ability and executive

functioning are mediated by language complexity and enrichment in the home environment (Hoff, 2003; Sarsour et al., 2011; Sheridan, Sarsour, et al., 2012). Interventions that increase children's access to learning opportunities and provide more consistent and structured interactions with adults improve cognitive development among children growing up in low-SES families (Campbell, Pungello, Miller-Johnson, Burchinal, & Ramey, 2001; Schweinhart, Berrueta-Clement, Barnett, Epstein, & Weikart, 1985), providing additional support for the role of cognitive and social stimulation in shaping children's cognitive development.

In sum, existing data support the hypothesis that deprivation is linked with thinning in cortex, reductions in surface area, and impairments in complex cognition such as executive function. These patterns are notably distinct from those most commonly observed among children exposed to threat, which primarily involve alterations in emotional processing, regulation, and learning. Together, existing studies are consistent with the notion that distinct types of adversity may have differential influences on aspects of cognitive, emotional, and neural development.

Current evidence for the dimensional model

Reflecting existing evidence related to both threat and deprivation, the DMAP proposes that these two dimensions of adversity exposure have distinct influences on developmental pathways that can be delineated in statistical models. We expect threat to primarily influence the development of emotional reactivity, emotion regulation, and fear learning processes as well as associated neural substrates such as the amygdala and vmPFC. In contrast, we expect deprivation to primarily influence the development of complex cognition, such as language and executive function, and associated neural substrates, such as the frontoparietal network.

Given that threat and deprivation-related adversities often co-occur (Green et al., 2010; McLaughlin et al., 2012), it is essential to examine their unique effects by adjusting for exposure to both forms of adversity simultaneously. The goal is not to identify children who have only experienced one particular form of adversity in isolation, but to demonstrate that despite the co-occurrence of adversity experiences, there is at least some specificity in the mechanisms that link particular forms of adversity with downstream outcomes. Such an approach is critical for isolating whether developmental processes are influenced by adversity globally or are specific to particular adversity dimensions. Thus, the primary prediction of the DMAP is that experiences of threat will have stronger influences on circuits involved in fear learning and emotional processing than experiences of deprivation and will persist after controlling for

co-occurring deprivation; in contrast, experiences of deprivation will be more strongly associated with neural circuits underlying complex cognitive abilities than experiences of threat and will persist even controlling for exposures to threat.

Recent work has supported these hypotheses. We have demonstrated that associations of threat with emotional reactivity, emotion regulation, and fear-learning processes are robust to controls for exposure to deprivation and find no associations of deprivation with these outcomes. Specifically, we have demonstrated that exposure to abuse and community violence is associated with elevated emotional reactivity (Weissman et al., 2019), heightened amygdala reactivity to negative emotional stimuli (McLaughlin et al., 2015), and disruptions in emotion regulation (Lambert, King, Monahan, & McLaughlin, 2017), after controlling for poverty. In all of these studies, markers of deprivation were unrelated to emotional reactivity and emotion regulation. We have also found a similar pattern for fear-learning processes. Specifically, children exposed to threat (abuse or domestic violence exposure) exhibited disruptions in fear learning such that they had difficulty discriminating threat and safety cues during learning, even after adjustment for poverty (McLaughlin et al., 2016). As with the prior studies, poverty was unrelated to fear learning. We have further demonstrated that exposure to abuse and community violence is associated with externalizing psychopathology, and that this association is mediated by blunted physiological reactivity (Busso, McLaughlin, & Sheridan, 2016). These associations were robust to controls for poverty and poverty was unrelated to physiological reactivity after adjusting for threat. In more recent studies, we have found that the associations of threat with amygdala reactivity and emotion regulation are robust to controls for more extreme forms of deprivation, such as neglect (Jenness et al., under review; Milojevich et al., 2019). Finally, in early childhood, we have found that exposure to threat (i.e., a composite measure taking into account abuse and domestic violence) was associated with early fear learning after controlling for deprivation (i.e., a composite measure taking into account family SES, neglect, and lack of cognitive enrichment in the home) (Machlin et al., 2019). Thus, in early childhood and adolescence, we consistently observe associations between threat exposure and heightened emotion reactivity, difficulties with emotion regulation, disruptions in fear-learning processes, and the neural correlates of these processes even after controlling for indicators of deprivation. Importantly, in these same studies, we did not observe associations between deprivation and these processes once we controlled for threat exposure (Busso et al., 2016; Lambert, King, Monahan, & McLaughlin, 2016; Machlin et al., 2019; McLaughlin, Peverill, et al., 2015).

We have similarly found specificity in the associations of deprivation with cognitive outcomes and associated neural circuitry. In a community sample of adolescents, we observed that low parental SES was linked with

disruptions in executive function (i.e., performance on an inhibitory control task), even after controlling for exposure to abuse and community violence (Lambert et al., 2017). In a replication of this finding in a sample with high levels of exposure to family violence (~38% of the sample reported clinically significant exposure to maltreatment), we observed that low parental SES predicted poor adolescent executive function measured by either performance on a behavioral task or parental report on a questionnaire measure (Sheridan, Peverill, Finn, & McLaughlin, 2017). In this same sample, low SES was associated with differences in recruitment of the frontoparietal network during a working memory task. These associations were robust to controls for exposure to violence (Sheridan et al., 2017). These initial tests of DMAP revealed evidence consistent with our predictions, but relied on low parental SES instead of a direct measure of deprivation exposure.

While low SES in families has been consistently associated with a lack of opportunity for cognitive enrichment (Bradley, Corwyn, McAdoo, & Coll, 2001), SES remains a risk factor for this exposure and not evidence of exposure. In follow-up analyses, we addressed this concern by directly measuring enrichment in the home environment. We demonstrated that directly measured opportunities for cognitive enrichment in the home environment during early childhood mediated the impact of SES on executive function and cortical thickness in the frontoparietal network (Rosen, Sheridan, Sambrook, Meltzoff, & McLaughlin, 2018) and that exposure to complex language in the family environment mediated the association of family SES with prefrontal cortex function (Sheridan, Sarsour, et al., 2012). In a longitudinal study of young children, we have shown that the degree of cognitive stimulation in the home environment mediates the association of SES with multiple forms of executive functions as well as growth in executive function over time (Rosen et al., in press). In more recent work, associations between a composite score reflecting deprivation (i.e., family SES, neglect exposure, and lack of cognitive enrichment) predicted executive function (i.e., performance on an inhibitory control task), after controlling for exposure to threat (i.e., a composite score of abuse and domestic violence exposure) (Machlin et al., 2019). Finally, we demonstrated that a lack of enrichment in the home environment predicted psychopathology in young adulthood via an indirect pathway through linguistic ability measured in early adolescence, and that this association was robust to controls for family violence exposure (Miller et al., 2018). In sum, in recent investigations, we have accumulated robust evidence that associations between deprivation and complex cognitive function, in particular executive function, are robust to controls for exposure to abuse and other forms of community and family violence exposure. Importantly, these associations have been observed in both early childhood and adolescence, longitudinal predictions of cognitive function, and multiple methods of assessing complex cognitive function, including through parent report, functional

activation using fMRI, and direct measures of task performance. Finally, we did not observe associations between threat exposure (e.g., abuse, community violence) and cognitive function in models which included both deprivation and threat (Lambert et al., 2016; Machlin et al., 2019; Miller et al., 2018; Sheridan et al., 2017), even when exposure to threat was significant and more severe than exposure to deprivation (i.e., exposure to physical or sexual abuse versus exposure to low family SES).

The evidence we have collected thus far in our direct tests of the DMAP robustly supports the hypotheses in our originally proposed model (McLaughlin et al., 2014; Sheridan & McLaughlin, 2014) and in subsequently published articulations and extensions of this model (McLaughlin & Sheridan, 2016; McLaughlin, Sheridan, & Nelson, 2017; Sheridan & McLaughlin, 2016). Importantly, we, like others (Farah et al., 2008; Humphreys & Zeanah, 2015; Manly, Kim, Rogosch, & Cicchetti, 2001), have observed multifinality with regards to associations between indicators of deprivation and threat and psychopathology (e.g., Busso et al., 2016). However, none of our existing studies suggests that the same multifinality exists for the more proximal developmental measures (e.g., emotional reactivity or executive function), which we hypothesize and observe to be mechanisms through which different forms of adversity influence risk for psychopathology (e.g., Miller et al., 2018). This distinction is central to DMAP, and makes this model substantively congruent with and complementary to existing cumulative risk approaches. While cumulative risk approaches can facilitate identification of *who* is most at risk, the DMAP approach can help identify *why* these associations exist and, thereby, identify potential targets for early interventions.

Directions for future research

While our existing work robustly supports the DMAP, the findings have primarily relied on self-report and have been in small nonrepresentative and cross-sectional samples. Future work should prospectively link direct measures of both threat and deprivation in the home during early childhood with psychopathology in later childhood or adulthood while demonstrating mediation by separate neurocognitive pathways. This would constitute a full test of DMAP. In addition, timing of both exposure and measurement of developmental outcome will almost certainly affect our observed associations between exposure to adversity and developmental outcomes. As an example of this, we observe that, in adolescence, exposure to threat is linked with a lack of differentiation between stimuli which do and do not predict threat (McLaughlin et al., 2016). In contrast, in early childhood, threat exposure predicts developmentally earlier acquisition of fear learning; that is, younger children (ages 4–5 years) who

have been exposed to family violence are able to distinguish between stimuli which do and do not predict a fear-eliciting stimulus, whereas same-age children without threat exposure do not (Machlin et al., 2019). This developmental distinction is consistent with theory, as the fear-learning system is developing during early childhood (Britton, Lissek, Grillon, Norcross, & Pine, 2011; Rudy, 1993), and animal models would suggest that exposure to threat would enhance this learning process early in development (e.g., Gunnar, Hostinar, Sanchez, Tottenham, & Sullivan, 2015). However, across time, iterative exposure to threats and the consequences of disrupted fear learning would likely function to blunt distinctions between fear and safety cues (McEwen, 1998, 2007). It is precisely this kind of interaction between development and adversity exposure that longitudinal studies could better characterize and disentangle.

Policy and practice implications

As we have articulated earlier, we theorize and have empirically observed that different forms of adversity exposure give rise to many forms of psychopathology via separable neurobiological pathways. This observation leads to the novel implication that not all forms of psychopathology related to adversity should be treated similarly. In fact, the etiology of a set of symptoms may influence the way in which those symptoms are treated. For example, a child with emotion regulation difficulties following exposure to traumatic violence and a child with executive function deficits following a lack of cognitive stimulation at home both may display what appears to be similar disruptive behavior; yet, interventions for these two hypothetical children could be very different. In the case of threat exposure, the child may benefit from a trauma-focused therapy designed to increase self-regulatory capacity via emotional awareness, whereas, in the case of an executive function deficit, the child may benefit from increased scaffolded learning opportunities at home and in the classroom. Of course, many children will have multiple exposures and require multiple and varied interventions. Even in these complicated cases, we expect that understanding the etiological "source" of behavioral deficits could enhance and refine future interventions.

Conclusion

The DMAP presents an alternate conceptual model of how adversity comes to influence developmental outcomes and addresses a specific limitation in the cumulative risk approach involving a lack of specificity concerning how early adverse experiences influence developmental

processes and, in turn, health outcomes. First, our model encompasses a wide range of adverse experiences. Traditionally, the ACEs model specifically focuses on a set of experiences within the family, which, while demonstrably important in development, are limited in scope (Felitti et al., 1998). Such models do not take into account a robust literature which links early deprivation related to a lack of cognitive stimulation or exposure to violence within the community with negative developmental outcomes (e.g., Bradley, Convyn, Burchinal, McAdoo, & Coll, 2001; Margolin & Gordis, 2000). Second, our model provides a way of distilling complex environmental experiences into core underlying dimensions that can be used to examine multiple adversity types that share core features (e.g., physical abuse and community violence), and evaluating the specificity with which these dimensions relate to developmental outcomes. Third, our model outlines neurobiological mechanisms that are specific to particular kinds of experiences that are both testable and falsifiable. Although adverse experiences co-occur, they can and should be measured separately to identify specificity in the cognitive, emotional, and neurobiological processes that they influence. Importantly, although threat and deprivation each impact psychopathology, they appear to do so through distinct cognitive, emotional, and neurobiological pathways.

DMAP builds on existing models of the impact of adversity on child development. The concept of deprivation is derived from the poverty literature identifying reduced cognitive stimulation as one pathway through which poverty influences education. The concept of threat is related to stress exposure postulated in the traditional ACEs model. Our model brings together multiple dimensions of adversity and pathways through which these adversities could be embedded to yield novel testable hypotheses, which recent evidence supports. This approach is an alternate to existing models of the impact of adversity on psychopathology that promises to generate novel and more targeted intervention strategies, which have the potential to enhance opportunities for our most disadvantaged children.

Conflict of interest statement

The authors have no conflicts of interest, which impact this work.

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