



Child maltreatment and the development of substance use and disorder

Dante Cicchetti^{a,b,*}, Elizabeth D. Handley^b

^a Institute of Child Development, University of Minnesota, USA

^b Mt. Hope Family Center, University of Rochester, USA



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ABSTRACT

Children who experience maltreatment are at well-documented risk for the development of problematic substance use and disorder in adolescence and beyond. This review applies a developmental psychopathology framework to discuss the complex multilevel probabilistic pathways from child maltreatment to substance use and substance use disorder (SUD). We begin with an overview of the myriad vulnerabilities associated with child maltreatment, including the development of substance use and SUD. Prominent pathways that may potentiate liability for SUD are discussed. Specifically, we highlight the robust empirical support for the prominent externalizing pathway of risk, and also discuss the state of the research regarding the internalizing pathway. Consistent with the developmental psychopathology perspective, we then review biological processes such as neuroendocrine mechanisms, allostatic load, and neurobiological pathways that may underlie child maltreatment risk, as well as discuss broader contextual issues. Elucidating the processes underlying the development of substance use and disorder among children exposed to this form of early adversity is paramount for not only informing developmental theories, but also designing effective prevention and intervention programs. Thus, implications for preventive interventions are provided. Finally, critical next steps for research within the area of child maltreatment and the developmental psychopathology of substance use and SUD are proffered.

1. Overview of child maltreatment risk

Child maltreatment has been frequently identified in the life histories of adolescents and adults in treatment for substance use disorders (SUDs),¹ as well as in epidemiological studies of risk factors for substance use and SUD (Cicchetti and Rogosch, 2018; Oshri et al., 2011; Rogosch et al., 2010). However, limited research has charted the unfolding developmental progression of maltreated children from the early years to demonstrate the emergence of substance use problems (Cicchetti and Luthar, 1999; Cicchetti and Rogosch, 2018).

In this review, we apply a developmental psychopathology framework to discuss the complex multilevel probabilistic pathways from child maltreatment to substance use and substance use disorder (SUD). Developmental psychopathology is an integrative scientific discipline that represents a movement toward comprehending the causes and determinants, pathways, sequelae, and prevention and treatment of high-risk conditions and mental disorders through its synthesis of knowledge from multiple disciplines and levels of analysis with the goal of understanding the mutual interplay between psychopathology and normative adaptation (Cicchetti, 1990, 1993; Sroufe, 1990). Developmental psychopathologists seek to engage in a comprehensive

evaluation of genetic, neurobiological, physiological, psychological, and social processes and how these multiple levels of analysis may influence the pathways by which normal and pathological outcomes may be achieved (Cicchetti and Sroufe, 2000). Accordingly, such a developmental perspective may aid in the prevention and reduction of the individual and societal burden of substance use disorder and mental illness.

Children in maltreating families are exposed to a progression of risk factors related to adolescent substance involvement, thereby heightening their vulnerability for problematic substance use outcomes. Adolescence is a developmental period fraught with neurobiological, physiological and psychological changes that often increase risk for exposure to substances (Cicchetti and Rogosch, 2002; Spear, 2000). Among the prominent risk factors for alcohol and drug use and disorder in adolescence, co-occurring psychopathology has received particular attention (Cicchetti and Rogosch, 1999; Weinberg et al., 1998). Disruptive behavioral problems are routinely identified as major contributors to adolescent substance use. Costello (2007) provided an overview of several large-scale, epidemiological studies examining linkages of various forms of psychopathology to substance use and disorder in adolescence and early adulthood. She concluded that a

* Corresponding author. Institute of Child Development, University of Minnesota, Twin Cities, 51 E. River Parkway, Minneapolis, MN, 55455, USA.
E-mail address: cicchett@umn.edu (D. Cicchetti).

¹ Throughout this review paper, and consistent with the DSM-5, we use the term “substance use disorder” to include substance abuse and substance dependence.

wealth of prospective data demonstrated that conduct problems precede drug use and disorder.

Internalizing problems, including major depression, bipolar disorder, and panic disorder, have been shown to predict cannabis use and cannabis use disorder as adolescents progress into adulthood (Wittchen et al., 2007), although some of these relations were attenuated when co-occurring externalizing problems were controlled. Thus, for maltreated children who are at substantial risk for the development of early externalizing and internalizing psychopathology, the developmental course poses vulnerability for engaging in substance use and developing SUDs.

Child maltreatment is a pathogenic relational experience that represents one of the most adverse and stressful challenges that confront children (Cicchetti and Lynch, 1995). Maltreatment during childhood ushers in motion a probabilistic path of epigenesis for abused and neglected children that is marked by an increased likelihood of failure and disruption in the successful resolution of salient developmental tasks. These failures may be isolated to specific domains of functioning, or they may occur in combination with failures in other domains. Maltreated children are likely to exhibit atypical physiological regulation, difficulties in affect differentiation, recognition, and regulation, dysfunctional attachment relationships, anomalies in self-system processes, perturbations in representational development, problematic peer relationships, and trouble adapting successfully to school (Cicchetti and Barnett, 1991; Cicchetti and Toth, 2015, 2016; DePasquale et al., 2019; Pollak et al., 2000; Pollak et al., 1997; Schneider-Rosen and Cicchetti, 1984; Shields and Cicchetti, 1997, 2001; Toth and Cicchetti, 1996; Toth et al., 2000).

Repeated disruptions compromise the positive organization of diverse developmental systems, thereby increasing the probability of maladaptation, psychopathology and problematic substance use, as negative transactions between the child and the environment ensue (Cicchetti and Lynch, 1993). Furthermore, if maltreatment persists, then stability in behavioral symptomatology increases and exacerbates risk for the emergence of SUDs. Because the majority of children are affected by adverse experiences (Cicchetti, 2017), child abuse and neglect may exemplify the greatest failure of the caregiving environment to provide opportunities for normal genetic, neurobiological, neuroendocrinological, and immunological development (Cicchetti and Lynch, 1995; Cicchetti and Toth, 2015). However, some maltreated children function in an adaptive resilient fashion despite their negative and traumatic experiences.

Discovering the processes underlying resilient functioning offers considerable promise for affirming, challenging, and expanding upon extant developmental theories (Howe et al., 2002), as well as for translating these findings to inform prevention, intervention, and social policy initiatives (Barnett et al., 1993; Cicchetti et al., 2006; Cicchetti and Toth, 1993; Toth et al., 2006). Moreover, epigenetic research suggests that with effective intervention and treatment, many maltreated children can be assisted to move toward resilience (Cicchetti, 2013; Szyf and Bick, 2013; Toth et al., 2013).

2. Developmental pathways

Since its inception as an emergent interdisciplinary science, diversity in process and outcome has been conceived as among the hallmarks of a developmental psychopathology perspective (Cicchetti and Rogosch, 1996; Sroufe, 1990). Equifinality refers to the observation that in any open system (Mayr, 1964, 1988) a diversity of pathways may lead to the same outcome. Stated differently, in an open system (i.e., one where there is maintenance in change, dynamic order of processes, organization, self-regulation, etc.) the same end state may be reached from a variety of different initial conditions and through different processes. Within the field of developmental psychopathology, equifinality has been invoked to explain why a variety of developmental pathways may eventuate in a given outcome, rather than

expecting a singular primary pathway to the adaptive or maladaptive outcome.

The concept of multifinality (Cicchetti and Rogosch, 1996) suggests that any one component may function differently depending on the organization of the systems in which it operates. In other words, a particular adverse event should not necessarily be viewed as leading to the same outcome in every individual. The meaning of any one attribute, process, psychopathological, or substance use/disorder condition needs to be considered in light of the complex matrix of individual characteristics, experiences, and social-contextual influences involved, the timing of events and experiences, and the developmental history of the individual (Sroufe et al., 1990).

Equifinality and multifinality are particularly important to consider when creating and delivering interventions for those who have experienced stress during childhood. For example, children who have experienced maltreatment might respond to the stressor or to an intervention in distinct ways that will likely have implications for their risk for future psychopathology or SUD.

3. Child maltreatment risk for substance use and disorder

Child maltreatment is a well-documented risk factor for the development of substance use and disorder (e.g., Buckingham and Daniolos, 2013; Hamburger et al., 2008; Huang et al., 2011; Tonmyr et al., 2010; Wendland et al., 2017; White and Widom, 2008; Widom et al., 2006). For instance, individuals who experienced maltreatment during childhood are at risk for an earlier initiation into drinking (Dube et al., 2006), faster increases in heavy episodic drinking during adolescence (Shin et al., 2013), and persistently elevated heavy episodic drinking throughout adolescence and young adulthood (Shin et al., 2013). Indeed, childhood emotional maltreatment, physical maltreatment, and sexual abuse have each been associated with increased risk for tobacco use, alcohol use, illicit drug use, and polydrug use (Alvarez-Alonso et al., 2016; Moran et al., 2004). Furthermore, adolescent girls with a history of childhood sexual abuse are approximately five times more likely to be heavy polysubstance users compared to adolescent girls without experiences of childhood sexual abuse (Shin et al., 2010). Although numerous forms of childhood adversity have been linked with risk for substance use later in development, Elliott et al. (2014) found that over and above other forms of childhood adversities (e.g., parental death, parental incarceration, parental divorce), child maltreatment uniquely predicted persistent alcohol dependence in adulthood (Elliott et al., 2014).

4. Externalizing and internalizing pathways

Identifying the underlying mechanisms, or pathways, by which maltreated children are at risk for the development of substance use and disorder is necessary for further elucidating the consequences of child maltreatment and understanding the etiology of SUDs, as well as for informing the design of preventive interventions for children and families. Consistent with the notion of equifinality, there are multiple pathways implicated in child maltreatment risk for substance use and disorder.

Specifically, there is robust support for an externalizing pathway to the development of SUDs (Chassin et al., 2016; Chassin et al., 2013; Mezquita et al., 2014; Sher et al., 2005; Zucker et al., 2011). This pathway, also referred to as the behavioral undercontrol-disinhibition pathway, antisocial pathway, and/or deviance-proneness pathway, has developmental roots in infancy marked by a difficult temperament. Throughout childhood, behavioral disinhibition, aggression, poor self-regulation, and rule-breaking behaviors are common temperament and behavioral hallmarks of this pathway.

Normative adolescent development is characterized by increased time spent with peers, and decreased time spent with parents and family (Spear, 2000), making the peer context particularly salient

throughout this period. Indeed affiliation with deviant, substance using peers is a robust proximal predictor of substance use throughout adolescence (e.g., Chuang et al., 2005). In spite of the normative shift away from family, parents continue to be influential in shaping adolescent substance use behavior (e.g., Wood et al., 2004). Specifically, parents may deter their adolescents' substance use via general parenting behaviors (i.e., social support) as well as via substance-specific socialization (i.e., alcohol-specific parenting strategies; Handley and Chassin, 2013). Moreover, affiliation with substance-using peers has been shown to mediate the effects of parenting behaviors on youth substance use (Kiesner et al., 2010).

Within the externalizing pathway of risk, maladaptive parenting practices and family contexts often interact with child temperament and behavior and peer affiliation to enhance risk (Chassin et al., 2009; Chassin et al., 2013; Costello, 2007; King et al., 2004; Sher, 1991; Zucker et al., 2011). Moreover, the family context may also be marked by parental SUD, a robust predictor of offspring SUD (e.g., Chassin et al., 1996). For example, a study by Fergusson et al. (2008) demonstrates the multifaceted complexity of this pathway. Results indicated that exposure to childhood physical abuse, childhood conduct problems, parent illicit drug use, and affiliation with substance-using peers all uniquely predicted late adolescent/emerging adult illicit drug use and disorder.

In accordance with the broader substance use literature, there is clear empirical evidence for an externalizing pathway underlying the link between child maltreatment and substance use and disorder (e.g., Handley et al., 2015; Handley et al., 2017; Jones et al., 2013; Mezquita et al., 2014; Oshri et al., 2011; Wardell et al., 2016). For example, Rogosch et al. (2010), showed that the effect of child maltreatment on early adolescent cannabis disorder symptoms was partially mediated by childhood externalizing problems. Similarly, using a ten-year prospective design, Handley et al. (2017) found that conduct problems during childhood significantly mediated the effect of child maltreatment on problematic alcohol use during emerging adulthood. Moreover, among a sample of adolescent girls, childhood sexual abuse predicted later substance use by way of a behavioral undercontrol pathway (Bailey and McCloskey, 2005).

Importantly, child maltreatment often occurs within the context of parental substance use disorder. Results of the Adverse Childhood Experiences (ACEs) study indicated that adults who reported being raised by one or more alcoholic parents were twice as likely to also have experienced child maltreatment (Dube et al., 2001). Indeed prospective studies show that parental SUD is a robust risk factor for child maltreatment (e.g., Appleyard et al., 2011; Chaffin et al., 1996; Kotch et al., 1999). Given that parental SUD is a well-documented risk factor for offspring development of problematic substance use (see Chassin et al., 2016 and Zucker et al., 2016 for reviews), parental SUD may represent an important familial context for this externalizing pathway among many maltreated individuals.

An additional, and not mutually exclusive, pathway underlying the link between child maltreatment and substance use is the internalizing pathway. The internalizing, or negative affect pathway, to SUD is marked by an early inhibited temperament style and internalizing symptoms throughout childhood, with continuity into adolescence and adulthood (Hussong et al., 2011; Zucker, 2006). It is also theorized to include positive beliefs about the benefits of substance use (e.g., tension-reducing alcohol use expectancies) and motivations to use substances to cope with distress and negative affect (Hussong et al., 2011; Sher, 1991), both of which are associated with problematic substance involvement (e.g., Cooper et al., 2016; Jones et al., 2001).

Empirical support for this general internalizing pathway to the development of SUD has been mixed. Although some prior studies have shown that internalizing symptoms predict problematic drinking behaviors, over and above externalizing symptoms (e.g., Menary et al., 2017; Pesola et al., 2015), others have not found an association (e.g., Chassin et al., 1999; King and Chassin, 2008). Moreover, studies have

also shown a protective effect of internalizing symptoms such as separation anxiety and social withdrawal on the development of substance use and disorder (Kaplow et al., 2001; Rogosch et al., 2010).

Within the context of child maltreatment, evidence for an internalizing pathway is emerging (e.g., Goldstein et al., 2010; Grayson and Nolen-Hoeksema, 2005; Hudson et al., 2017; Jester et al., 2015; Mezquita et al., 2014). For example, Mezquita et al. (2014) found childhood emotional abuse was associated with higher levels of negative emotionality, which in turn predicted coping motivations to drink and problematic drinking. Similarly, Lewis et al. (2011) showed that child maltreatment prospectively predicted cigarette use at age 16 via internalizing symptoms at age 14. Interestingly, Hudson et al. (2017) also found support for an internalizing pathway from child maltreatment to alcohol use, albeit moderated by gender. Specifically, anxiety was found to mediate the link between childhood sexual abuse and problem drinking among women; however, for men, anger was a significant pathway, suggesting potential gender differences in this mechanism of risk. Finally, post-traumatic stress disorder (PTSD) has also been shown to mediate the association between childhood maltreatment and adult alcohol and illicit drug use among women (White and Widom, 2008).

Investigators have recently begun to explicate the role of genotype within this internalizing pathway. Specifically, the *FKBP5* gene is involved in the stress-response symptom and it has been repeatedly documented that variation in *FKBP5* interacts with early adversity to predict various negative outcomes, including depression, anxiety, and aggressive behavior (see Zannas and Binder, 2014 for review). Regarding child maltreatment risk for SUD, Handley et al. (2017) found support for moderated mediation of this pathway such that childhood internalizing symptoms mediated the effect of child maltreatment on the development of emerging adult tension-reduction alcohol expectancies only for individuals with a particular *FKBP5* genotypic profile. Future research examining whether certain individuals may be more vulnerable to traversing the internalizing pathway of risk due to genetic variation may clarify prior seemingly inconsistent findings.

Neuroendocrine dysregulation and an altered stress response may represent an additional aspect of the internalizing pathway. Although more research on the associations between hypothalamic-pituitary-adrenal axis (HPA axis) regulation and reactivity and substance use among humans is necessary, HPA dysregulation likely plays a critical role in this mechanism. The links between child maltreatment and the HPA axis system are complex and the majority of research with maltreated children have examined basal levels, rather than reactivity. Results of these studies are largely mixed (see Cicchetti and Toth, 2016; McCrory et al., 2010; Tarullo and Gunnar, 2006 for reviews). Interestingly though, the consideration of internalizing disorders may clarify these inconsistencies. For instance, Cicchetti et al. (2010) showed that children who experienced physical and sexual abuse prior to age 5, and had high levels of internalizing symptoms, demonstrated a pattern of cortisol levels across the day, indicative of neuroendocrine dysregulation. This pattern of atypical flattening of cortisol was unique to individuals with these specific forms of early maltreatment in combination with high internalizing symptoms only. In addition to internalizing disorders, gender may also play a clarifying role in these associations. Doom et al. (2013) found that among girls, those who experienced late onset and recent maltreatment evidenced higher cortisol compared to nonmaltreated girls and girls who experienced early, but not recent, maltreatment, thus highlighting the criticality of examining both gender and maltreatment timing within these complex associations.

Although more research is needed to explicate direct links between the HPA axis system and the development of problematic substance use, given the evidence that maltreated children are at-risk for subsequent dysregulation of the HPA axis, and that dysregulation of the HPA axis enhances risk for psychopathology, neuroendocrine dysregulation may also play a key role in maltreated children's liability for the development of substance use and disorder. This is consistent with the stress-

incubation/corticolimbic developmental cascade hypothesis proffered by Andersen and Teicher (2008, 2009) in which it is theorized that the link between early life adversity and SUD may be partially mediated by a highly reactive HPA axis and using substances to cope with negative affect. Future investigations into the complex relations between child maltreatment, neuroendocrine dysregulation, internalizing symptoms and the development of SUD are necessary.

In summary, consistent with equifinality, there are multiple complex pathways whereby maltreated individuals are at risk for the development of SUDs. Elucidating these underlying mechanisms is critical for the advancement of knowledge regarding the etiology of SUDs, as well as for informing the development of prevention and intervention efforts. It is worth emphasizing, however, that child maltreatment does not lead to the development of SUD for all individuals. Consistent with multifinality, risk associated with child maltreatment does not lead to SUD in a deterministic manner. Rather, these are probabilistic pathways and child maltreatment may lead to a number of diverse outcomes for various individuals.

5. Developmental cascades framework

Developmental cascades refer to effects that spread across multiple levels (micro to macro levels), across multiple domains at the same level, or across systems (Cicchetti and Dawson, 2002; Masten and Cicchetti, 2010). These models strive to demonstrate a developmental sequence of risk processes, whereby early risk factors generate subsequent vulnerabilities in development, which in turn transact to produce further risk for competent adaptation. An illustration of a cascade model of SUD is demonstrated by Oshri et al. (2011). The cascade model of these investigators charted a developmental sequence from family risk due to child maltreatment to early childhood difficult temperamental traits (e.g., ego undercontrol), the emergence of childhood aggression and disruptive behavior problems, and ensuing in substance disorder in adolescence. This cascade model illustrates the influence of compromises in one domain unfolding to difficulties in subsequent areas of behavioral control and regulation. Notably, early risk processes coalesced to promote conduct disturbance as an important link in the cascade from child maltreatment to adolescent substance problems.

Thus, problems in one domain can cascade to multiple domains, suggesting that an early risk factor may not remain confined to one domain over time and can alter the course of development. Developmental cascades may explain why early problems following childhood stress can cascade to problems at multiple levels and across domains in adolescence and adulthood. Cascading effects can be direct or indirect through a number of pathways, and they may be either adaptive or maladaptive. However, it is important to note that cascades are not deterministic; not all early problems spread to other domains and there is great variability between individuals in the characteristics of cascades.

6. Multiple levels of analysis considerations

The majority of research on the sequelae of child maltreatment has focused predominately on psychosocial outcomes. In recent decades, research on the effects of maltreatment has incorporated multilevel investigations of biological and psychosocial sequelae (Cicchetti and Valentino, 2007; De Bellis, 2001, 2005; McCrory et al., 2010; Pollak et al., 1997). Shonkoff et al. (2009) differentiated among three types of stress that children may experience. Normative and routine life challenges that are embedded within a context of protective factors are examples of positive stress. Time-limited stresses within supportive relationships are considered tolerable stress. Toxic stress involves conditions in which the child is exposed to chronic severe, and prolonged stress, often occurring in the absence of protective factors. As chronic and toxic stressors (Shonkoff et al., 2009), child abuse and neglect are implicated in the disruption of biological systems, including

neuroendocrine and immune functioning, physical and mental health outcomes, and neurobiology (Cicchetti and Rogosch, 2001a, b; Cicchetti et al., 2010).

Developmental considerations within the context of multilevel processes are important. In this regard, the timing of periods of severe stress may be critical. For example, genotypic variation and variation in the age of maturation of brain structures, notably the hippocampus, prefrontal cortex, and the amygdala, may result in differential effects on functioning and health (Lupien et al., 2009; Shonkoff et al., 2009). Sensitive periods in the development of these brain structures may generate heightened vulnerability to the neurotoxic effects of excess glucocorticoids, thereby creating a long-term liability as development proceeds.

Alternatively, the cumulative exposure to stressful experiences and concomitant dysregulation of the HPA axis may contribute to ongoing wear and tear on these brain structures. These effects of chronic stress are heightened, given that these areas of the brain have dense concentrations of glucocorticoid receptors, thereby promulgating progressive inefficiency in brain structure and function. For children in low-income environments and those subjected to abuse and neglect, the consequences may be particularly salient for health outcomes across the lifespan. Consolidated, multisystemic intervention approaches beginning early in development are necessary to reduce environmental stress exposure, child maltreatment, and allostatic overload to improve physical and mental health. Not only is the extensive rate of psychopathology among maltreated children a dire consequence in its own right (Vachon et al., 2015), but also psychopathology in childhood has been linked to negative physical health outcomes many years later in adulthood (Von Stumm et al., 2011). Accordingly, the extent to which the experience of maltreatment generates high rates of psychopathology and substance use and disorder in abused and neglected children may, in turn, have negative ramifications for physical health (Cicchetti et al., 2016).

Attention to individual differences in the organization of multiple biological and psychological systems in response to the chronic stress of maltreatment is crucial for attaining a more complete understanding of processes contributing to vulnerability to SUD. In particular, chronic stress disrupts the regulation of the endocrine system, and maltreated children exhibit varied extremes of HPA axis functioning (Cicchetti and Rogosch, 2001a; Cicchetti et al., 2010) which in turn relates to different patterns of psychopathology (Cicchetti and Rogosch, 2001b), including substance use and disorder (Goodman, 2008). Glucocorticoids induce effects on brain development and organization, and dysregulation in the HPA axis can thereby contribute to variation and atypicalities in executive cognitive functions, attention, and emotion regulation, as well as personality organization, which increase susceptibility to substance use and disorder. Such stress-compromised children may be even more vulnerable to familial and peer contextual influences that promote drug use as development proceeds and these youth enter late adolescence.

7. Allostatic load

The concepts of allostasis and allostatic load (AL) provide an integrative framework for understanding how exposure to stress, such as child maltreatment, potentiates long-term liabilities for physical and mental health (Juster et al., 2010). Allostasis is a process that involves the activation of multiple interactive physiological systems (e.g., cardiovascular, neuroendocrine, immune, and metabolic systems). Epinephrine, norepinephrine, cortisol, dehydroepiandrosterone (DHEA), and pro- and anti-inflammatory cytokines are considered the primary mediators of AL because they operate on the cellular level (Miller et al., 2011; Shonkoff et al., 2009).

The concept of allostatic load (McEwen and Stellar, 1993) has been invoked to describe the wear and tear that the body experiences because of repeated cycles of allostasis that are inefficiently handled.

Allostatic load refers to cumulative physiological dysregulation across multiple biological systems. Chronic or toxic stress, as is often the case in child maltreatment, can lead to allostatic load through a cascade of causes and sequelae that can damage the brain, organ systems, and the neurochemical balance that undergirds cognition, emotion, mood, personality and behavior (Lupien et al., 2009).

In the short term, mobilization of these systems exerts a protective effect on the body and promotes an adaptive response to stress; however, with chronic activation, physiological reactions to stress become less efficient in protecting the individual. It is the collective impact of alternations across multiple systems that contribute most strongly to morbidity, rather than changes within any one system (Rogosch et al., 2011). Allostatic load processes may unfold very early in the development of maltreated children, setting up the possibility of life-long difficulties in the regulation of physiological stress systems. Maltreatment during childhood increases allostatic load later in life, resulting in a number of emotional and physical difficulties. These include depression, aggressions, substance use and substance use disorder, as well as inflammation, cardiovascular disease, and telomere shortening (Danese et al., 2008; Gunnar and Vaszquez, 2001, 2006; Juster et al., 2010; Tyrka et al., 2010).

8. Neurobiological development of maltreated children

We know that the mechanisms of neural plasticity cause the brain's anatomical differentiation to be dependent on stimulation from the environment (Cicchetti and Tucker, 1994). For example, early maltreatment may alter young neural networks, resulting in cascading effects through the course of later development, possibly constraining the child's capacity to adapt flexibly to new challenging situations and environmental demands. Accordingly, early psychological trauma may eventuate not only in emotional sensitization, but also in pathological sensitization of neurophysiological reactivity. Thus, it is not surprising that maltreatment experiences exert an impact on biological and psychological processes across the lifespan. For example, Cicchetti and White (1990) hypothesized that the difficulty that maltreated youngsters have verbally expressing their feelings to their caregivers may not only be a reflection of psychological intimidation (Beeghly and Cicchetti, 1994), but also a manifestation of the neuroanatomical and neurophysiological changes that occur secondary to abuse and neglect.

Children who are endowed with normal brains may encounter a number of experiences (e.g., poverty, community violence, child maltreatment) that exert a negative impact on developing brain structure, function, and organization and contribute to distorting these children's experiences of the world (Hackman et al., 2010). Physiological and behavioral responses to maltreatment are interrelated and contribute to children's making choices and responding to experiences in ways that typically produce pathological development.

Numerous interconnected neurobiological systems are affected by the various stressors associated with child abuse and neglect. Each of these neurobiological systems influences and is influenced by multiple domains of biological and psychological development, including psychopathology and substance use disorder. Moreover, in keeping with the principle of multifinality, the neurobiological development of maltreated children is not affected in the same way in all individuals. Furthermore, not all maltreated children exhibit anomalies in their brain structure or functioning and identifying protective mechanisms in these children emerges as an important area for future research.

9. Ecological contexts

Cicchetti and Lynch (1993) proposed the ecological/transactional model which asserts that child maltreatment must be studied within the broader environmental and cultural context in which it occurs. Indeed children exposed to child maltreatment are more likely to be from socioeconomically disadvantaged families and reside in communities

marked by more violence, as compared to nonmaltreated children (Lynch and Cicchetti, 1998; National Incidence Study; Sedlak et al., 2010). Moreover, Cicchetti and Lynch (1993) assert that pervasive community violence may function as a risk factor for child maltreatment and that community factors and child maltreatment experiences may interact and transact to exert harmful effects on development. For example, community violence and child maltreatment have been shown to each uniquely, and in interaction, affect anger in young adults (Cecil et al., 2014). Additional research investigating interactive effects of community violence and maltreatment in the development of SUD is necessary for a more complete understanding of the etiology of SUD among this vulnerable population.

In addition to community violence, another important contextual factor is neighborhood disadvantage/disorder. There is growing evidence to suggest that individuals with a history of child maltreatment may be especially susceptible to disadvantageous neighborhood contexts. For example, Handley et al. (2015) found that neighborhood disadvantage, as indicated by constructs such as census poverty data, neighborhood safety, and neighborhood drug availability, was associated with higher levels of adolescent marijuana dependence symptoms only for children who experienced maltreatment, but not for low-income demographically matched nonmaltreated children. Similarly, Keyes et al. (2012) showed that neighborhood physical disorder, as measured by observer ratings of the neighborhood physical environment (i.e., boarded up windows, vacant buildings, etc) predicted binge drinking only among adults with a history of child maltreatment. These results highlight the vulnerability associated with child maltreatment that may heighten risk for developing problems with substances in certain contexts. Finally, results of a study by Duprey et al. (2017) supported an internalizing pathway from childhood neglect to adolescent substance use; however, this pathway was moderated by neighborhood disorder. Contrary to expectations, higher levels of internalizing symptoms were associated with higher substance use in less disordered neighborhoods. Together these studies indicate the criticality of examining maltreated youth within the context of their neighborhood environments.

10. Preventive and intervention implications

Because individuals who experienced child maltreatment are at heightened risk for the development of substance use and SUD, prevention efforts aimed at the avoidance of maltreatment are imperative. Two such examples that begin working with families prenatally or in the early postpartum period are Building Healthy Children (BHC; Paradis et al., 2013) and the Nurse Family Partnership (NFP; Olds, 2006). Both seek to support high-risk mothers in an effort to promote positive parenting and avoid child maltreatment.

In addition to prevention efforts, targeted interventions for families affected by maltreatment are also required to alter the probabilistic negative developmental cascade from child maltreatment to subsequent substance use and disorder among offspring. Cohen, Mannarino, Murray, and Igelman (2006) provide a comprehensive review of the evidence-base for psychosocial interventions for maltreated and violence-exposed children. For instance, trauma-focused cognitive-behavioral therapy (TF-CBT; Cohen and Mannarino, 1993), originally developed for children exposed to sexual abuse but expanded for children exposed to any type of trauma, enjoys robust empirical support with maltreated children (Cohen et al., 2006).

Moreover, the empirical evidence for various pathways from child maltreatment to SUD and associated negative outcomes can inform clinical practice and decision making for this vulnerable population. Specifically, because child maltreatment has a marked negative impact on the parent-child relationship (e.g., Cicchetti and Toth, 2015), and because a positive parent-child relationship is protective against the development of substance use and disorder (e.g., Handley and Chassin, 2013), relational interventions present a theoretically salient approach

to the prevention of SUD among maltreated children (Suchman et al., 2004; Suchman et al., 2006). See Toth et al. (2013) for a complete review of relational interventions for child maltreatment.

Given the robust support for the externalizing pathway, and the cascading of negative outcomes across multiple systems that may begin with early externalizing behavior, evidence-based treatments targeting childhood externalizing symptoms will also be beneficial to thwarting the development of SUDs (see Eyberg et al., 2008 review of evidence-based treatments for childhood disruptive behavior). Moreover, effective school-based programs targeting the substance-use norms of the school community may be beneficial to curbing peer substance use, a proximal and salient predictor of youth substance use. Additionally, given the robust associations between parental SUD, disruptions in the parent-child relationship, and child maltreatment, treatment for parental SUD may also be indicated.

11. Future directions

Although it is evident that individuals who experience childhood maltreatment are at risk for substance use and disorder, much work remains. For instance, as previously described, child maltreatment is a broad umbrella term used to describe adverse experiences such as physical abuse, sexual abuse, physical neglect (failure to provide), supervisory neglect (lack of supervision), emotional abuse, and educational neglect (Barnett et al., 1993). Maltreated children often experience more than one subtype of maltreatment (Cicchetti and Rizley, 1981; Cicchetti and Toth, 2016). Among studies that employed Child Protective Service (CPS) record data for maltreatment classifications, results indicated that 33–94% of maltreated children experienced more than one subtype of maltreatment (Herrenkohl and Herrenkohl, 2009). Moreover, child maltreatment occurs across various sensitive developmental periods throughout childhood and adolescence.

Evidence suggests there are implications to not only the subtype experienced, but also the chronicity, severity, and developmental timing of the maltreatment. For example, Manly et al. (2001) found that children who experienced chronic maltreatment beginning in the preschool years demonstrated significantly higher externalizing symptoms compared to children who experienced maltreatment in infancy/toddlerhood only, and those who experienced maltreatment during the preschool years only. In addition, Cicchetti et al. (2015) found that the timing of maltreatment, in terms of the onset and recency of experiences, interacted with C-reactive protein (CRP) genotypic variation, a gene associated with the inflammatory process, to predict salivary CRP levels, a marker of inflammation. Although replication is necessary, this study provides preliminary evidence that developmental timing of maltreatment may be differentially related to outcomes depending on an individuals' genotype. Finally, Cowell et al. (2015) showed that children maltreated in infancy demonstrated worse performance on neurocognitive tasks involving cognitive control compared to children who were maltreated later in development. Importantly, there may be critical implications of the *pattern* of maltreatment subtypes experienced, the chronicity and severity of the experiences, and the developmental timing of these patterns of experiences, especially with regards to the development of substance use and disorder. These complexities call for a person-centered approach to the study of child maltreatment effects on SUDs.

Person-centered methods, such as latent class analysis and latent profile analysis, seek to describe population heterogeneity by identifying classes of individuals based on various patterns or profiles of experiences or characteristics (Collins and Lanza, 2010; Lanza and Cooper, 2016). Given the vast heterogeneity in maltreatment experiences in terms of subtype, chronicity, severity, and developmental timing, person-centered approaches represent an important tool for explicating the development of substance use and disorder among individuals with child maltreatment histories.

Research is emerging illustrating the utility of these approaches

within the examination of child maltreatment. A recent review of the 16 studies that employed person-centered methods to classify maltreatment heterogeneity concluded that poly-victimization was associated with the most severe outcomes in all studies reviewed (Debowska et al., 2017). Moreover, the authors also concluded that the consequences of childhood sexual abuse may be intensified when the sexual abuse occurs with other forms of maltreatment. Although these person-oriented approaches have been useful for identifying commonly occurring patterns of maltreatment experiences, many unanswered questions remain, especially with regards to substance use and disorder. For example, which pattern of maltreatment subtypes and developmental timing are associated with early onset substance use, rapid escalation in substance use, and the development of disorder? Questions such as these will be best answered by employing person-centered methods.

In addition to the use of person-centered methods, future research on child maltreatment and the development of SUDs will also benefit from a continued examination of the relevant contexts in which the experience of child maltreatment is embedded. As described above, child maltreatment often co-occurs within the context of parental SUD, community violence, and neighborhood disorder. It is important to consider the ways in which these community and family-level risk factors may each uniquely, and interactively, affect the development of offspring SUDs. This information will be critical to effective intervention and prevention programs for families and for a more nuanced understanding of the etiology of SUDs.

Moreover, future randomized control trials (RCTs) examining the efficacy and effectiveness of prevention and intervention programs for child maltreatment and the development of SUDs must continue to move toward a multi-level conceptualization, consistent with the developmental psychopathology framework (Luthar and Cicchetti, 2000; Toth et al., 2013), including multi-level mediators, moderators, and outcomes. Examples may include investigations of epigenetic change as a result of intervention, examination of genotypic moderators of treatment efficacy, and the assessment of multi-level mechanisms and outcomes such as neurocognitive, neuroendocrine, immune, and metabolic processes. See Masten and Cicchetti (2016) for a detailed discussion of the criticality of a multiple-levels-of-analysis approach to general preventive intervention. Moreover, RCTs will also benefit from a strong developmental conceptualization, not only in terms of the developmental salience of the active components of the interventions, but also in relation to the optimal developmental timing of prevention or intervention efforts.

12. Conclusion

Childhood maltreatment initiates a probabilistic negative cascade across myriad multilevel processes increasing risk for the development of problematic substance use and disorder. Because substance use and SUD unfold over time in a developing individual (Fitzgerald and Puttler, 2018), changes in contexts, processes, and developmental tasks all play critical roles in the evolution of substance use and SUD (Windle et al., 2009). The heightened vulnerability is a consequence of both the continuity of risk from earlier developmental stages and the unique neurobiological, cognitive, and socio-emotional changes that occur (Cicchetti, 2010; Spear, 2000; Zucker et al., 2016). Accordingly, it is necessary to consider developmental variations in cognitive, socio-emotional, representational, interpersonal, and social-cognitive capacities, in addition to biological domains of functioning, in order to ascertain how individual differences in these domains, as a result of childhood maltreatment, may underlie and interact to affect the development of substance use and SUD over time.

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