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REVIEW ARTICLE

# Is There an Ace Up Our Sleeve? A Review of Interventions and Strategies for Addressing Behavioral and Neurobiological Effects of Adverse Childhood Experiences in Youth

Namik Kirlic[1] · Zsofia P. Cohen[1] · Manpreet K. Singh[2]



**Abstract**
Exposure to early life adversity (ELA) is a major public health crisis posing as a significant risk of immediate and sustained mental and physical health consequences. While a remarkable body of knowledge has been amassed showing psychological, cognitive, social, developmental, and neurobiological consequences of ELA exposure, little has been done to improve the long-term mental and physical health outcomes for youth exposed to ELA. Furthermore, neurobiological processes underlying poor outcomes in this population have been largely left out of prevention and intervention target efforts. In this review, we first describe ELA-related alterations across psychological and neurobiological systems in children and adolescents. Next, we describe existing evidence-based interventions targeting ELA-related outcomes. We then turn to experimental studies examining individual differences in mechanistic functioning consequent to ELA exposure, and strategies that target these mechanisms and modulate disrupted functioning. Finally, we highlight areas of future research that may be promising in engaging behavioral and neurobiological targets through novel preventive interventions or augmentation of existing interventions, thereby reducing negative mental and physical health outcomes later in life.

**Keywords** Adverse childhood experience · Trauma · Adversity · Stress · Treatment · Intervention · Cognitive behavioral · Mindfulness · Children · Adolescent · Resilience · Neurobiological

## Introduction

Exposure to early life adversity (ELA) poses as a significant risk of immediate and sustained mental and physical health consequences. With high incidence rates and yearly cumulative direct and indirect costs, ELA exposure is a major public health crisis. Although a remarkable body of knowledge has been amassed in the past several decades showing psychological, cognitive, social, developmental, and neurobiological consequences of ELA exposure, little has been done to actually improve the long-term outcomes for those affected by maltreatment in childhood and adolescence. Furthermore, given that some maltreated adults fare poorer in current first-line psychological and pharmacological therapies, there is a dire need to identify preventive interventions that directly target behavioral and neurobiological disruptions seen in maltreated individuals and subsequently cultivate resilience.

In this review, we aim to bridge the gap between basic findings regarding the effects of ELA exposure, existing treatments, and outcomes in maltreated children and adolescents, henceforth referred to as youth. We pay particular attention to the knowledge-base that may inform improvement of existing or development of novel neuroscience-based and scalable preventive interventions. We begin by discussing ELA-related systemic disruptions across psychological and neurobiological domains. Next, we describe existing evidence-based interventions targeting ELA-related outcomes, focusing on mechanisms of change along these domains where possible. We then turn to experimental studies examining individual differences in mechanistic functioning consequent to ELA exposure, and strategies that target these mechanisms and modulate disrupted functioning. Finally, we highlight areas of future research that may be promising in engaging behavioral and

✉ Namik Kirlic
nkirlic@laureateinstitute.org

[1] Laureate Institute for Brain Research, 6655 South Yale Ave., Tulsa, OK 74136, USA

[2] Department of Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

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neurobiological targets through novel interventions or augmentation of existing interventions in order to prevent negative mental and physical health outcomes later in life.

## Early Life Adversity

In this review, we define early life adversity (ELA) as sustained exposure to negative events between birth and 18 years of age. Examples of ELA include, but are not limited to, emotional and physical abuse and neglect, sexual abuse, household dysfunction, parental psychopathology, parental substance abuse, parental incarceration, interpersonal violence, and peer bullying. Retrospective reports from a large nationally representative adult sample show that 64% experienced some form of adversity in early life (Dube, Felitti, Dong, Giles, & Anda, 2003b; Felitti, Anda, Nordenberg, Williamson, Spitz, & Edwards, 1998), while approximately 40% experienced two or more types of adversity (Dube et al., 2003b). Although regarded as a conservative representation, in 2017, 674,000 children and adolescents in the USA were newly confirmed victims of abuse and neglect as defined by state laws, resulting in 1720 deaths, while the number of Child Protective Services investigations involved 5% of all American youth (US Department of Health & Human Services, 2017).

ELA is associated with profound and long-term health and societal costs. In the landmark Adverse Childhood Experiences (ACEs) study of nearly 10,000 individuals (Felitti et al., 1998), it was discovered not only that ELA is common, but also that there was a dose-response effect of ELA on mental and physical health problems in these individuals. Two decades of research since then across a number of independent samples have confirmed these findings. ELA is perhaps the single strongest predictor of mental illness, accounting for nearly half of all childhood-onset disorders and up to 32% of all later-onset disorders (Kessler, McLaughlin, Green, Gruber, Sampson, & Zaslavsky, 2010), including posttraumatic stress disorder (PTSD), depression, anxiety, panic attacks, disruptive behavior, substance abuse, sleep disturbance, and suicide attempts (Alisic, Zalta, Van Wesel, Larsen, Hafstad, Hassanpour, & Smid, 2014; Carliner, Keyes, McLaughlin, Meyers, Dunn, & Martins, 2016; Dube et al., 2001; Dube et al., 2003a; Dube et al., 2003b; Kendler, Bulik, Silberg, Hettema, Myers, & Prescott, 2000; McLaughlin, Green, Gruber, Sampson, Zaslavsky, & Kessler, 2012; Scott, Smith, & Ellis, 2010). In addition, ELA is associated with greater risks for borderline and antisocial personality disorders (Herman, Perry, & Van der Kolk, 1989; Jovev, McKenzie, Whittle, Simmons, Allen, & Chanen, 2013; Reich, Vera, Marino, Levin, Yong, & Frankenburg, 1997), as well as psychosis and bipolar disorder (Arseneault, Cannon, Fisher, Polanczyk, Moffitt, & Caspi, 2011; Bendall, Jackson, Hulbert, & McGorry, 2007; Cutajar, Mullen, Ogloff, Thomas, Wells, & Spataro, 2010; Etain, Mathieu, Henry, Raust, Roy, & Germain, 2010; Leverich, McElroy, Suppes, Keck, Denicoff, & Nolen, 2002). Among maltreated individuals, earlier onset, greater severity, and more comorbidity in psychopathology are also observed (Teicher & Samson, 2013), as well as a 3-fold increase in prescription rates for antidepressants, 2-fold for anxiolytics, 10-fold for antipsychotics, and 17-fold for mood-stabilizers (Anda, Brown, Felitti, Bremner, Dube, & Giles, 2007). With respect to physical health, maltreated individuals are observed to have poorer health behaviors (e.g., smoking, physical inactivity, and unsafe sexual behaviors), and multiple physical health conditions and diseases, including obesity, heart disease, hypertension, obstructive pulmonary disease, and chronic lung disease, resulting in premature mortality (Brown, Anda, Tiemeier, Felitti, Edwards, Croft, & Giles, 2009; Dube et al., 2003b).

The costs of ELA exposure and subsequent short- and long-term negative outcomes to society are staggering. Current estimates of ELA-related direct (e.g. hospitalization and mental health care) and indirect (e.g. special education and lost productivity) costs in the USA range between $80.3 and $124 billion per year (Fang, Brown, Florence, & Mercy, 2012; Gelles & Perlman 2012). Therefore, ELA exposure is a major public health crisis requiring novel approaches for preventive interventions that are best optimized for maltreated individuals.

Currently, the data on how maltreated individuals respond to treatment are scarce, and the lack of available evidence raises concern about how their clinical needs are being addressed. For example, findings among individuals being treated for depression with both psychological and pharmacological interventions suggest that ELA is associated with a significant lack of response or remission (Nanni, Uher, & Danese, 2012). The unique factors driving these unfavorable outcomes are not well-understood. Outcomes in youth are also not understood. In this review, we aim to summarize the current evidence-based psychological interventions for exposure to maltreatment and trauma in youth, seeking to establish potential neurobiological targets for current and novel interventions. First, however, we present a brief review of neurobiological effects of ELA.

## Neurobiological Consequences of Early Trauma

The neurobiological consequences of ELA have been well-described in previously published comprehensive reviews (Bremner, 2003; De Bellis & Zisk, 2014; Nemeroff, 2016; Teicher, Samson, Anderson, & Ohashi, 2016). Briefly, negative outcomes associated with ELA are believed to stem from a cascade of closely intertwined alterations in neurobiological processes responsible for the regulation of stress, including

those mediated by endocrine, immune, epigenetic, metabolic, and brain systems. Stress acutely mobilizes a coordinated response across endocrine, sympathetic nervous, and immune systems in order to best prepare an organism for coping with the stressor and its consequences. Data describing the central and peripheral endocrine effects of ELA youth are also beginning to emerge (Sun, Watson, Angal, Bakkila, Gorelik, & Leslie, 2018).

Extant data now show that ELA alters the functioning of the hypothalamic–pituitary–adrenal (HPA) axis, which plays a prominent role in responses to and regulation of stress. Psychological and physical stressors characteristic of ELA activate the HPA axis, ultimately resulting in the release of cortisol, which is necessary for the integration of appropriate responses to stress and the subsequent return to homeostasis via a negative feedback loop terminating in the hypothalamus and in the pituitary gland (Gunnar & Vazquez, 2006). Quick activation and quick subsequent recovery of the stress response is suggested to represent an adaptive response, whereas an exaggerated or blunted response is associated with dysfunction (Karatsoreos & McEwen, 2013). Both hyper- (Fernando, Beblo, Schlosser, Terfehr, Otte, & Löwe, 2012; Heim, Newport, Bonsall, Miller, & Nemeroff, 2001) and hypo-activity (Carpenter, Shattuck, Tyrka, Geracioti, & Price, 2011; MacMillan, Georgiades, Duku, Shea, Steiner, & Niec, 2009; Ouellet-Morin, Odgers, Danese, Bowes, Shakoor, & Papadopoulos, 2011) of the HPA axis have been associated with ELA exposure. Although hyperactivity is attributed to the damage to hippocampal neurons containing glucocorticoid receptors which signal the termination of the HPA axis response, the hypoactivity of the HPA axis is thought to relate to insufficient glucocorticoid signaling. A number of factors, including the nature, timing, and chronicity of adverse events, and genetic factors, are thought to account for these divergent outcomes (Nemeroff, 2016). Changes in HPA axis functioning consequent to ELA are also, in part, due to epigenetic modifications (i.e. DNA methylation, histone modification, and changes in mRNA levels) of the key HPA axis regulatory genes (e.g., FKBP5, NR3C1, and NR3C2) (Ladd, Huot, Thrivikraman, Nemeroff, & Plotsky, 2004; Makino, Smith, & Gold, 1995; McGowan, Sasaki, D'alessio, Dymov, Labonté, & Szyf, 2009; Medina, Seasholtz, Sharma, Burke, Bunney, & Myers, 2013; Silberman, Acosta, & Zubilete, 2016), which may result in altered glucocorticoid and mineralocorticoid receptor availability and efficiency.

The immune system is regulated by the glucocorticoids released by the HPA stress axis. Sustained stress exposure compromises the immune system, resulting in systematic inflammation, which is characterized by enhanced production of pro-inflammatory cytokines, such as the interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and C-reactive protein (CRP) (Danese, Caspi, Williams, Ambler, Sugden, & Mika, 2011; Pace, Mletzko, Alagbe, Musselman, Nemeroff, Miller, & Heim, 2006; Slopen, Kubzansky, McLaughlin, & Koenen, 2013). In turn, elevated cytokines further impair glucocorticoid receptor functioning, thereby inhibiting negative feedback and promoting inflammation (Raison & Miller, 2003). Indeed, individuals with ELA exposure show compromised immune functioning both at baseline (Danese, Pariante, Caspi, Taylor, & Poulton, 2007; Taylor, Lehman, Kiefe, & Seeman, 2006) and in response to immune challenges (Bertone-Johnson, Whitcomb, Missmer, Karlson, & Rich-Edwards, 2012; Kiecolt-Glaser, Gouin, Weng, Malarkey, Beversdorf, & Glaser, 2011; Slopen et al., 2013). Elevated inflammation has been implicated in the etiology of a number of medical conditions and, thus, represents an early marker of disease risk in maltreated individuals and likely contributes to associated poor physical health outcomes (Danese & McEwen, 2012).

Finally, an additional consequence of chronic stress exposure related to elevated inflammation and glucocorticoid-associated oxidative stress damage is the shortening of the length of telomeres (Drury, Theall, Gleason, Smyke, De Vivo & Wong, 2012; Kiecolt-Glaser et al., 2011; Shalev, Moffitt, Sugden, Williams, Houts, & Danese, 2013; Tyrka, Price, Kao, Porton, Marsella, & Carpenter, 2010). Telomeres are DNA–protein structures at both ends of each chromosome that play a vital role in preserving genomic information. Accelerated telomere shortening is associated with biological aging, aging-related diseases, and mortality, and may further explain the poor physical health outcomes and shortened lifespan observed in maltreated individuals (Drury et al., 2012).

## Neural Correlates of ELA

Brain development is shaped by experience, and ELA exerts profound effects on this process. As a chronic activator of the stress response, ELA elicits widespread neurobiological reactions which, over time, disrupt developmental trajectories in brain structure and function (Teicher, Samson, Anderson, & Ohashi, 2016). Overall, structural neuroimaging studies show smaller intracranial, cerebral, and cerebellar volumes in maltreated relative to non-maltreated youth (Bauer, Hanson, Pierson, Davidson, & Pollak, 2009; De Bellis, Keshavan, Frustaci, Shifflett, Iyengar, Beers, & Hall, 2002b; De Bellis, Keshavan, Shifflett, Iyengar, Beers, Hall, & Moritz, 2002a; De Bellis & Kuchibhatla, 2006; Hanson, Chung, Avants, Rudolph, Shirtcliff, & Gee, 2012). These volumetric differences may be regionally pronounced in prefrontal cortical white matter and right temporal lobe volumes. Maltreatment is also associated with attenuated development in the anterior cingulate, orbitofrontal, and dorsolateral prefrontal cortex (De Bellis, Keshavan, Spencer, & Hall, 2000; Hanson, Chung, Avants, Shirtcliff, Gee, Davidson, & Pollak, 2010; Tomoda Suzuki, Rabi, Sheu, Polcari, & Teicher, 2009). In addition, smaller volume of the midsagittal middle and posterior

regions of the corpus callosum, as well as a reduced fractional anisotropy, indicate less myelin integrity in maltreated youth (Jackowski, Douglas-Palumberi, Jackowski, Win, Schultz, & Staib, 2008; Teicher, Dumont, Ito, Vaituzis, Giedd, & Andersen, 2004). Reduced ventral and inferior prefrontal gray matter volumes are also described to distinguish youth with posttraumatic stress disorder from typically developing controls (Carrion, Weems, Richert, Hoffman, & Reiss, 2010). Thus, structural neuroimaging studies suggest aberrant gray and white matter structure across multiple brain regions in ELA exposed youth.

Perhaps the strongest support for the effect of maltreatment on brain structure has been observed in the hippocampus. However, reduced overall hippocampal volume has been observed in adults (Smith, 2005; Stein, Koverola, Hanna, Torchia, & McClarty, 1997; Teicher, Anderson, & Polcari, 2012; Vythilingam, Heim, Newport, Miller, Anderson, & Bronen, 2002), but not in youth. Similarly, amygdala volume has been found to be decreased in adults exposed to maltreatment (Driessen, Herrmann, Stahl, Zwaan, Meier, & Hill, 2000; Malykhin, Carter, Hegadoren, Seres, & Coupland, 2012; Schmahl, Vermetten, Elzinga, & Bremner, 2003; Vermetten, Schmahl, Lindner, Loewenstein, & Bremner, 2006), but is inconsistently reduced in maltreated youth. Developmental differences alone may explain these inconsistencies in regions that are critical for emotion and stress regulation (Carrion et al., 2010; De Bellis, Keshavan, Clark, Casey, Giedd, & Boring, 1999; De Bellis & Kuchibhatla, 2006; Teicher & Samson, 2016), such that youth may not yet demonstrate the deleterious effects of cumulative stress on these temporal lobe regions. In addition, the presence or absence of psychopathology may play a role in varied outcomes, as well as that some changes may reflect adaptive or compensatory modifications.

With respect to brain function, enhanced amygdala response to emotional stimuli in maltreated relative to non-maltreated individuals has been well-described (Teicher et al., 2016). Findings in children and adolescents are consistent with adult studies in this regard, suggesting that functional differences may be observed sooner than structural differences and may even precede the embedding of psychopathology that may occur after chronic ELA exposure. For example, family history of psychopathology and severity of childhood stress exposure are positively related to amygdala reactivity to threatening faces in adolescents (Swartz, Williamson, & Hariri, 2015). Similarly, heightened amygdala reactivity is found in youth with early deprivation, victims of family violence, and PTSD (Garrett, Carrion, Kletter, Karchemskiy, Weems, & Reiss, 2012; McCrory, De Brito, Sebastian, Mechelli, Bird, Kelly, & Viding, 2011; Tottenham, Hare, Millner, Gilhooly, Zevin, & Casey, 2011). During processing of emotional conflict, maltreated children exhibit greater amygdala reactivity (Marusak, Martin, Etkin, & Thomason, 2015b), as well as greater fronto-insular responses compared with non-maltreated children (Marusak, Etkin, & Thomason, 2015a). Moreover, maltreated youth fail to dampen dorsolateral prefrontal cortex (dlPFC) activity, as well as engage amygdala–pregenual cingulate inhibitory circuitry during the regulation of emotional conflict (Marusak et al., 2015a). In response to threatening faces, maltreated youth exhibit a response bias compared with non-maltreated youth, as well as increased activity in ventromedial prefrontal cortex (vmPFC) and anterior cingulate cortex (ACC) when viewing fearful expressions (Hart, Lim, Mehta, Simmons, Mirza, & Rubia, 2018). Decreased PFC responses during a verbal working memory task in maltreated youth relates to trait impulsivity (Hallowell, Oshri, Liebel, Liu, Duda, Clark, & Sweet, 2019), while reduced activation in the ACC in maltreated youth relates to poorer inhibitory control during the Stroop task (Zhai, Yip, Lacadie, Sinha, Mayes, & Potenza, 2019). Maltreated youth show further evidence of impaired cognitive control with longer response times and elevated responses in the dorsal ACC, inferior PFC, and striatum when switching from prepotent to alternative responses (Mueller, Maheu, Dozier, Peloso, Mandell, & Leibenluft, 2010). Children with attachment disorder, orphaned children experiencing early deprivation, and maltreated children at high risk for depression show diminished responses in striatal regions during anticipation of rewards during the monetary incentive delay task (Hanson, Hariri, & Williamson, 2015; Mehta, Gore-Langton, Golembo, Colvert, Williams, & Sonuga-Barke, 2010; Takiguchi, Fujisawa, Mizushima, Saito, Okamoto, & Shimada, 2015). Further, even in a stage of health, youth offspring of parents with bipolar disorder have reduced pregenual ACC activation and connectivity during the anticipation of loss and reward compared with healthy youth without any psychopathology, providing additional evidence that parental psychopathology has an early and significant impact on neural responses to reward in youth (Singh, Kelley, Howe, Reiss, Gotlib, & Chang, 2014).

Other studies suggest dysconnectivity in brain networks in youth exposed to ELA. Childhood maltreatment appears to predict lower PFC–hippocampus connectivity in females and males, but lower PFC–amygdala connectivity only in females, which in turn predicts internalizing symptoms (Herringa, Birn, Ruttle, Burghy, Stodola, Davidson, & Essex, 2013). Youth who have experienced maternal deprivation have negative amygdala-medial PFC coupling (Mueller et al., 2010). During processing of threatening faces, maltreated youth show reduced connectivity between the vmPFC and insula relative to both healthy controls and psychiatric patients without maltreatment (Hart et al., 2018). Further, in maltreated youth, resting-state functional connectivity data reveal increased connectivity of the insula to regions of the salience network (SN), as well as altered connectivity between the salience and default mode networks (DMN) compared with non-maltreated youth (Marusak et al., 2015a). Childhood

**Table 1** Summary of randomized controlled trials on interventions for maltreatment exposed youth

| Citation | Age group | Special populations | Intervention | Condition | Outcomes |
|---|---|---|---|---|---|
| Ahmad et al., (2007) | 6–16 years | Norway, Sweden | EMDR | Waitlist control | ↓ Scores PTSS-C: PTSD symptom subscale, re-experiencing and avoidance subscales |
| Ahrens & Rexford (2002) | Adolescents | Incarcerated and/or conduct disorders | CPT | Waitlist control | ↓Anxiety, depression, intrusions, avoidance, numbing |
| Auslander et al., (2017) | 12–18 years | Girls in child welfare | GAIN–CBITS | Treatment as usual | ↓ Number of girls with PTSD and depression<br>↑ Social problem-solving skills |
| Cohen & Mannarino, (1998b) | 3–7 years | Sexually abuse | SAS-CBT | Non-directive supportive therapy | ↓ Sexually inappropriate and externalizing behavior, PTSD symptoms |
| Cohen et al., (2004) | 8–14 years | Sexual abuse | TF-CBT | Child-centered therapy | ↓ Behavioral problems, shame-related attributions<br>↑ PTSD and depression symptom reduction |
| Crooks et al., (2011) | 14–15 years | Violent delinquency | Fourth R | Health class | ↓ Delinquency |
| Damra et al., (2014) | Not specified; children | Jordan: children with abuse histories | TF-CBT | Waitlist control | ↓ PTSD, depression symptoms |
| Deblinger et al., (2011) | 4–11 years | Sexual abuse | TF-CBT ± trauma narrative | 8 or 16 weeks of TF-CBT; with or without trauma narrative component | ↓Abuse-related fear and anxiety<br>↑ Personal safety skills; effective regardless of trauma narrative |
| Deblinger et al., (2001) | 2–8 years | Sexually abused children + non-offending mother | CBT | Supportive therapy | ↑ Knowledge of body safety |
| Fantuzzo et al., (1996) | 3–5 years | Project Head Start; socially withdrawn children with physical abuse and neglect histories | RPT | Waitlist control | ↓ Solitary play<br>↑ Positive peer interactions |
| Farkas et al., (2010) | Not specified; adolescents | – | EMDR | Treatment as usual | ↓ PTSD symptoms, behavioral problems |
| Foa et al., (2013) | Not specified; adolescents | Sexual abuse | PE | Supportive counseling | ↓ PTSD symptom severity, depression<br>↑ Global functioning |
| Ford et al., (2012) | 13–17 years | Girls involved in delinquency | TARGET | Enhanced treatment as usual | ↓ Re-experiencing, avoidance, anxiety, posttraumatic cognitions<br>↑ Emotion regulation |
| Jee et al., (2015) | 14–21 years | – | Mindfulness | Treatment as usual | ↑ Stress management skills, self-awareness |
| Jensen et al., (2014) | 10–18 years | – | TF-CBT | Treatment as usual | ↓ Posttraumatic stress, functional impairment<br>↑ General mental health |
| Kim & Leve (2011) | 12–17 years | Substance use and delinquency in girls in foster care | Middle school success | Treatment as usual | ↓ Substance use, internalizing and externalizing behaviors<br>↑ Prosocial skills |
| King et al.,(2000) | 5–17 years | Sexual abuse | CBT (individual or family) | Waitlist control | ↓ PTSD, anxiety, fear<br>↑ Global functioning<br>= Parent or individual CBT |

**Table 1** (continued)

| Citation | Age group | Special populations | Intervention | Condition | Outcomes |
|---|---|---|---|---|---|
| McMullen et al., (2013) | 13–17 years | Democratic Republic of Congo: child soldiers and other war-affected youth | TF-CBT | Waitlist control | ↓ Posttraumatic stress symptoms, overall distress, depression, anxiety, conduct problems<br>↑ Prosocial behavior |
| Murray et al., (2015) | 5–18 years | Zambia: orphans | TF-CBT | Treatment as usual | ↓ Trauma symptom score, overall functioning |
| O'Callaghan et al., (2015) | 13–17 years | Democratic Republic of Congo: child soldiers and other war-affected youth | TF-CBT | Child friendly spaces (non-trauma-focused intervention) or waitlist control | Both:<br>↓ Posttraumatic stress, internalizing symptoms, conduct problems, prosocial behavior |
| O'Callaghan et al., (2013) | 12–17 years | Democratic Republic of Congo: sexually exploited girls | TF-CBT | Waitlist control | ↓ Posttraumatic stress symptoms, psychosocial difficulties |
| Poulton et al.,(2014) | 13–17 years | Delinquent girls in foster care | TFCO | Group care | ↓ Symptoms of psychosis |
| Rahman et al., (2018) | 11–12 years | Pakistan | Forgiveness therapy | Treatment as usual | ↓ Anger<br>↑ Levels of hope and forgiveness |
| Scheeringa et al., (2011) | 3–6 years | Heterogeneous maltreatment histories | TF-CBT | Waitlist Control | ↓ PTSD, depression, social anxiety disorder symptoms |
| Smith et al., (2010) | 12–17 years | Chronic delinquency | TFCO | Group care | ↓ Drug and substance use |
| Swart & Apsche, (2014) | 14–17 years | Conduct and personality disorders | MDT | CBT | ↓ Anger, internalizing and externalizing behaviors |
| Swenson et al., (2010) | 10–17 years | – | MST-CAN | Enhanced outpatient treatment | ↓ Psychopathology (anxiety, depression, anger, dissociation, posttraumatic stress), parent emotional distress, negative parenting behavior, changes in youth placement<br>↑ Social support for parents |
| Taussig & Culhane, (2010) | 9–11 years | Foster care | Fostering healthy futures | Treatment as usual | ↓ Dissociative symptoms<br>↑ Quality of life, positive coping skills, social acceptance, self-worth |
| Thomas & Zimmer-Gembeck, (2012) | 3–9 years | – | PCIT | Waitlist control | ↓ Internalizing and externalizing behaviors, stress<br>↑ Positive parenting verbalizations |

*CBT*, cognitive behavioral therapy; *CPT*, cognitive processing therapy; *EMDR*, eye movement desensitization and reprocessing; *GAIN–CBITS*, Girls Aspiring towards independence–Cognitive Behavioral Intervention for Trauma in Schools; *MDT*, mode deactivation therapy; *MST-CAN*, multisystemic therapy for child abuse and neglect; *PCIT*, parent–child interaction therapy; *PE*, prolonged exposure therapy; *RPT*, resilient peer treatment; *SAS-CBT*, sexual-abuse-specific cognitive behavioral therapy; *STAIR*, Skills Training in Affective and Interpersonal Regulation; *TARGET*, Trauma Affective Regulation: Guide for Education and Therapy; *TF-CBT*, trauma-focused cognitive behavioral therapy; *TFCO*, Treatment Foster Care Oregon

maltreatment may also alter the functionality of DMN, such that it disrupts the anterior–posterior integration of its key regions, the ventromedial prefrontal cortex (vmPFC) and posterior cingulate cortex (PCC) (Daniels, Frewen, McKinnon, & Lanius, 2011). This is further accompanied by disrupted connectivity within the SN, including reduced PCC connectivity with amygdala and hippocampus/parahippocampal gyrus relative to healthy controls (Bluhm, Williamson, Osuch, Frewen, Stevens, & Boksman, 2009). Finally, maltreatment also appears to affect brain network architecture, such that maltreated children exhibit significant reductions in global connectivity strength and local connectivity and increased path length associated with psychopathology in other studies (Puetz, Parker, Kohn, Dahmen, Verma, & Konrad, 2017). This was particularly pronounced in regions within the vmPFC where lower connectivity strength was found.

Together, these findings may help explain the association between ELA and the subsequent development and maintenance of psychopathology in youth. The literature suggests that ELA results in widespread effects during critical sensitive windows in development, resulting in global and regional structural, functional, and network differences compared with non-ELA exposed youth. In some, these differences, in turn, underlie the observed deficits in executive function (e.g., working memory, cognitive control, inhibition), emotional awareness and regulation (e.g., threat responses), reward, motivation, social cognition (e.g., theory of mind) and behavior, self-referential processes, and interoception. However, longitudinal studies will help elucidate whether the observed changes represent the biological basis of vulnerability or resilient outcomes. Regardless, our understanding of these systemic disruptions provides an opportunity for development of preventive approaches and interventions that can target the underlying disrupted neural mechanisms.

## Treatments, Interventions, and Programs

As summarized above, some neurobiological negative consequences associated with ELA in youth are well-known, but the question remains which interventions are capable of improving outcomes for maltreated youth. Although many interventions exist, we discuss those that (1) have shown efficacy using empirical research methodology (i.e., randomized clinical trials) and (2) employ strategies that may relate to the disrupted underlying mechanisms of ELA described above. Table 1 summarizes randomized clinical trials in youth exposed to ELA.

### Cognitive Behavioral Therapies

Perhaps the most well-known and widely used psychological interventions to date are cognitive behavioral therapies (CBT) (David, Cristea, & Hofmann, 2018). CBTs target dysfunctional cognitions and behaviors that are associated with and perpetuate distressing emotional states. Specifically, CBTs involve modeling, cognitive restructuring (e.g., reframing, reappraisal), problem solving, and developing personalized coping skills (Benjamin, Puleo, Settipani, Brodman, Edmunds, Cummings, & Kendall, 2011) in response to stress. There are many adaptions of CBTs that have been tailored to address negative reactions to childhood trauma, maltreatment, and early life adversity. A meta-analysis of trauma-focused CBTs (TF-CBT) found large effect sizes for TF-CBT relative to no treatment, and small-to-moderate improvements over other alternative therapies (e.g., supportive therapy, family therapy, child-centered play therapy) (Lenz & Hollenbaugh, 2015). Similarly, in a meta-analysis of child and adolescent survivors of natural and man-made disasters, CBTs showed improvements in posttraumatic reactions with large effect sizes (Newman, Pfefferbaum, Kirlic, Tett, Nelson, & Liles, 2014). CBTs have also been efficacious across different cultures (Newman et al., 2014; Pityaratstian, Piyasil, Ketumarn, Sitdhiraksa, Ularntinon, & Pariwatcharakul, 2015; Shein-Szydlo, Sukhodolsky, Kon, Tejeda, Ramirez, & Ruchkin, 2016), but this should not be understood to imply absolute cross-cultural generalizability, and care should be taken to ensure that the administration of CBTs is appropriately placed within the relevant cultural contexts. We next describe TF-CBT, adaptations of CBTs designed to address ELA, as well as a range of other therapies that have been found to be efficacious for maltreated individuals.

**Trauma-Focused Cognitive Behavioral Therapy** TF-CBT is an evidence-based treatment that meets the well-established criteria and has shown to be the best supported treatment for youth with maltreatment histories (Leenarts, Diehle, Doreleijers, Jansma, & Lindauer, 2013; Silverman, Ortiz, Viswesvaran, Burns, Kolko, Putnam, & Amaya-Jackson 2008). It is based on a flexible-components model, containing psychoeducation, parenting skills, overcoming avoidance of traumatic memories, relaxation, affective modulation, cognitive coping skills (e.g., changing maladaptive cognitions), processing of the event(s) and cues, and focusing on the future trajectory (Cohen & Mannarino, 2008; Cohen, Mannarino, & Murray, 2011). One key aspect of TF-CBT is the trauma narrative, which helps to organize fragmented sensory and emotional memories and integrate them into an autobiographical memory. In TF-CBT dismantling studies, youth randomly assigned to the trauma narrative condition showed less anxiety and diminished fear regarding their abuse when compared to youth receiving TF-CBT without the trauma narrative component (Deblinger, Mannarino, Cohen, Runyon, & Steer, 2011). These effects appear to persist, such that follow-up assessments show additional improvements in symptoms 12 months later (Mannarino, Cohen, Deblinger, Runyon, & Steer, 2012).

TF-CBT is equally as effective in reducing internalizing symptoms as treatment as usual, but excels in reducing

subsequent diagnoses of PTSD (Jensen, Holt, Ormhaug, Egeland, Granly, & Hoaas, 2014). TF-CBT has been examined in children as young as 3 to 6 years of age, where effect sizes are large in PTSD symptom reduction, but less robust in addressing comorbidities such as anxiety, depression, and defiance (Scheeringa, Weems, Cohen, Amaya-Jackson & Guthrie, 2011). Notably, TF-CBT is more effective in those with fewer comorbid disorders (Goldbeck, Muche, Sachser, Tutus, & Rosner, 2016), suggesting a potential moderator of its effects. Finally, when compared with child-centered psychotherapy, TF-CBT demonstrates significant improvement in levels of PTSD and depression symptoms, behavioral problems, and abuse-related cognitions (Cohen, Deblinger, Mannarino, & Steer, 2004).

One randomized controlled trial (RCT) assigned sexually abused children to either child-alone CBTs, family CBTs, or waitlist control (King, Tonge, Mullen, Myerson, Heyne, & Rollings, 2000). Children assigned to treatment arms exhibited reduced self-reported measures of PTSD symptoms, fear, anxiety, and parent-reported measures of overall functioning. Notably, caregiver presence did not moderate this effect. TF-CBT has also been shown to be effective in treating single event traumas in youth, such as natural disasters and motor vehicle accidents, with up to as much as 92% of participants no longer meeting diagnostic criteria for PTSD upon completion of 10 sessions and at 6-month follow-up (Smith, Yule, Perrin, Tranah, Dalgleish, & Clark, 2007). The psychoeducation component of TF-CBT has also been effective in increasing knowledge regarding healthy sexuality and body safety in children aged 2–8 who had been sexually abused (Deblinger, Mannarino, Cohen, Runyon, & Steer, 2001).

TF-CBT is also applicable in group settings, with shorter duration, cross-culturally, and across wide arrays of trauma. TF-CBT effectively reduced PTSD symptoms and increased psychosocial functioning in children within protection agencies in Jordan (Damra, Nassar, & Ghabri, 2014), child soldiers and other war-affected youth in the Democratic Republic of Congo (McMullen, O'Callaghan, Shannon, Black, & Eakin, 2013; O'Callaghan, McMullen, Shannon, Rafferty, & Black, 2013), and sexually exploited girls in the Democratic Republic of Congo (O'Callaghan, McMullen, Shannon, & Rafferty, 2015). In Zambia, orphans and vulnerable children randomized to TF-CBT saw significantly reduced trauma and stress-related symptoms (Murray, Skavenski, Kane, Mayeya, Dorsey, & Cohen, 2015), reinforcing TF-CBT's flexibility in addressing a host of concerns associated with traumatic and adverse life events early in life. Finally, adolescents with a diagnosis of PTSD four years after the 2004 tsunami in Thailand received an abbreviated, 6-h CBT treatment delivered over 3 days and showed immediate reduction in PTSD symptoms (Pityaratstian et al., 2015), indicating that short-term interventions can leave meaningful and lasting results. Further, street children in Mexico randomized to receive 12 sessions of individual CBTs reported lower levels of depression, anxiety, and anger when compared with the waitlist condition, with results maintained three months post-treatment (Shein-Szydlo et al., 2016).

**Prolonged Exposure Therapy for Posttraumatic Stress Disorder** Prolonged exposure therapy (PE) is a gold-standard treatment for trauma-related reactions in adults and shows strong research support by the APA Division 12 list of Empirically Supported Treatments. Based on the emotional processing theory, the PE focuses on the repeated exposure and confrontation of trauma-related cues through imaginal and in vivo exposures in a safe setting with a clinician present. Among the primary goals of therapy is the habituation to escaped and avoided trauma-related fear-evoking images and situations. Randomized controlled trials comparing the PE to waitlist and active control conditions have shown meaningful improvements in PTSD and depression symptoms in adults (Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010).

Although the research is limited with respect to youth, the evidence to date is promising. For example, sexually abused adolescent girls randomly assigned to the PE or supportive counseling benefited from PE as indicated by a significant reduction in PTSD symptoms and improvement in quality of life (Foa, McLean, Capaldi, & Rosenfield, 2013). Further, a pilot study with adolescents in South Africa maintained lower scores on the Child PTSD Symptom Scale Severity Interview and Beck Depression Inventory postintervention and at 12-month follow-up (Rossouw, Yadin, Alexander, Mbanga, Jacobs, & Seedat, 2016; Rossouw, Yadin, Alexander, & Seedat, 2018).

**Cognitive Processing Therapy for Posttraumatic Stress Disorder** Like PE, cognitive processing therapy (CPT) has been classified as having strong research support by the APA Division 12 list of Empirically Supported Treatments. Based on the social cognitive theory of PTSD, as well as emotional processing theory in PE, CPT focuses on how the traumatic event is understood and coped with. In addition to eliciting memories of the trauma and subsequent habituation, CPT directly confronts the maladaptive beliefs surrounding the event (Resick & Schnicke, 1993). It is believed that modifying the faulty interpretations of the event through cognitive restructuring drives recovery and symptom remission. Dismantling studies have shown that both the cognitive and exposure aspects of CPT are effective in treating the symptoms associated with PTSD (Resick, Galovski, Uhlmansiek, Scher, Clum, & Young-Xu, 2008).

Although CPT was originally used to treat trauma involving rape or interpersonal violence (Chard, 2005), in recent years, it has been used to treat reactions to a range of traumatic events, including combat-related trauma (Monson, Schnurr, Resick, Friedman, Young-Xu, & Stevens, 2006). Additionally, it has been used to address reactions related to

complex traumatic events, including childhood trauma. Resick, Nishith, and Griffin, (2003) showed that women with significant childhood sexual trauma history, despite greater self-regulatory problems at baseline, were just as likely to benefit from CPT as women without childhood sexual trauma. A formal adaptation of CPT for women survivors of childhood sexual abuse found this protocol to be superior to minimal attention control active comparison in reducing trauma-related beliefs and PTSD symptoms (Owens, Pike, & Chard, 2001). However, a recent study in women with a broader range of childhood trauma histories saw a weakened reduction in PTSD symptoms when compared with women who experienced fewer types of trauma (Bosch, Mackintosh, Wells, Wickramasinghe, Glassman, & Morland, 2019).

As with PE, evidence for CPT efficacy for youth is limited. In incarcerated adolescents with PTSD, a the short-term CPT resulted in declined self-report outcomes for anxiety, depression, intrusions, and avoidance symptoms (Ahrens & Rexford, 2002). A small pilot study modified CPT to be developmentally appropriate for use with adolescents (D-CPT) (Matulis, Resick, Rosner, & Steil, 2014). The results showed D-CPT to reduce PTSD and comorbid disorders with modest improvements in posttraumatic reactions and symptoms of depression.

**Eye Movement Desensitization and Reprocessing Therapy** Eye movement desensitization and reprocessing (EMDR) therapy is a conditionally recommended evidence-based, trauma-focused therapy that involves the use of bilateral physical stimulations (e.g., eye movements or tones) during simultaneous engagement in the trauma memory and its associated images, cognitions, affect, and physical sensations. Although EMDR shows efficacy, there is a significant amount of controversy surrounding the components that drive symptom improvement—some argue that improvements are largely attributed to exposure and cognitive restructuring, rather than bilateral stimulations of eye movement (Davidson & Parker, 2001).

EMDR has been less examined in youth, but there is data that show its efficacy in decreasing trauma symptoms and externalizing behaviors in maltreated adolescents (Farkas, Cyr, Lebeau, & Lemay, 2010). Additionally, youth receiving 8 weekly sessions of EMDR saw reductions in PTSD (particularly re-experiencing) symptoms when compared with the waitlist control group (Ahmad, Larsson, & Sundelin-Wahlsten 2007). Six sessions of EMDR following a single-event trauma yielded clinically significant reductions in child and parent-reported symptoms of PTSD, with additional improvements toward remission at 3- and 12-month follow-up (de Roos, van der Oord, Zijlstra, Lucassen, Perrin, Emmelkamp, & de Jongh, 2017). In children experiencing disaster-related PTSD, three sessions of EMDR substantially lowered participant scores on the Child Reaction Index, with additional decreases at the 6-month follow-up (Chemtob, Nakashima, & Carlson, 2002).

**Skills Training in Affective and Interpersonal Regulation** Skills Training in Affective and Interpersonal Regulation (STAIR) is an evidence-based adaptation of CBTs aimed at addressing mood symptoms, emotion regulation, and interpersonal problems in adolescent and adult survivors of a wide array of traumas (Cloitre, Koenen, Cohen, & Han, 2002). STAIR targets the negative impact trauma has on emotion regulation and social engagement. It may be delivered over 8–12 sessions, though the manual has flexibility to address the unique challenges each individual faces (Cloitre et al., 2002). STAIR begins with discussing the impacts of trauma and its effect on social and emotional disturbances and providing survivors with a toolkit of relaxation techniques and cognitive reappraisals to build self-efficacy. The second half of treatment involves personalizing emotional reactions to specific interpersonal connections, such as skill-building to appropriate communication of negative emotions (e.g., disappointment, anger), building connectedness, and developing flexible expectations and reactions. Finally, treatment concludes with self-compassion exercises.

One large-scale RCT in STAIR compared STAIR/Exposure, Support/Exposure (exposure comparator), and STAIR/Support (skills comparator) in women with child abuse-related PTSD. Results indicated the STAIR/Exposure group was most likely to achieve PTSD remission, and secondary outcomes of depression and anxiety measures also decreased when compared with the other two conditions (Cloitre, Stovall-McClough, Nooner, Zorbas, Cherry, & Jackson, 2010). Other analyses have shown therapeutic alliance largely contributes to treatment completion, lowering of PTSD symptoms, and negative mood regulation during exposure exercises (Cloitre, Chase Stovall-McClough, Miranda, & Chemtob, 2004). STAIR has also been adapted for use with adolescents (STAIR-A), where pilot data showed enhanced resilience, improved emotion regulation and interpersonal skills, and reductions in PTSD, depression, and anxiety symptoms (Gudiño, Leonard, & Cloitre, 2016).

**Sexual Abuse Specific Cognitive Behavioral Therapy** Sexual abuse–specific cognitive behavioral therapy (SAS-CBT) was designed specifically to address the behavioral manifestations of sexual abuse in preschool-aged children. Moderators of outcomes in sexually abused preschoolers include maternal support, maternal depression, and duration of the abuse, as well as the child's abuse-related attributions and locus of control (Cohen et al., 2004). As such, SAS-CBT has been shown to be effective in reducing inappropriate sexual and other externalizing behaviors in preschool children, as reported by parents through the Child Behavior Checklist and Weekly Behavior Report (Cohen & Mannarino, 1998a). More specifically, a number of studies evaluated treatment outcomes in sexually abused preschool children receiving either SAS-CBT or non-directive supportive counseling (Cohen & Mannarino,

1997, 1998a, 1998b). Initial findings, as well as findings at 6- and 12-month follow-up, show that SAS-CBT was more effective in reducing the aforementioned behaviors, when compared with the non-directive therapy (Cohen & Mannarino, 1998a). Notably, non-offending parental support became a strong predictor of prolonged outcomes, indicating the importance of the role of the caregiver and a potential avenue for future interventions (Cohen & Mannarino, 1998a).

**Game-Based Cognitive Behavioral Therapy** Game-based cognitive behavioral therapy (GB-CBT) is a relatively new approach to CBT and focuses on youth with sexual abuse histories, drawing from components of both TF-CBT and play therapy. The model mainly targets internalizing symptoms, externalizing behaviors such as learned sexually inappropriate behaviors, trauma symptoms such as avoidance and arousal, and aims to instill self-protection, positive social skills, and healthy knowledge about sexuality (Misurell, Springer, Acosta, Liotta, & Kranzler, 2014; Springer & Misurell, 2012). Sessions may involve both children and their non-offending caregivers working through a number of techniques, such as token economies, psychoeducation, and role plays to systemically desensitize anxiety-related cues and improve daily functioning (Springer & Misurell, 2010). Preliminary outcome data suggests that the GB-CBT improved symptoms of all domains in the positive direction in the majority of participants (Misurell et al., 2014), though none of these findings reached statistical significance (Misurell, Springer, & Tryon, 2011).

## Emotion Regulation Approaches

In recent years, emotion regulation has begun to receive significant attention as a potentially important mediator between ELA and PTSD symptoms, depression, and poor physical health outcomes and therefore may be an important treatment target (Cloitre, Khan, Mackintosh, Garvert, Henn-Haase, Falvey, & Saito, 2019; Rudenstine, Espinosa, McGee, & Routhier, 2018). A meta-analysis of 41 studies found a moderately strong relationship between children and adolescents diagnosed with PTSD and difficulties with emotion regulation (Villalta, Smith, Hickin, & Stringaris, 2018). Emotion regulation has further been shown to significantly mediate the changes seen in emotion dysregulation, severity of PTSD and depression symptoms, and physical health in a sample of women enrolled in a PTSD clinical trial (Cloitre et al., 2019).

**Trauma Affective Regulation: Guide for Education and Therapy** One RCT compared Trauma Affective Regulation: Guide for Education and Therapy (TARGET), an emotion regulation therapy, with enhanced treatment as usual in delinquent adolescent girls meeting full or partial criteria for PTSD and showed marked reductions in PTSD symptoms, depression, and anxiety scores (as measured by the Trauma Symptom Checklist for Children (TSSC)). TARGET takes place over twelve sessions and educates survivors about the brain's alarm system after a trauma and provides the skills and support to reprogram those alarms (Ford, Steinberg, Hawke, Levine, & Zhang, 2012).

**Ecological Momentary Stress Management** With new technology, opportunities for novel interventions have come about, including web- or smartphone-based methods. Ecological momentary assessments (EMAs) and ecological momentary interventions (EMIs) are delivered through cell phones at scheduled intervals to provide psychological support. EMIs and EMAs have been used in a number of samples since their conception as a way for clinicians to improve the impact between therapy sessions in clients. It appears that emotional self-monitoring, which in turn may raise self-awareness and promote positive behaviors and coping, is the mechanism upon which this intervention acts (Runyan & Steinke, 2015). To test the efficacy of this new intervention outside of a therapy setting, college students with and without emotional abuse histories were randomly assigned to receive either EMIs that taught stress management skills or EMAs that focused on monitoring stressors and affect. Preliminary data shows that EMIs were more effective than EMAs for those with histories of emotional abuse, while the opposite showed to be true for those without histories of abuse (Nguyen-Feng, Romano, & Frazier, 2019).

## Mindfulness-Based Approaches

One category of treatment that has gained traction in recent years is mindfulness-based interventions. Mindfulness has been shown to have a myriad of benefits, such as enhanced emotion regulation and reactivity, decreased stress levels, improved focus and attention, and improved overall physical and mental health (Davis & Hayes, 2011; Ortiz & Sibinga, 2017). Mindfulness centers around three maxims—intention, attention, and attitude—to view each moment of experience with objectivity and non-judgment. Together, these lead to a process of "re-perceiving," which is accompanied by shifts in perspective, and subsequently enhanced self-regulation, flexibility in behaviors, and exposure (Shapiro, Carlson, Astin, & Freedman, 2006). Research in both adults and youth shows that mindfulness reduces symptoms of depression and anxiety, and improves cognitive and social outcomes (Borquist-Conlon, Maynard, Brendel, & Farina, 2017; Creswell, 2017; Zack, Saekow, Kelly, & Radke, 2014; Zenner, Herrnleben-Kurz, & Walach, 2014). Mindfulness may also promote extinction learning by reducing experiential avoidance, increasing awareness of internal states and attention to conditioned stimuli (Treanor, 2011), and uncoupling associative learning (Brewer & Garrison, 2014).

Literature regarding mindfulness in youth, however, has just begun emerging, and questions about how to adapt these interventions to youth and adolescents remains to be explored (Kostova, Levin, Lorberg, & Ziedonis, 2019). For example, plasticity as a function of mindfulness practice is still largely unknown within the developing brain, even though it has been shown in adults (Bauer, Caballero, Scherer, West, Mrazek, & Phillips, 2019). Additionally, mindfulness practice has been shown to benefit individuals with ELA and other long-term stress; the mechanisms at work likely act upon enhancing stress-coping skills and targeting the underlying neurobiology of stress upon the HPA axis (Ortiz & Sibinga, 2017).

While mindfulness-based stress reduction (MBSR) has been shown to be an effective intervention when adapted to teens (MBSR-T) (Biegel, Chang, Garrett, & Edwards, 2014), few studies ($n = 11$) have investigated mindfulness in at-risk adolescents, and even fewer ($n = 3$) have been randomized controlled trials (Rawlett & Scrandis, 2015). Here, we highlight a few notable studies examining the impact of mindfulness in children and adolescents and their implications for mollifying negative consequences of ELA.

In one study, mindfulness training improved delayed gratification in a sample of internationally adopted children when compared with executive function training (active comparator) and control groups (Lawler, Esposito, Doyle, & Gunnar, 2019). Additionally, 10 weeks of mindfulness training in incarcerated male adolescents revealed gains in global well-being, self-awareness, and self-regulation (Himelstein, Hastings, Shapiro, & Heery, 2012), while a day-long retreat following the 10-week program reinforced these gains and led to future practice in the adolescents (Barnert, Himelstein, Herbert, Garcia-Romeu, & Chamberlain, 2014). Low-income adolescents who were tested positive for HIV received an age-appropriate version of MBSR and reported reduced hostility and physical and emotional discomfort (Sibinga, Kerrigan, Stewart, Johnson, Magyari, & Ellen, 2011). A mindful yoga intervention in an underserved, elementary-age population effectively reduced involuntary stress reactions, such as rumination, intrusive thoughts, and emotional arousal (Gould, Dariotis, Mendelson, & Greenberg, 2012; Mendelson, Greenberg, Dariotis, Gould, Rhoades, & Leaf, 2010). Similarly, a 12-session MBSR program for 7th and 8th grade boys in a low-income area resulted in less anxiety and rumination, and cortisol levels remained stable rather than increasing through the academic term, when compared with those receiving a health education course (Sibinga, Perry-Parrish, Chung, Johnson, Smith, & Ellen, 2013). A larger RCT replicated these findings in stress-vulnerable, low-income middle school students, with additional outcomes showing lower levels of somatization, depression, negative affect, and self-hostility in the MBSR group (Sibinga, Webb, Ghazarian, & Ellen, 2016). However, a similar RCT comparing MBSR and health education did not result in significant differences in psychosocial outcomes but did improve self-awareness, self-regulation, and conflict avoidance in the MBSR group (Sibinga, Perry-Parrish, Thorpe, Mika, & Ellen, 2014). Finally, 10 sessions of MBSR delivered to traumatized youth in foster and kinship care showed enhanced self-awareness and new stress-management skills, but did not have a strong impact on attention, internalizing, or externalizing behaviors (Jee, Couderc, Swanson, Gallegos, Hilliard, & Blumkin, 2015). These indicate that further research must be done to identify the most impactful aspects of mindfulness to employ in those with ELA.

## Forgiveness Therapy

Another approach that has been employed is forgiveness therapy, where the abuse survivor learns to respond to the abuser with beneficence through counseling. One such intervention consists of 24 weeks of individual therapy focused on uncovering anger, committing to forgiveness as a strength, and discovering when forgiveness is appropriate and complete (Lee & Enright, 2014). Following a person-centered approach, the hypothesized mechanism behind forgiveness therapy involves cognitive restructuring of the abuser and events (Lee & Enright, 2014).

A number of studies have shown forgiveness therapy to be effective. In a study of female incest survivors randomly assigned to forgiveness therapy or waitlist-control conditions, the treatment group had a significantly greater decrease in levels of depression and anxiety (Freedman & Enright, 1996). Furthermore, a similar trial in women diagnosed with fibromyalgia who experienced at least two ACEs in their childhood reported increases in forgiveness toward their abuser, lower levels of state anger, and improvements in physical health related to their fibromyalgia symptoms (Lee & Enright, 2014). This supports the idea that therapies targeting psychological distress related to ELA can also help improve aspects of physical health that may be dysregulated by maltreatment in childhood. Similar findings were also shown in a small sample of female Pakistani adolescents with histories of abuse, suggesting that forgiveness therapy may uphold in a cross-cultural context (Rahman, Iftikhar, Kim, & Enright, 2018).

## Home- and Family-Based Interventions

An important consideration in the prevention of ELA is thorough parent psychoeducation, particularly for those most at risk. Home-based interventions are primarily aimed at preventing or halting the occurrence of ELA and promoting healthy relationships between caregivers and their children. As many cases of child maltreatment occur within the cycle of violence and are related to chronic risk factors, many of these programs within the child welfare system are called for

by pediatricians (Landers, McLuckie, Cann, Shapiro, Visintini, & MacLaurin, 2018). As such, the first line of defense in preventing ELA is thought to include the modification of caregiver behavior. For example, families randomly assigned to receive home visits or a control group immediately post-natal and were followed for 4 months. Those receiving home visits saw improved family functioning compared with the control group, including mother–infant attachment and competence in the parenting role. Additionally, infants had greater health outcomes: receiving vaccinations on schedule, fewer injuries or bruising, and decreases in exposure to secondhand smoke (Armstrong & Morris, 2000). Moreover, a systematic review concluded that multicomponent interventions targeting caregivers can reduce the impact of ELA and improve parent–child interactions (Marie-Mitchell & Kostolansky, 2019).

The National Child Traumatic Stress Network cites several home- and family-based interventions that have been implemented by the organization, including Child Adult Relationship Enhancement (CARE), Early Pathways, Let's Connect, Risk Reduction through Family Therapy (RRFT), and Strengthening Family Coping Resources (SFCR). SFCR is a manualized skill-building intervention for families living in traumatic contexts that has shown promise in reducing youth PTSD symptoms, improving family functioning, and decreasing parenting stress (Kiser, Backer, Winkles, & Medoff, 2015). SFCR may be delivered in a multi-family group, individual family, or peer (parent to parent) setting. It combines attachment and social support theories to increase coping resources and improve emotion regulation and communication in order to prevent relapse of abuse. Early Pathways teaches caregivers to learn reasonable, developmentally appropriate expectations and employ calmer methods when responding to challenging behaviors in their children. An RCT showed significant improvements through decreased disruptive behaviors, increased prosocial behaviors, and decreased use of verbal and physical punishments when compared with a waitlist control (Harris, Fox, & Love, 2015). Similarly, preliminary efficacy trials have been conducted for Multisystemic Therapy for Child Abuse and Neglect (MST-CAN) (Swenson, Schaeffer, Henggeler, Faldowski, & Mayhew, 2010). This therapy has been shown to be effective for both parents and children in decreasing occurrences of maltreatment and PTSD symptomology and improving social support outcomes.

**Parent–Child Interaction Therapy** Parent–child interaction therapy (PCIT) is an empirically supported intervention for children with behavioral problems and has recently become an area of focus for maltreatment exposed youth and their caregivers. PCIT first aims to identify the cycle of negative parent–child interactions that often occurs in physically abusive families, then attempts to correct these maladaptive patterns by providing parents with alternative and consistent behaviors. For example, parents are taught to respond with positive attention when their child is engaging in appropriate behavior and ignore or appropriately discipline misbehavior (Ware, Fortson, & McNeil, 2003). In a meta-analysis of 63 studies, Lundahl, Risser, and Lovejoy, (2006) found PCIT to be effective in reducing behavioral problems regardless of child's age and symptom severity prior to treatment. However, socioeconomic status moderated these effects, such that families of lower SES experienced less change in parenting behavior (measured via self-report measures and rater observations). Furthermore, economically disadvantaged families saw greater benefits from individual rather than group parent training.

With respect to maltreated youth, there have been a number of studies examining the effectiveness of PCIT. Thomas & Zimmer-Gembeck, (2012) conducted an RCT with families with maltreatment histories to examine the effectiveness of a standard, 12-session PCIT protocol compared with a waitlist control. Between baseline and 12 weeks post-assessment, parent-reported measures of child internalizing symptoms and externalizing behaviors, parent stress levels, depression ratings, and abuse potential all saw significant reductions in PCIT group. Lanier, Kohl, Benz, Swinger, & Drake, (2014) examined recidivism 13 to 40 months after a community-based implementation of PCIT. Overall, PCIT was found to be effective in preventing maltreatment in families with prior histories of abuse and neglect. Importantly, attrition from PCIT program had no significant effect on later reports of abuse or neglect. The greatest predictors of recidivism were prior perpetration by the caregiver, as well as greater parenting stress scores.

**Child–Parent Psychotherapy** As in PCIT, child–parent psychotherapy (CPP) centers around improving the child's functioning through the joint construction of the trauma narrative with a non-offending or victimized parent. A randomized controlled trial comparing CPP with case management and individual psychotherapy found CPP to be effective in reducing child behavioral problems (Child Behavior Checklist) and caregiver symptomology (SCL-90 Symptoms Checklist) over the course of 50 weekly sessions and at the 6-month follow-up. The proposed mechanisms of action are the mother's sense of agency and psychological well-being. It is believed that these are improved through both growing the mother–child relationship and the child's decline in externalizing behaviors (Lieberman, Ippen, & Van Horn 2006).

**Filial Relationship Enhancement** Filial Relationship Enhancement (FRE) is a comparable, strength-based intervention where parents learn to conduct child-centered play therapy sessions (Ginsberg, 2002; Topham & VanFleet, 2011). It is

grounded in a blend of orientations, including humanistic, psychodynamic, behavioral, and social learning theories. With play as a central part of healthy child development, filial therapy offers a unique opportunity for parents to empathically listen to and understand their child, driving the process of adaptive changes in parenting skills (Topham & VanFleet, 2011). In a study of children and their incarcerated fathers, FRE showed greater levels of empathy and acceptance in fathers and improved self-concept children had toward their fathers, when compared with the control group (Landreth & Lobaugh, 1998). Similarly, Patterson, Stutey, and Dorsey, (2018) found that a combination of individual and group play therapy demonstrated significant decreases in anxiety and negative intrusions in children exposed to ELA, providing support for variations of child-centered play as a possible intervention to mitigate the impact of ELA.

## School- and Community-Based Interventions

Youth with maltreatment histories frequently engage in more violent behaviors in adolescence (Crooks, Scott, Ellis, & Wolfe, 2011). Other factors, such as being male and attending a school with lower levels of perceived safety, are predictors of delinquent behaviors (Crooks, Scott, Wolfe, Chiodo, & Killip, 2007). As such, school-based programs with mandatory curriculum may be useful in diminishing this trend and promoting more positive outcomes.

One such intervention, named the Fourth R (Crooks, Wolfe, Hughes, Jaffe, & Chiodo, 2008), is delivered by teachers in physical and health education classes over the course of 21 weeks. Topics emphasized include personal safety, healthy growth and sexuality, substance abuse, and targeted problem-solving and interpersonal skills. In a randomized controlled trial, the risk of subsequent delinquency was lower in schools receiving the intervention when compared with the control schools (Crooks, Scott, Ellis, & Wolfe, 2011).

Another context of school-based interventions combines social modeling through play. Socially withdrawn child victims of physical abuse and neglect were paired with non-maltreated peers for resilient-peer treatment (RPT) for 15 play sessions over a 2-month period (Fantuzzo, utton-Smith, Atkins, Meyers, Stevenson, & Coolahan, 1996). After randomization and RPT, children paired with resilient peers saw increases in positive interpersonal interactions and decreases in solitary play. Results upheld 2 months later (Fantuzzo et al., 1996) and have been replicated in wider settings with free-play sessions (Fantuzzo, Manz, Atkins, & Meyers, 2005).

Finally, Cognitive Behavioral Intervention for Trauma in Schools (CBITS) is a program delivered by clinicians and combines psychoeducation, relaxation techniques, and cognitive restructuring to youth exposed to a variety of trauma. Preliminary data evidences small reductions in PTSD symptoms, but these reductions were not maintained beyond 6 months (Jaycox, Langley, Stein, Wong, Sharma, Scott, & Schonlau, 2009; Stein, Jaycox, Kataoka, Wong, Tu, Elliott, & Fink, 2003). Support for Students Exposed to Trauma (SSET) and Girls Aspiring toward Independence (GAIN) are two adaptations of CBITS for children and teens exposed to a range of traumas with moderate levels of associated impairment. Pilot studies have shown small reductions in depressive and PTSD symptoms in program completers, though current literature on CBITS is limited (Auslander, McGinnis, Tlapek, Smith, Foster, Edmond, & Dunn, 2017; Jaycox, Kataoka, Stein, Langley, & Wong, 2012; Jaycox et al., 2009; McInerney and McKlindon 2014).

## Foster Care Settings

Children with maltreatment histories who are placed into foster care face elevated risks for negative outcomes later in life, with foster care often counteracting the protective factors against poorer health outcomes (Pears, Kim, Fisher, & Yoerger, 2013; Rebbe, Nurius, Ahrens, & Courtney, 2017; Villegas & Pecora, 2012). Moreover, foster care is disproportionately represented by ethnic minorities who often face greater risks due to lower socioeconomic status (Culpin, Stapinski, Miles, Araya, & Joinson, 2015; Villegas & Pecora, 2012). Quasi-experimental studies that have traced foster care alumni in private (child placement agencies) versus public (state department) programs have found that those in private programs were diagnosed with fewer mental disorders, gastrointestinal problems, and cardiometabolic disorders, indicating protective factors on long-term health outcomes (Kessler, Pecora, Williams, Hiripi, O'Brien, & English, 2008). In addition, school engagement is seen as a protective factor in preventing negative outcomes for all children in the general population, and children in foster care have shown lower levels of school engagement (Pears et al., 2013).

One particular program in foster care, Fostering Healthy Futures (FHF), is a 9-month individual mentoring program, where mentors spent 2–4 h per week with the child and individualized the program based on the child's strengths, presenting problems, and placement family characteristics. In a sample of 9–11-year olds, those in the FHF sought therapy less and reported higher quality of life when compared with the control group (Taussig & Culhane, 2010). A second program, Middle School Success (MSS), aimed to reduce substance use and delinquency in girls in foster care through an RCT and 3 years of follow-up assessments. Overall, girls in the MSS program reported significantly lower levels of substance use, increased prosocial behavior and decreased delinquency, and fewer placement changes (Kim & Leve, 2011).

Finally, the Treatment Foster Care Oregon (TFCO) is a well-established 6-month-long intervention for adolescents in the foster care system with a history of abuse and delinquency (McCart & Sheidow, 2016). Drawing from social

learning theory, family interactions, and behavior change, TFCO provides adolescents with an adult mentor who sets boundaries for appropriate behavior, establishes applicable consequences, and rewards points that the teen may apply to various freedoms and increasing levels of independence. TFCO also provides individual and family therapy, emphasizing interpersonal skills and community involvement, as a means of providing alternatives to delinquency (O'Loughlin, Althoff, & Hudziak, 2017). To date, a number of RCTs have been conducted and have found medium-to-large effect sizes in the program's impact (Dishion, Forgatch, Chamberlain, & Pelham III, 2016). For example, TFCO greatly reduced pregnancy rates at 6, 12, 18, and 24 months after program completion when compared with group care treatment as usual (Kerr, Leve, & Chamberlain, 2009). TFCO also showed decreases in severe antisocial behavior (Eddy & Chamberlain, 2000); ameliorated psychotic symptom trajectories (Poulton, Van Ryzin, Harold, Chamberlain, Fowler, & Cannon, 2014); and decreased the use of tobacco, marijuana, and alcohol (Smith, Chamberlain, & Eddy, 2010). Finally, TFCO outcomes were found to be mediated by the mentor–mentee relationship and ongoing associations with delinquent peers outside of the program (Eddy & Chamberlain, 2000; Leve, Chamberlain, & Reid, 2005).

### Other Approaches

There are a number of other emerging interventions worth discussing. Acceptance and commitment therapy (ACT) is based on modern behavioral psychology and emphasizes values, cognitive restructuring, and commitment to behavior change (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). Research with trauma has been limited to case studies only, but one subject with treatment-resistant PTSD receiving 21 sessions of the ACT found reductions on trauma-related beliefs near the end of treatment (Twohig, 2009). Similarly, mode deactivation therapy (MDT) incorporates aspects of dialectical behavior therapy, ACT, and mindfulness to target maladaptive schemas related to complex traumas. In a sample of adolescents, MDT outperformed the CBT across all measures—externalizing and internalizing behaviors, anger and expression, coping behaviors (Swart & Apsche 2014). In sum, MDT shows promise in treating adolescents with complex trauma histories that have shown resistance to other types of treatments. Third, component-based psychotherapy (CBP) is a new framework combining previous schools of thought centered around four pillars: relationship, regulation, aspects of the self-lost to the trauma, and narrative; the primary driver of change is the therapeutic alliance (Grossman, Spinazzola, Zucker, & Hopper, 2017). Finally, the Intergenerational Trauma Treatment Model (ITTM) educates parents about the impact of trauma and promotes stronger parent–child interactions through 21 sessions of manualized intervention (Scott & Copping, 2008). Exclusive to the ITTM is the focus on the trauma cycle and patterns of transmission. Future research is needed to demonstrate the potential for the use of these interventions in maltreated youth.

### Trials Currently Under Way

Finally, we mention a few current studies posted on Clinical Trials that are aimed to intervene on the disruptive natural course of ELA. Interestingly, many of the studies involve mindfulness-based interventions. First, a community-based program entitled Weaving Healthy Families in Native American families with violence and substance abuse histories is examining recidivism rates, cardiovascular health, emotional stress, and improved parent–child dyads (ClinicalTrials.gov Identifier: NCT03924167). Second, animal-assisted therapy in combination with TF-CBT is being delivered to maltreated 6–17-year olds (CTI: NCT03135119). Main outcomes involve changes in scores on the UCLA PTSD Reaction Index, Strengths and Difficulties Questionnaire, Mood and Feelings Questionnaire, and Emotion Regulation Index. Third, Massachusetts General Hospital (CTI: NCT02447744) is examining the neural changes, such as hippocampal volume, associated with MBSR training in young adults, as well as measures of perceived stress, depression, and state and trait anxiety. Fourth, a multisite trial in London, India, and Nepal (CTI: NCT03625206) is employing cognitive bias modification training to modify attentional bias toward threat cues, along with self-report outcomes of emotional, behavioral, and social difficulties; outcomes of interest include visual search task reaction times and electroencephalography event-related potentials. Fifth, PCIT and a health and safety parenting program are being compared to evaluate their effectiveness in preventing future reports of child maltreatment. Finally, our group is conducting two separate trials in which we are examining the feasibility of employing mindfulness for youth with ELA exposure and the effect on neurobiological systems and symptoms. Specifically, one trial examines the change in cortisol reactivity during the Trier Social Stress Test, as well as symptoms of depression and anxiety, from pre- to post-mindfulness intervention (CTI: NCT03633903), while the other utilizes real-time fMRI neurofeedback in maltreated youth during mindfulness practice with an aim of enhancing its effects on brain activation and perceived stress (CTI: NCT04053582).

## Effect of Intervention on Neural and Biological Outcomes

Advances in neuroimaging have not only allowed for investigations of effects of ELA on brain structure and function in

youth, but also potential changes in these disruptions as a result of psychological interventions. Although these types of data are in their very infancy, promising evidence is beginning to emerge. Additionally, few studies have examined other neurobiological outcomes, mainly cortisol responses.

## Cognitive Behavioral Approaches

Cisler et al., (2015, 2016a, b) examined neural correlates of TF-CBT in adolescent girls exposed to maltreatment. First, they found that PTSD symptom trajectories during TF-CBT were significantly related to pre-treatment bilateral amygdala activation during threat processing (Cisler, Sigel, Kramer, Smitherman, Vanderzee, Pemberton, & Kilts, 2015). Greater amygdala activation to threatening and safe stimuli predicted poorer symptom improvement (suggesting impairment in discrimination), whereas adolescents with greater symptom improvement were characterized by amygdala activation only to threat images. Additionally, maltreated adolescents with greater temporal improvement of PTSD symptoms during TF-CBT had network connectivity and organization that more resembled the matched healthy controls than maltreated adolescents with flatter trajectory slopes (Cisler, Sigel, Kramer, Smitherman, Vanderzee, Pemberton, & Kilts, 2016a). Finally, maltreated adolescent girls with greater post-treatment symptom reduction following TF-CBT were also able to suppress amygdala–insula connectivity during task-instructed cognitive reappraisal, unlike the maltreated girls with less symptom reduction. Incidentally, these pre- to post-treatment changes in amygdala to insula functional connectivity were also related to overall improvements in emotion dysregulation (Cisler, Sigel, Steele, Smitherman, Vanderzee, & Pemberton, 2016b).

Cognitive reappraisal is a technique used in CBTs that involves reframing the subjective interpretation of present states with a goal of lessening the emotional and/or behavioral consequences of the initial interpretation (Gross, 2007). Among maltreated youth, habitual reappraisal is associated not only with a lessened negative mood but also increased resting state functional connectivity between the vmPFC and amygdala (El Khawli, Fan, Aust, Wirth, Bönke, & Stevense, 2018). When instructed to use reappraisal to reduce negative emotion versus passively viewing negative stimuli, maltreated youth exhibited greater recruitment of the superior frontal gyrus and dorsal ACC relative to non-maltreated youth (McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015). Interestingly, both groups then exhibit similar amygdala response during reappraisal, despite showing increased activity during passive viewing. This suggests that maltreated youth had to exert greater effort to modulate heightened amygdala responses (McLaughlin et al., 2015). Further, greater recruitment of prefrontal regions in these youth predicted lower risk for depression over time (Rodman, Jenness, Weissman, Pine, & McLaughlin, 2019).

Repeated exposure to fear-provoking stimuli without the occurrence of feared outcomes leads to habituation and extinction. This process is a cornerstone of exposure-based therapies. Although there have not been studies in maltreated youth, adult data show the effect of repeated exposure to traumatic memory on strengthening of functional connectivity between the insula and hippocampus, amygdala, and the medial PFC, and hippocampus and striatum, dorsal ACC and orbitofrontal cortex (Cisler, Steele, Lenow, Smitherman, Everett, Messias, & Kilts, 2014). Given the similar alterations in functional connectivity, comparable results may be evident in maltreated youth as well.

Psychological interventions also appear to modify the functioning of the HPA axis in maltreated youth. A randomized clinical trial of family-based therapeutic intervention targeting developmental and social–emotional needs in preschoolers in foster care demonstrated a normalizing effect of intervention on morning cortisol levels (Fisher, Stoolmiller, Gunnar, & Burraston, 2007). Using a range of cognitive behavioral and parent-training techniques to treat adolescent males exposed to ELA, Schechter, Brennan, Cunningham, Foster, and Whitmore, (2012) further demonstrated that lower levels of cortisol in the afternoon interacted with early life adversity to predict greater externalizing behaviors after treatment. Therefore, cortisol levels may be an important target either by behavioral or pharmacological means in order to optimize outcomes in some maltreated youth. Indeed, in adult women with maltreatment exposure, cortisol administration resulted in reduced depression-related negative memory bias and improved recall for pleasant stimuli (Abercrombie, Frost, Walsh, Hoks, Cornejo, & Sampe, 2018). This was accompanied by increased activation in the supplementary motor area while viewing unpleasant images.

## Mindfulness-Based Approaches

Mindfulness targets the development of control over one's thoughts, emotions, and behaviors by increasing the ability to observe and direct internal experiences (Creswell, 2017). Mindfulness has been recognized as an important approach to treating adverse outcomes of ELA by exerting its effect on the disrupted underlying neurobiological mechanisms (Ortiz and Sibinga, 2017). Preliminary data in adults indicate that mindfulness may positively influence a number of immune and endocrine system markers (e.g., C-reactive protein (CRP) and cortisol levels, (Black & Slavich, 2016; Creswell, Pacilio, Lindsay, & Brown, 2014)), gene expression (e.g., RIPK2 and COX2; (Kaliman, Álvarez-López, Cosín-Tomás, Rosenkranz, Lutz, & Davidson, 2014)), and brain regions (e.g., PFC, amygdala, and insula (Hölzel, Ott, Hempel, Hackl, Wolf, Stark, & Vaitl, 2007; Tomasino & Fabbro, 2016; Zeidan, Emerson, Farris, Ray, Jung, McHaffie, & Coghill, 2015)) and networks (e.g., DMN coupling (Brewer,

Worhunsky, Gray, Tang, Weber, & Kober, 2011); amygdala–subgenual ACC functional connectivity at rest (Taren, Gianaros, Greco, Lindsay, Fairgrieve, & Brown, 2015)). Together, this points to a mechanism of change whereby the stress responses in the body may be downregulated with mindfulness practice.

Early studies in youth show similar trends. In a study of 40 middle-schoolers, randomized to either 8 weeks of mindfulness training or active control (i.e., coding training), greater perceived life stress positively related to greater amygdala activation while viewing fearful faces at baseline (Bauer et al., 2019). Following intervention, mindfulness training resulted in reduced amygdala activation to fearful faces, as well as lower perceived stress. Furthermore, mindfulness training led to increased vmPFC–amygdala functional connectivity in response to fearful faces, and changes in perceived stress levels persisted beyond meditative states.

With respect to cortisol responses, in a sample of low-income, urban middle-schoolers, mindfulness intervention brought on attenuation of cortisol response to academic stress from baseline to post-treatment as compared with the control group. In another adolescent study, greater dispositional mindfulness predicted lower cardiovascular and emotional responses during the Trier Social Stress Test (Lucas-Thompson, Miller, Seiter, & Prince, 2019). Interestingly, this was related to greater cortisol reactivity in those perceiving less life stress and may reflect adaptive responding during stressful situations in maltreated youth. Although these data are only beginning to emerge, they suggest that cognitive behavioral and mindfulness-based approached may exert positive effects on neurobiological systems affected by ELA.

## Conclusion and Future Directions

It has been 20 years since the first epidemiological study on exposure to multiple forms of adverse childhood experiences was published, and yet little progress has been made in the way of ameliorating the long-term negative outcomes associated with ELA. ELA continues to profoundly impact the well-being of those affected and exert significant costs on the society. While it is important to acknowledge that interventions exist that are not only feasible, but also efficacious in reducing symptoms associated with trauma, adversity, and stress exposure in youth, the field currently lacks evidence (1) whether there are long-term improvements in mental and physical health outcomes as a result of these interventions, and whether (2) these interventions prevent, reverse, or compensate for ELA-related alterations in neurobiological processes underlying associated mental and physical disorders.

There are several potential explanations for the overall lack of these data. First, clinical trials have typically focused on treatment of a single DSM diagnosis. Comorbid conditions are often seen as confounding and thus deemed exclusionary. Given the observed clinical presentation complexity in maltreated youth, they may be consequently underrepresented in RCTs targeting specific disorders. Second, individuals participating in clinical trials are not routinely assessed for ELA, or these data are not reported, leaving the moderating effect of ELA on intervention outcome unknown. Third, there is evidence that maltreated adolescents and young adults are reluctant to seek mental health services (Bonabi, Mueller, Ajdacic-Gross, Eisele, Rodgers, & Seifritz, 2016; Rickwood, Deane, & Wilson, 2007), which may reduce their participation in such clinical trials. Therefore, the generalizability of current evidence-based psychological interventions for a range of mental health conditions may be limited with respect to maltreated individuals. Finally, RCTs examining the effect of treatment on improvement of outcomes in maltreated individuals to date, by and large, have not focused on psychological and neurobiological mechanisms that underlie the associated pathology. Specifically, not only have RCTs failed to include neurobiological variables as primary and/or secondary outcomes, but interventions have also not been designed with these targets in mind.

We have identified a number of studies and approaches that appear to be successful in reducing symptoms and improving outcomes for youth exposed to trauma and maltreatment. Indeed, findings are encouraging in that they not only show the feasibility of these interventions with children and adolescents but also show their applicability in a variety of settings and efficaciousness across a number of domains impacted by ELA. Neurobiological studies of consequences of ELA tell us that the most altered are the mechanisms underlying threat detection and stress response, emotion regulation, reward anticipation, interoception, and self-referential processes (Teicher et al., 2016), which also increase the risk for psychiatric and physical health disorders. Furthermore, there are preliminary data to suggest that cognitive behavioral and mindfulness-based interventions are related to changes in the functioning of the associated neurobiological mechanisms. Therefore, we conclude that they are well-suited for and hold promise to exert immediate preventive and sustained changes in outcomes for maltreated youth.

Nevertheless, significant future work is needed to establish the efficacy of such interventions in improving long-term outcomes for maltreated youth. First, randomized clinical trials contrasting different interventions in maltreated youth are needed to not only solidify their relative efficacy but also to establish any unique effects on divergent outcome measures. Development of new and testing of current interventions that have not yet been examined in this population are also warranted. For example, approaches targeting positive valence systems, such as behavioral activation therapy and future-oriented positive thinking, may prove to be beneficial in this population. Third, using behavioral tasks with appropriate

reliability and ecological validity will allow for assessment of intervention effects on behavior independent of clinician observation and participant self-report. Fourth, the use of neurobiological outcome measures across systems is paramount. Specifically, neurobiological predictors of varying trajectories may significantly increase personalized treatment selection and delivery. Moreover, treatment-related change (e.g., normalization) in previously implicated processes, or identification of additional ones, would identify targets that are engaged by interventions, as well as the degree to which their variability may mediate health outcomes. In turn, this would provide an opportunity for augmentation of interventions by means that may directly target these processes, including the use of neurofeedback, brain stimulation, EMA/Is, or pharmacotherapy. Finally, all approaches will require long-term and repeated follow-ups across multiple levels of assessment to firmly establish prevention of ELA-related poor mental and physical health outcomes later in life. Therefore, given our knowledge and recent advancements in neuroscience and biology, there is an immense opportunity for optimization of current strategies to intervene, as well as development of novel interventions to prevent the negative long-term consequences of early life adversity and chronic maltreatment.

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