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Neurobiological Development in the Context of Childhood Trauma

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Abstract

Neurobiological systems may be particularly susceptible to deleterious impact of childhood trauma, and the impact of childhood trauma on development and subsequent functional outcomes across the lifespan has been well-documented. The current review addresses the neurobiological impact of exposure to interpersonal trauma in childhood in the context of executive function, emotion regulation, and dissociation/interoceptive awareness. Subsequent risk for PTSD and depression is also discussed. The pathway of risk from childhood trauma to these cognitive, emotional, and psychiatric outcomes is addressed in terms of potential structural and functional alterations within the hippocampus, prefrontal cortex, and amygdala resulting from chronic or repeated activation of the hypothalamic-pituitary-adrenal (HPA) axis and its interaction with and influence on genetic and epigenetic processes during sensitive periods of development. Implications for practice are discussed.

Keywords

childhood trauma; childhood maltreatment; dissociation; executive function; emotion regulation; neurobiology

Neurobiological Development in the Context of Childhood Adversity

A robust body of research demonstrates that prolonged or repeated exposure to stress and trauma can have serious negative consequences for physical and mental health (Schneiderman, Ironson, & Siegel, 2005), particularly when stress is experienced early in

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development (Lupien, Ouellet-Morin, Herba, Juster, & McEwen, 2016). A clear dose-response relationship exists between exposure to stress or trauma in early life and risk for psychiatric morbidity over the lifespan, including for posttraumatic stress disorder (PTSD) and depression (Norman et al., 2012). This facilitation of risk may be partly the result of cascading neurobiological changes over the course of development which influence neurocognitive and emotion regulation abilities and ultimately interfere with adaptive stress responses to future stressful events (Teicher, Samson, Anderson, & Ohashi, 2016; Dunn, Nishimi, Powers, & Bradley, 2017).

For this review, with regard to childhood stressful and traumatic experiences, we focus on findings related to childhood exposure to interpersonal trauma because, relative to non-interpersonal trauma, interpersonal trauma may be more likely to recur across development and to present in multiple forms (Masten & Wright, 1998) such that children are often exposed to multiple types of abuse and/or neglect (i.e., physical, sexual, emotional abuse, and/or physical and emotional neglect; Finkelhor, Turner, Ormrod, & Hamby, 2009), as well as to witnessed family violence (Zolotor, Theodore, Coyne-Beasley, & Runyan, 2007). Because children are likely to spend a large majority of their time during the first several years of life with family or other caregivers, exposure to violence, abuse, or neglect in a primary setting, such as the home, may promote persistent fear and anticipation of recurrence and, thus, represent just the kind of stressor that can profoundly alter neurobiological development (Tarullo & Gunnar, 2006).

Therefore, the current review considers the impact of childhood interpersonal trauma, as a form of chronic stress exposure, on neurobiological development. We address the impact of chronic stress exposure on neurobiological development during childhood, in part through the potential roles of repeated activation of the physiological stress response system, environmental influence on gene expression, and specific sensitive periods of development. Given the broad-reaching impact of trauma on development (i.e., multifinality), we focus not only on the impact of childhood trauma on neurobiological development with respect to risk for specific diagnoses (e.g., depression, PTSD), but also on the impacts on three areas of functioning that cut across diagnoses: 1) executive function 2) emotion regulation, and 3) dissociation/interoceptive awareness.

Overview of the Neurobiological Impact of Childhood Trauma

Exposure to childhood trauma can impact brain development over time, leading to changes in the structure and function of multiple stress-sensitive areas, including the hippocampus, prefrontal cortex (PFC), and the amygdala (Cerqueira, Mailliet, Almeida, Jay, & Sousa, 2007; Stevens et al., 2013; Tomoda et al., 2009; van Harmelen et al., 2014). Under normal neurobiological conditions, the hippocampus receives input regarding perceptual information (“who and what”) and binds it to contextual information (“when and where”), and the PFC facilitates future recollection of and attributions about that information (“why”) (Ranganath, 2010). The PFC also modulates amygdala activity via inhibitory mechanisms (Banks, Eddy, Angstadt, Nathan, & Phan, 2007) and communicates with the hippocampus to promote the consolidation of emotional and perceptual information (Kajiwara, Takashima, Mimura, Witter, & Iijima, 2003). Under adverse neurobiological conditions, such as those

shaped by frequent or enduring trauma, the individual and connected functions of the hippocampus, PFC, and amygdala can be impacted in ways that not only facilitate inappropriate associations among perceptual, contextual, and attributional information about traumatic events (Acheson, Gresack, & Risbrough, 2012), but also diminish capacity for consciously managing recollections of the events and moderating fear responses to the recollections. (Stevens et al., 2013). Importantly, the pathways from chronic stress exposure during childhood to these differences in brain region structure, function, and connectivity are potentially many, and chief among them is the pathway through the stress response system.

Chronic fear, whether in response to actual or anticipated threat, can lead to repeated activation of the physiological stress response system, the hypothalamic-pituitary-adrenal (HPA) axis, altering the regulation of glucocorticoids, such as cortisol (Tarullo & Gunnar, 2006; Trickett, Noll, Susman, Shenk, & Putnam, 2010). Childhood trauma is associated with HPA axis upregulation (i.e., elevated baseline cortisol, as well as greater increase and slower decline of cortisol following stress-exposure; Tarullo & Gunnar, 2006). At elevated levels or with repeated exposure, cortisol is thought to have neurotoxic effects, particularly early in development (Lupien et al., 2016). Notably, however, lower cortisol levels and attenuated cortisol reactivity (i.e., HPA axis downregulation) are observed in some individuals exposed to childhood trauma, and the onset of downregulation is typically during adolescence (Trickett et al., 2010). Downregulation of the HPA axis follows a period of chronic upregulation and may be the result of increased glucocorticoid receptor sensitivity leading to blunted stress reactivity and lower baseline cortisol levels, potentially as a compensatory strategy. Nevertheless, upregulation and associated neurobiological differences likely precede and persist beyond the onset of downregulation (Slattery, Grieve, Ames, Armstrong, & Essex, 2013).

The impact of HPA axis dysfunction on the neurobiology of childhood trauma may be better understood when considered in the context of genetic and epigenetic processes that influence and are influenced by glucocorticoid exposure. Although a more complete consideration is beyond the scope of this review (see Sharma, Powers, Bradley, & Ressler, 2016, and Heim & Binder, 2012), a particularly relevant area of research is the study of gene-environment (G × E) interactions of the FKBP5 gene with childhood adversity. FKBP5 is a gene that contributes to the regulation of glucocorticoid receptor sensitivity, and risk variants of FKBP5 polymorphisms are associated with reduced receptor sensitivity, which can lead to diminished HPA axis negative feedback (i.e., slower “off-switch” for the stress response) and subsequent maintenance of glucocorticoids in the absence of threat (Dias, Maddox, Klengal, & Ressler, 2015). Sustained elevations of glucocorticoids may interfere with neurotrophic gene expression and protein synthesis across the brain, but particularly within the hippocampus and PFC, resulting in reduced neurogenesis and neuroplasticity in, as well as degraded connectivity between, the two regions (Cerqueira et al., 2007; Daskalakis, De Kloet, Yehuda, Malaspina, & Kranz, 2015). There is now substantial evidence of an interaction between FKBP5 polymorphisms and early childhood maltreatment in predicting adult PTSD symptoms (Binder et al., 2008; Boscarino et al., 2012; Xie et al., 2010). This effect is not driven by total trauma exposure and appears directly related to childhood exposure, suggesting a developmental window in which FKBP5-mediated cellular interactions have lasting effects on neurobiology that increase the risk of developing PTSD

in adulthood. G × E interactions of childhood trauma and FKBP5 polymorphisms also predict adult risk for other psychopathology, including depression and psychosis (Appel et al., 2011; Collip et al., 2013; Zimmerman et al., 2011), and there is emerging evidence of a similar G × E effect of FKBP5 polymorphisms and childhood maltreatment on adult executive function (Green et al., 2015; Lovallo et al., 2015).

In addition to G × E interactions, there appears to be an important role of epigenetic mechanisms, such as DNA methylation, in understanding how childhood trauma leads to neurobiological changes and subsequent development of psychopathology (Heim and Binder, 2012; McGowen et al., 2009). For example, in a sample of low-income, primarily African American adults with high levels of trauma exposure across the lifespan, Klengel et al. (2013) found evidence that epigenetic mechanisms mediated the G × E effect of early life trauma and FKBP5 on the development of PTSD and depression symptoms in adulthood. Epigenetic changes in the form of differential transcriptional activation of FKBP5 by glucocorticoid receptor activation in the presence of childhood abuse may enhance FKBP5 responsiveness, leading to both long-term changes in the body's stress response system and alterations of neuronal circuits, resulting in higher risk for trauma-associated psychiatric disorders in adults. Similar to G × E effects, the effects on DNA methylation in this study were observed only for childhood trauma exposure, further highlighting the potential impact of traumatic events occurring in early development.

To fully understand the impact of childhood trauma on neurobiological development, the timing of the trauma exposure, as well as its chronicity across the course of development, should be taken into account. Foundational to the idea that childhood trauma can impact neurobiological development is the observation in human and non-human studies of sensitive periods of brain development marked by enhanced plasticity during which experience is inordinately influential to neurogenesis, synaptic growth, and organization of neural circuits (Heim & Binder, 2012; Knudsen, 2004). Thus, exposure to stress during these sensitive periods has the potential to alter the neurobiological landscape in powerful and lasting ways (Knudsen, 2004). Trauma occurring during early, sensitive periods of development can increase risk for psychological, behavioral, and neurocognitive problems across the lifespan. (Cowell, Cicchetti, Rogosch, & Toth, 2015; Dunn et al., 2017; Enlow, Egeland, Blood, Wright, & Wright, 2012)

In addition to broader neurobiological sensitivity during periods of early development, specific brain regions mature at unequal pace, affording differential, timing-dependent impacts of environmental input across development. If childhood trauma exposure acts through sensitive periods to impact neurobiological changes, timing-dependent effects on brain regions should be observed for relevant developmental periods. Recent research has provided some support for this idea showing age-dependent impacts of childhood environment, including trauma and abuse, on amygdala, hippocampal, and PFC volume (e.g., Pechtel, Lyons-Ruth, Anderson, & Teicher, 2014; Andersen et al., 2008; Rao et al., 2010). Although brain regions mature at unequal pace, regional development is anything but independent. Brain regions are structurally and functionally connected such that regions may facilitate or inhibit activity in other regions. Environmental input during sensitive periods may not only interfere with the normative development of one specific region, but also the

nature of its relationship to other regions (Knudsen, 2004). The hippocampus, PFC, and amygdala are part of a network of connected regions (Tottenham & Sheridan, 2010), chronic stress reduces connectivity within this network (Cerqueira et al., 2007), and reduced connectivity is associated with deficits across multiple domains (Cerqueira et al., 2007; Opitz & Friederici, 2003; Wendelken & Bunge, 2010; Stevens et al., 2013). Thus, even if a particular brain region, such as the PFC, is most vulnerable during a sensitive period later in development, its connectivity to regions, such as the hippocampus, with earlier sensitive periods may introduce opportunity for stressful or traumatic experiences earlier in development to nevertheless degrade both the structure and the function of that later-peaking brain region (Cerqueira et al., 2007).

Importantly, sensitive periods may be prolonged if environmental input is unexpected or inconsistent (Knudsen, 2004; Panchanathan & Frankenhuis, 2016). Childhood trauma is often characterized by unexpected or inconsistent caregiver interaction (Blair & Raver, 2012; Ross & Hill, 2002), and under uncertain conditions, the window of opportunity for neurobiological insult—and potentially recovery (Nelson et al., 2007)—remains open (Panchanathan & Frankenhuis, 2016). Moreover, unpredictability associated with childhood trauma and prolonged periods of neurobiological sensitivity may also contribute to increased HPA reactivity and cortisol levels (Sanchez, 2006), thereby potentially further compounding neurobiological risk during sensitive periods.

Taken together, these findings suggest that childhood trauma can alter neurobiological development, particularly within the hippocampus, PFC, and amygdala, and this may occur at least in part as a result of the chronic or repeated activation of the physiological stress response system acting together with genetic and epigenetic processes during sensitive periods of development. These neurobiological changes can, in turn, influence a number of critical cognitive and emotional processes (i.e., executive function, emotion regulation, and that, when disturbed, may represent transdiagnostic risk factors for trauma-related psychopathology, such as PTSD and depression.

Impact of Childhood Trauma on Executive Function

Executive function refers to a set of processes, supported largely by the PFC, that facilitate awareness of and adaptation to internal and external stimuli and goals, thus promoting flexible, context-appropriate, and goal-oriented emotional and behavioral responses (Miyake et al., 2000). Executive function comprises working memory (i.e., holding onto and actively manipulating multiple mental representations), cognitive flexibility (i.e., inhibiting previously learned responses to meet new demand), inhibitory control (i.e., inhibiting overlearned or automatic responses), and the ability to form abstract concepts. Exposure to childhood trauma is associated with relative impairments in each these processes (Cowell et al. 2015; DePrince, Weinzierl, & Combs, 2009; Gould et al., 2012; Kavanaugh & Holler, 2014; Nikulina & Widom, 2013; Nolin & Ethier, 2007; Skowron, Cipriano-Essel, Gatzke-Kopp, Teti, & Ammerman, 2014; Spann et al., 2012), and such impairment is associated with increased risk for PTSD and depression (Aupperle, Melrose, Stein, & Paulus, 2012; Joormann, 2010).

Trauma-related deficits in executive function appear to accumulate in a dose-response manner across development, and may be more pronounced if the onset of trauma is early. For example, in cross-sectional studies of childhood trauma, DePrince et al. (2009) found that for every 1.0 SD increase in the number of exposures to familial interpersonal traumatic events, children demonstrate a .30 SD reduction in overall executive function, and Cowell et al. (2015) found that inhibitory control and working memory were impaired in children exposed to maltreatment, particularly if maltreatment began in infancy and recurred across multiple developmental periods. Moreover, these deficits are likely to persist into adolescence (Kavanaugh & Holler, 2014; Spann et al., 2012) and adulthood. In retrospective studies of adults with self-reported histories of childhood maltreatment, maltreatment is negatively associated with adult working memory, inhibitory control, and cognitive flexibility (Gould et al., 2012; Navalta, Polcari, Webster, Boghossian, & Teicher, 2006), and in a prospective study, maltreatment and particularly neglect during childhood predicted cognitive flexibility at age 41 years (Nikulina & Widom, 2013).

Working memory, cognitive flexibility, and inhibitory control are each influenced substantially, though not exclusively, by PFC functioning (Miyake et al., 2000), so relative deficits observed in these domains in individuals exposed to childhood trauma point to the PFC as an important site of neurobiological response to early stress. Relatedly, differences in the structure and function of the hippocampus, PFC, and amygdala, as well as differences in the structural and functional connectivity of the PFC to both the hippocampus and amygdala have been observed between individuals who have and have not experienced childhood trauma (Cerqueira et al., 2007; Tomoda et al, 2009; van Harmelen et al., 2014). In fact, in a recent review, Teicher et al. (2016) identified the hippocampus, amygdala, and prefrontal regions (i.e., orbitofrontal cortices dorsolateral prefrontal) as among the brain regions most impacted by childhood maltreatment with prefrontal regions, as well as the anterior cingulate cortex, representing the most consistent sites of impact for abuse specifically. These maltreatment-related differences in the structure, function, or connectivity of prefrontal regions is associated not only with impairments in conflict-monitoring and decision-making, but also emotion regulation in adults with maltreatment-related PTSD compared to non-maltreated controls (Thomaes et al., 2010; van Harmelen et al., 2014).

Impact of Childhood Trauma on Emotion Regulation

Emotion regulation refers to a broad set of strategies to manage cognitive, behavioral, and physiological responses to emotion (Cole, Martin, & Dennis, 2004) and encompasses a number of components, including awareness, understanding, and acceptance of emotional experiences (Gratz & Roemer, 2004). Developmental research points to an important impact of trauma on children's emotional awareness, understanding, and regulation (Shields, Ryan, & Cicchetti, 2001; Shipman, Zeman, Penza, & Champion, 2000), which are typically developed in part through interactions with parents and other supportive adults (Bariola, Gullone, Hughes, 2011; Parke, 1994). Because exposure to childhood maltreatment often includes abuse or neglect from a primary caregiver or the presence of violence within the home, children are less likely to be exposed to modeling of appropriate emotional labeling, expression, and regulation behaviors often modeled by primary caregivers and may therefore develop deficits in appropriate emotion regulation.

In addition to the potential absence or scarcity of appropriate models, emotion regulation may also be diminished in the context of childhood trauma due to its partial reliance on executive function—itself diminished by childhood trauma. Executive function contributes to emotion regulation by controlling the contents of working memory to prevent excessive attention to negative thoughts or stimuli (Joormann, 2010), shifting to new coping strategies when old ones are no longer effective (Gilliom, Shaw, Beck, Schonberg, & Lukon, 2002), and inhibiting automatic emotional, behavioral, or cognitive responses that do not fit the situation or one's goals (Carlson & Wang, 2007), such as during cognitive reappraisal (Goldin, McRae, Ramel, & Gross, 2008).

Emotion dysregulation is considered a transdiagnostic risk factor for a broad range of psychiatric morbidity (Werner & Gross, 2010), including PTSD and depression (Bradley et al., 2011a), and exposure to childhood trauma is associated with emotion regulation deficits across the lifespan (Cloitre, Miranda, Stovall-McClough, & Han, 2005; Kim & Cicchetti, 2010; McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015; Powers, Etkin, Gyurak, Bradley, & Jovanovic, 2015). Similar to executive function, emotion regulation is most impacted by trauma that occurs early and often (Kim & Cicchetti, 2010). Associated deficits are diverse and may present as attentional bias to negative or threatening stimuli, trouble recognizing emotions in the self or others, and difficulty effectively modulating or reappraising distress (McLaughlin et al., 2015; Pollak, 2008; Tottenham et al., 2010).

Neuroimaging studies demonstrate an association of emotion regulation and childhood trauma in terms of both neurobiological structure and function and behavioral strategies. In a study of institutionally-raised children, Tottenham et al. (2010) found that prolonged placement was associated with increased attention to negatively-valenced stimuli, as well as with enlarged amygdala, a finding which could represent potential for a relative disadvantage of the PFC in modulating amygdala. For example, in a study of adolescents with histories of childhood maltreatment, McLaughlin et al. (2015) also found a bias toward negatively-valenced stimuli and, relative to non-maltreated adolescences, greater recruitment of the PFC during cognitive reappraisal to achieve comparable reduction of amygdala activity. In this study, both maltreated and non-maltreated adolescents were able to demonstrate emotion regulation ability via amygdala modulation, but maltreated adolescents expended more executive resources to so regulate, which could decrease the availability of those resources for regulating subsequent distress (Muraven & Baumeister, 2000). It is possible, therefore, for some individuals to present with a pattern of apparent emotion regulation—perhaps even overregulation—followed by depletion of regulatory resources. Efforts to overregulate may be associated with aspects of dissociation.

Impact of Childhood Trauma on Dissociation and Interoceptive Awareness

Dissociation refers to a state of altered conscious awareness of or engagement with one's internal or external experience and can manifest in numerous ways, including as feelings of unreality or separation from oneself or surroundings (i.e., derealization and depersonalization, respectively) or a sense that one's identity is fragmented or that one is disconnected from one's own body (Briere, Hodges, & Godbout, 2010). Dissociation often manifests in response to perceived threats that may be viewed on unmanageable or too

painful, and dissociative symptoms are often observed in individuals who have experienced childhood maltreatment, particularly sexual abuse, as a means of near total avoidance of thoughts, emotions, or sensations associated with traumatic memories (Putnam, Helmers, Horowitz, & Trickett, 1995; Stein et al., 2013; Steuwe, Lanius, & Frewen, 2012; Trickett, Noll, & Putnam, 2011).

Notably, individuals with histories of childhood trauma often report depersonalized dissociation, or feeling disconnected from their own bodies (Simeon, Guralnik, Knutelska, Hollander, & Schmeidler, 2001) and, paradoxically, often have high incidences of chronic somatic disorders and concerns (Friedrich & Shafer, 1994; McFarlane, Atchison, Rafalowicz, & Papay, 1994). Given these findings, it is not surprising that dissociation has been linked to impairments in interoception, or awareness of somatic states. For some individuals exposed to trauma—particularly abuse—attending to their current physiological state can evoke trauma-related reminders and subsequent distress and is thus avoided (Lanius et al., 2010).

The neurobiology of dissociative processes in childhood abuse survivors is distinct from a typical fear response. Compared to the “fight or flight” response thought to characterize PTSD, dissociative maltreated individuals often exhibit a pattern of autonomic response has been likened to a “freeze” response to incoming threat (Scaer, 2011) during which the person feels immobile, paralyzed, and detached from their body. The neurobiological signature of dissociation reflects a blunted physiological response to stress (Sack, Cillien, & Hopper, 2012; Zaba et al., 2015). In fact, highly dissociative maltreated individuals often do not demonstrate the expected increases in physiological arousal and overall sympathetic response to trauma-related stressors (Lanius et al., 2010). A proposed model of PTSD describes highly dissociative traumatized individuals as “overmodulators” of affect, who tend to demonstrate increased neural response in brain regions that are involved with control of emotional responses (i.e., medial prefrontal cortical regions), and dampened response in fear processing regions (i.e., the amygdala) as they attempt to control distressful emotional states (Lanius et al., 2010).

Opportunities for Intervention

Even in the midst of trauma, many children demonstrate sustained neurobiological resilience across development and into adulthood, due in part to the presence of protective social or biological factors (Dias et al., 2015; Gunnar & Donzella, 2002). For example, although childhood trauma may promote chronic HPA axis reactivity often leading to neurobiological changes, HPA axis functioning is not disturbed in every individual exposed to childhood trauma. Neurobiological resilience may be due in part to protective factors in the environment (e.g., social buffering; Gunnar & Donzella, 2002). Supportive and responsive parents, peers, or other adult caregiver can be important buffers against the effects of childhood trauma on neurobiological development (Gunnar & Donzella, 2002). Even in an inadequate or threatening environment, a child who expects to be attended to and protected may feel less distressed and may demonstrate less frequent or intense physiological response to stressors (Gunnar & Donzella, 2002), thereby limiting the opportunity for cortisol-related insult. Thus, enhancing social support for at-risk children may be an important intervention

tool to promote resilience in executive function and emotion regulation and to reduce reliance on dissociative strategies, in addition to treating early symptoms of PTSD and/or depression.

At the same time, individuals who are less resilient in terms of neurobiological changes, executive function, emotion regulation, or psychiatric morbidity can still benefit from psychotherapeutic and pharmacological intervention even in adulthood (Cloitre, Koenen, Cohen, & Han, 2002; Tyrka, Burgers, Philip, Price, & Carpenter, 2013). In fact, psychotherapy for adults with PTSD may calm HPA axis reactivity, decrease amygdala activity, and increase PFC and hippocampal activity, and pharmacotherapy may even promote structural changes (Olff, de Vries, Güzelcan, Assies, & Gersons, 2007; Thomaes et al., 2014). Additionally, psychotherapy with neurofeedback training may decrease depression and improve emotion regulation by facilitating upregulation of parts of the PFC and brain areas associated with positive emotion (Linden et al., 2012).

It is important, however, to consider environmental factors that may impact the success of trauma-related intervention. For example, for individuals living in environments with continued elevated risk of trauma exposure (e.g., neighborhoods with high rates of crime), therapists should be careful to consider that some fears may be based on realistic threats. In addition, particularly for individuals with few resources, little previous experience with mental health services, or discomfort seeking mental health services, offering interventions in and tailored to familiar and accessible settings (e.g., primary care clinics), may be critical for increasing access to care and reducing stigma (Machtinger, Cuca, Khanna, Rose, & Kimberg, 2015). Furthermore, using alternative approaches, such as mindfulness, that focus less directly on trauma but incorporate mind-body awareness and enhancing emotion regulation and interoceptive awareness may be more tolerable for individuals with complex trauma histories and symptom presentations who may otherwise refuse standard trauma-focused interventions. Dissociative symptoms are known to interfere with recovery from trauma, and can impede engagement in trauma-focused treatments; attempts to attend to trauma memories during imaginal exposure therapy often produce increased feelings of detachment with one's self and surroundings, interfering with adequate extinction of learned fear responses. Given their inherent focus on increasing interoception and emotion tolerance, mindfulness-based treatments have been proposed as a choice treatment option for childhood abuse survivors, and have shown long-term efficacy in treating symptoms of dissociation in addition to depression, PTSD, and overall anxiety (Earley et al., 2014; Price, Wells, Donovan, & Rue, 2012). Enhancing awareness of body states during mindfulness-based practices is a naturally attractive target for highly dissociative childhood trauma survivors, and is the focus of a current clinical trial designed for this population (NCT02754557); this trial uses physiological feedback to enhance participants' ability to maintain focus on breathing and associated body and emotional states during mindfulness meditation. Although intervening in childhood trauma-related psychopathology is challenging (Nanni, Uher, & Danese, 2012), recovery is very much possible (Ehring et al., 2014) and may be even more effective if adapted to patients' individual needs and concerns (Cloitre, 2014).

Importantly, although childhood trauma is associated with risk for psychopathology, many individuals will not develop a diagnosable mental illness, will not present for treatment, but will nevertheless exhibit dysregulated physiological stress response and neurobiological changes—imprints of childhood trauma that can nevertheless inhibit management of daily stressors and overall well-being (Geoffroy, Pereira, Li, & Power, 2016; Juul et al., 2016; McLaughlin et al., 2015; Spann et al., 2012). Given that the impact of childhood trauma can persist across the lifespan in manners both subtle and profound, efforts should be made to reduce its occurrence and intervene early. Early interventions could include increasing access to mental health services for parents and children (Poobalan et al., 2007), educating physicians and parents about the importance of positive parent-child interactions to neurobiological development (Gunnar & Donzella, 2002), and promoting a better understanding of trauma-related cognitive, emotional, or behavioral problems that may present in a classroom (Brunzell, Stokes, & Waters, 2016).

Limitations

This review should be considered in light of the following limitations. First, much of the reported literature is based on retrospective studies of childhood trauma, limiting the ability to make causal interpretations; however, some prospective studies do lend support to interpretations of childhood maltreatment as potentially contributing to risk for depression, PTSD, and dissociation, as well as to deficits in executive function and emotion regulation (Enlow et al., 2012; Geoffroy et al., 2016; Nikulina & Widom, 2013; Trickett et al., 2011; Zimmermann et al., 2011).

Second, the potential causes of childhood trauma-related changes to neurobiological development presented in the current review are by no means exhaustive. For example, this review does not address the impacts of poverty or racism, both of which have been shown to exert pernicious influence on neurobiological development (Blair & Raver, 2012; Chae et al., 2014). Children living in poverty are confronted with distressed and less responsive caregivers, and may also be at increased risk of experiencing maltreatment (Blair & Raver, 2012; Brooks-Gunn, Schneider, & Waldfogel, 2013). Furthermore, African-American and Hispanic children are disproportionately impacted by poverty (Macartney, 2011), and compared to all other racial/ethnic groups, African-American children are more likely to be exposed to violence (Goldmann et al., 2011) and to demonstrate dysregulated HPA axis functioning in infancy, childhood, and adulthood (Blair et al., 2011; Kuzawa & Sweet, 2009). Although outside the scope of this review, these findings highlight the troubling intersection of poverty and racism with trauma that must not be ignored when addressing the role of childhood trauma in adult functioning.

In addition, this review does not address all physiological sequelae of childhood trauma that may impact neurobiological development. For example, inflammation is elevated across development for individuals exposed to childhood trauma (Coelho, Viola, Walss-Bass, Brietzke, & Grassi-Oliveira, 2014), increasing risk to physical and mental health and contributing additional influence to neurobiological development (Hagberg & Mallard, 2005). Finally, this review does not address potential intergenerational effects of trauma on neurobiological development. Elevated cortisol levels in utero are associated with long-term

relative deficits in neurocognitive ability (LeWinn et al., 2009), and childhood trauma may also interfere with later parenting behavior (Smith, Cross, Winkler, Jovanovic, & Bradley, 2014), potentially creating adverse conditions in the next generation. Certainly, consideration of intergenerational effects is important for better understanding the individual effects in broader context.

Conclusion

Childhood trauma, particularly if experienced early and often, is associated with neurobiological changes that may influence important processes, such as executive function and emotion regulation, as well as increase risk for dissociation and trauma-related disorders, such as PTSD and depression. This neurocognitive, emotion regulation, and psychiatric risk may result from cascading changes to neurobiology facilitated by chronic HPA axis reactivity and interaction with genetic and epigenetic processes during sensitive periods in development in ways that ultimately interfere with the structure, function, and functional connectively of the hippocampus, PFC, and amygdala and limit resilience to future stressors.

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