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Practitioner Review: Neurobiological consequences of childhood maltreatment – clinical and therapeutic implications for practitioners

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Background: Childhood maltreatment is one of the most important preventable risk factors for a wide variety of psychiatric disorders. Further, when psychiatric disorders emerge in maltreated individuals they typically do so at younger ages, with greater severity, more psychiatric comorbid conditions, and poorer response to established treatments, resulting in a more pernicious course with an increased risk for suicide. Practitioners treating children, adolescents, and young adults with psychiatric disorders will likely encounter the highest prevalence of clients with early-onset maltreatment-associated psychiatric disorders. These may be some of their most challenging cases. **Method:** In this report, we explore key validated alterations in brain structure, function, and connectivity associated with exposure to childhood maltreatment as potential mechanisms behind their patients' clinical presentations. **Results:** We then summarize key behavioral presentations likely associated with neurobiological alterations and propose a toolkit of established trauma and skills-based strategies that may help diminish symptoms and foster recovery. We also discuss how some of these alterations may serve as latent vulnerability factors for the possible development of future psychopathology. **Conclusions:** Research on the neurobiological consequences of childhood adversity provides a vastly enriched biopsychosocial understanding of the developmental origins of health and pathology that will hopefully lead to fundamental advances in clinical psychology and psychiatry. **Keywords:** Trauma; neurobiology; therapy.

Recently, the American Academy of Pediatrics (Forkey et al., 2022) proposed integrating trauma-informed care into pediatric practice. This report identified the importance of socially induced stressors in the ontogeny of various childhood illnesses and emphasized the importance of screening for adverse events. More importantly, the Academy emphasized that the first line of defense for mitigating the adverse biological effects of these stressors is the presence of a nurturing caregiver who helps the child with adaptive skills in the context of a strong attachment relationship.

But what if the caregiver is not able to provide that buffer? It appears many are not. In the United States, almost 700,000 substantiated cases of maltreatment were reported to child protection agencies in 1 year (Widom, 2019) with estimates being as high as one in seven children experiencing some form of abuse (Lippard & Nemeroff, 2020). Incidence rates in the UK Primary Care database were reported at 60.1 per 100,000 cases in 2017, with higher rates reported for females, ethnic minority groups, and economically deprived children (Chandan et al., 2020).

While exposure to childhood maltreatment does not constitute a diagnosis, it defines a population at heightened risk for developing psychiatric or physical disorders, and several subsyndromal behavioral presentations that may bring these individuals into treatment. What can be done to help maltreated youth (beyond prevention or removal from the source) remains to be demonstrated. While there is now a convincing body of evidence that supports the effectiveness of trauma-focused cognitive-behavioral therapy and other trauma-focused interventions (including EMDR) for the treatment of PTSD in children and adolescents (Chen et al., 2018; Gillies et al., 2016; John-Baptiste Bastien et al., 2020; Mavranezouli et al., 2020; Smith et al., 2019), it is unclear how effective these modalities are in treating the vast array of other psychiatric disorders that emerge in maltreated youths. In a Cochrane review of treatments for children and adolescents exposed to trauma, Gillies et al. (2016) reports that most PTSD treatments studied produce moderate improvement for PTSD symptoms but no clear evidence of improvement for anxiety (total, state, or trait), depression, negative behaviors (total, internalizing, or externalizing), functional impairment, or quality of life. They also note that outcomes for subjects with exposure to trauma who did not meet criteria for PTSD were less favorable than outcomes for those diagnosed with PTSD. Addressing a similar issue, Karatzias et al. (2019) reviewed outcome studies of adult PTSD treatment to identify a subset of subjects meeting additional ICD-11 criteria for complex PTSD. The resulting meta-regression analysis revealed that subjects with complex PTSD did not respond as well to standard PTSD treatments.

Further, not all maltreated children develop PTSD or meet criteria for complex PTSD. Famularo

et al. (1993) reported that only 35% of severely maltreated and psychologically traumatized children removed from parental custody met structured interview criteria for PTSD.

Patients with a history of childhood maltreatment can present with a wide variety of symptoms or none at all. Differences in type and timing of exposure, mitigating environmental circumstances and genetic predispositions affect clinical presentation. Moreover, symptoms can come and go depending on the brain state and level of emotional activation. It can be difficult to separate emotional or somatic flashbacks related to earlier childhood events from present-day symptoms of comorbid psychiatric illness (such as depression, panic disorder, or psychosis). Further, when formal psychiatric disorders emerge in maltreated individuals, they typically respond more poorly to established treatments, resulting in a more pernicious course with an increased risk for suicide (Lippard & Nemeroff, 2020; Teicher & Samson, 2016). Perhaps most importantly, maltreatment trauma occurs during periods critical for healthy brain development and alterations to the developmental trajectories of brain structures and circuits can create a cascade of developmental and functional abnormalities (Astle et al., 2022; McCrory et al., 2022).

A growing body of neuroimaging research shows that early exposure to maltreatment can alter trajectories of brain development and affect a wide variety of regions and circuits. We have proposed that these alterations are not due to the damaging effects of stress hormones, as previously believed, but instead represent environmentally induced phenotypic adaptations. Moreover, while these adaptations may have helped the individual cope and survive under the deleterious childhood circumstances, they may be highly maladaptive in their current life (Teicher, 2002; Teicher & Samson, 2016). Alterations have been reported in several brain regions, with many playing a pivotal role in threat detection and response. Others are involved in emotional regulation, reward processing, interhemispheric integration, autobiographical memory, and sensory processing. Admittedly, these observations are based on group averages, and maltreated individuals will vary in which, if any, of these alterations they manifest. However, for the clinician treating victims of childhood maltreatment, it is helpful to understand the neuropsychobiological consequences of maltreatment as potential mechanisms behind their patients' clinical presentations and then to find ways to explain this to their patients and their caregivers in an age-appropriate and compassionate manner. Here, we summarize key findings of relevance.

Altered threat detection and response

Detecting and responding appropriately to threats is fundamental to survival and shaped by our experiences. We have assembled a model of this system (Figure 1) primarily based on work from LeDoux (2002; LeDoux & Brown, 2017; LeDoux & Pine, 2016), Mujica-Parodi et al. (2017), Herringa et al. (2013); Herringa et al., 2016), Miles and Maren (Giustino et al., 2020; Goode et al., 2019; Miles & Maren, 2019), and our earlier models (Teicher et al., 2016; Teicher & Samson, 2013). Briefly, two interconnected circuits govern threat detection as well as defensive actions and reactions. Both circuits receive sensory input from the thalamus but they bifurcate at this point before reconverging on the amygdala. One circuit follows a long high road to integrate responses from multiple cortical regions and brings information regarding potential threats into perceptual awareness and provides top-down moderating effects on the amygdala. The other circuit follows a direct low road enabling rapid reactions below perceptual or conscious awareness. The focal point of both circuits are the amygdalae, which are small, bilateral, subcortical structures that contain several discrete nuclei. Of note are the lateral amygdala nucleus, where sensory inputs converge, the central nucleus, from which the primary outputs emerge, and the basal nuclear group (basolateral, basomedial) which receives reciprocal modulatory inputs and outputs to cortical and other subcortical regions. The amygdala is also tightly connected to the bed nucleus of the stria terminalis and together, they constitute the extended amygdala. The immediate presence of a threat can initiate defensive reactions through low-road outputs to the amygdala and then through inputs from the extended amygdala. Our reactions to threats (including activation of the hypothalamic–pituitary–adrenal axis), defensive reactions such as freezing or fleeing, and defensive actions such as fighting are largely enabled through connections of the extended amygdala to the hypothalamus, periaqueductal gray, and nucleus accumbens (NAc).

In contrast, the high road brings information signaling threat to perceptual awareness by connections with cortical sensory regions (such as primary visual and auditory cortices). These regions, in turn, connect to higher-order association cortices, such as the inferior frontal gyrus, which is part of the lateral prefrontal cortex (PFC) and plays a critical role in attentional focus and language production. Incorporating high-road information regarding potential threats into our cognitive stream may be essential for our experience of emotions such as fear and anxiety (LeDoux, 2002; LeDoux & Brown, 2017; LeDoux & Pine, 2016). Other portions of the PFC (particularly the ventromedial aspect) moderate and inhibit amygdala response to perceived threat via the uncinate fasciculus tract (UFC), which also conveys information back to the prefrontal regions from the amygdala. The dorsal anterior cingulate, which lies between the PFC and the limbic system, appears to

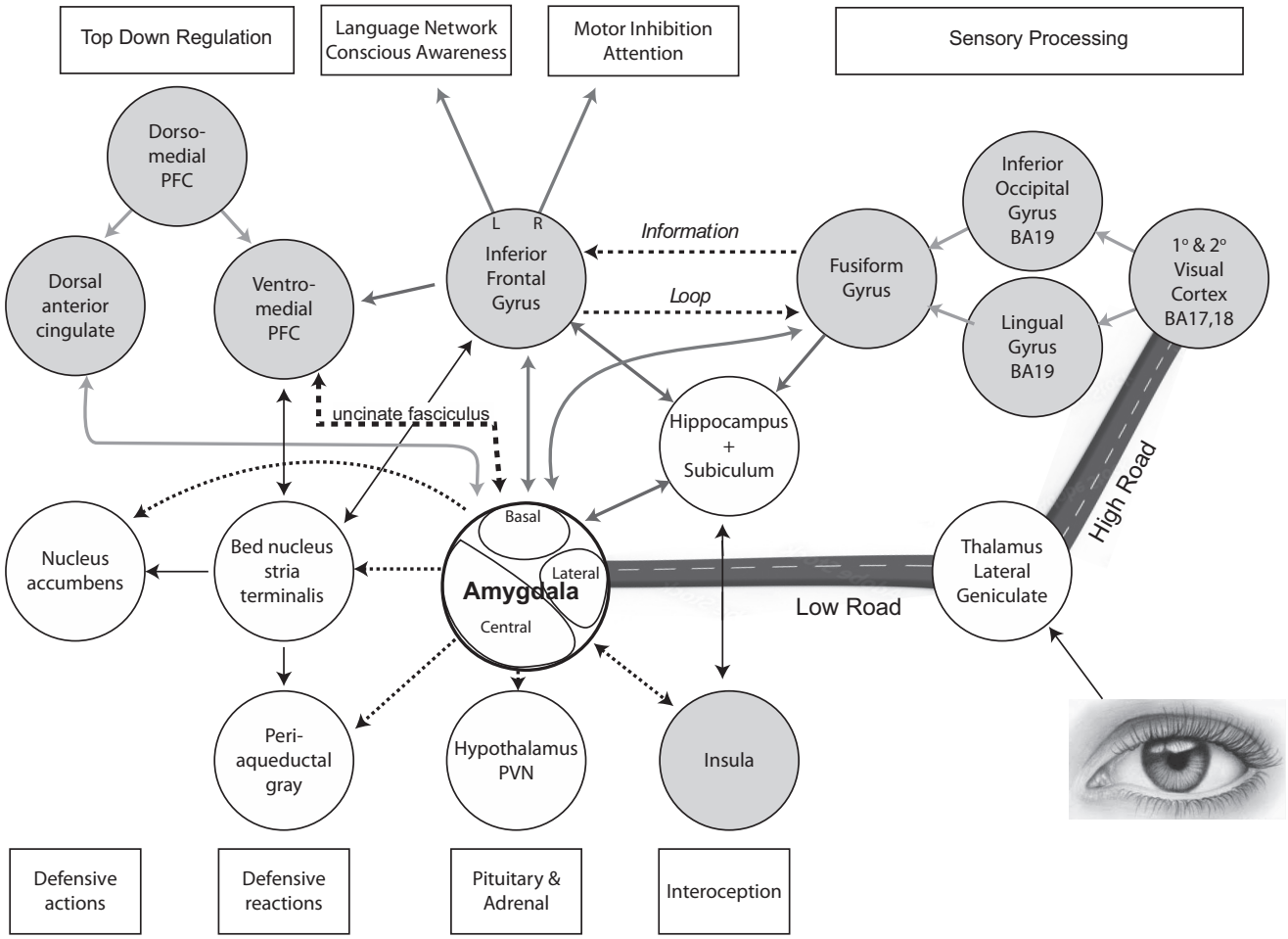

Figure 1 Threat detection and response circuit. Key components and pathways regulating the detection, perception, physiological, and behavioral response to threatening visual stimuli. BA, Brodmann area; L, left; PFC, prefrontal cortex; PVN, paraventricular nucleus; R, right.

act oppositely to enhance amygdala response to potential threats.

Significant developmental changes occur in this system due to the increasing connectivity of the PFC and hippocampus to the amygdala (Meyer & Lee, 2019). The most noteworthy is a shift from positive, mutually reinforcing amygdala-prefrontal connectivity in early childhood to negative amygdala-prefrontal connectivity at around age 10 years. This developmental shift enables the vmPFC to down-regulate amygdala response and is associated with a steady decline in amygdala reactivity over time (Gee, Humphreys, et al., 2013). Accordingly, in early childhood, parental cues are typically associated with decreased threat-related amygdala response, which likely represents the child's ability to use the parent as a buffer against stress. However, with the maturation of the PFC and the UFC tract, the effectiveness of parental cues decreases, and adolescent brain pathways switch over to self-regulate amygdala activation (Gee et al., 2014).

Many structural neurobiological changes associated with childhood maltreatment affect threat detection and response. First, groups of individuals with a history of childhood maltreatment show alterations in amygdala volume and responsivity. Many studies report reduced volume and greater response, but a substantial number show opposite associations (Teicher & Samson, 2016). In general, threat but not deprivation is associated with a smaller amygdala size and greater response (McLaughlin et al., 2019). Timing may be a critical factor (Fonzo, 2019). Our findings suggest that increased volume and blunted response result from exposure to maltreatment before puberty but not after (Zhu et al., 2019).

This finding is consistent with the suggestion that early maternal deprivation is associated with premature emergence and maturation of a negative pattern of connectivity between the PFC and the amygdala, which may enable dampening of amygdala response in younger children who do not have maternal cues to protect from symptoms of anxiety (Gee, Gabard-Durnam, et al., 2013). By contrast, teenaged exposure to maltreatment appears to be associated with exaggerated amygdala response to threatening stimuli, particularly on the right side (Dannlowski et al., 2012), which may be due, at least in part, to diminished connectivity between vmPFC and the amygdala (Wolf & Herringa, 2016). This is

consistent with the general finding that maltreatment may be associated with a reduction in the white matter integrity of the UFC and hence, reduced input from the PFC to the amygdala (McCarthy-Jones et al., 2018).

Third, data collected from groups of maltreated individuals show structural alterations in sensory areas receiving repeated exposure to adverse sensory experiences. For example, exposure to parental verbal abuse has been associated with later observations of gray matter alterations in left auditory cortex (Tomoda et al., 2011) and reduced white matter integrity of the left arcuate fasciculus (Choi et al., 2009). This important language pathway interconnects Broca and Wernicke's areas. In contrast, visual exposure to repeated acts of domestic violence has been associated with gray matter volume reduction in primary visual cortex (Tomoda et al., 2012) and reduced white matter integrity of the inferior longitudinal fasciculus (Choi et al., 2012) which interconnects visual and limbic systems and plays a vital role in our emotional and memory response to what we see. Similarly, groups of females exposed to repeated episodes of penetrative sexual abuse show relative thinning of specific components of the somatosensory cortex responsible for perception of clitoral and genital tactile sensation. In contrast, other groups of maltreated individuals exposed to emotional abuse showed relative thinning in cortical regions relevant to self-evaluation and self-awareness (Heim et al., 2013). While these sensory adaptations may protect a child from fully processing frightening experiences, later they may lead to problems, such as impaired sexual response (Knop et al., 2022) when sensory awareness is needed.

Fourth, childhood maltreatment has been associated with structural changes in the PFC, including the anterior cingulate, dorsolateral, dorsomedial, ventromedial and ventrolateral PFC (Teicher et al., 2016; Teicher & Samson, 2016; Zhu et al., 2023) in groups of children and adults. These alterations, in combination with the effects of maltreatment on sensory cortex, may serve to diminish the influence of the high road conscious cortical component while preserving the functioning of the low road unconscious subcortical behavioral component (Teicher & Samson, 2013).

In summary, childhood exposure to maltreatment may be associated with specific structural brain alterations that include decreases or increases in amygdala size and responsivity, modifications of cortical structures that may affect conscious perception of sensory input, reductions in top-down regulation of the amygdala by prefrontal regions, reduced hippocampal size and decreased myelination of the UFC that impairs communication of contextual input to the amygdala and BNST from the hippocampus and vPFC. These alterations preserve the more rapid activation of the unconscious threat alerting and survival behavior subsystems but also decrease activation of the conscious upper cortical systems. Hence, it is understandable that individuals with trauma history can report feeling flooded by extreme defensive physiological responses but with limited understanding of their source. Alternatively, other survivors may have a blunted functional response to threats and an impaired ability to accurately perceive threats in their environment. This could explain the tendency of some maltreated individuals to repeatedly become involved with other individuals who are harmful or abusive.

Reduced area or integrity of white matter tracts

White matter tracts undergo dramatic transformation in adolescence with increased myelination and microstructural integrity (Lebel et al., 2019). In groups of maltreated youth and adults, decrements in white matter tract integrity can be seen in the corpus callosum, corona radiata, and uncinate fasciculus (McCarthy-Jones et al., 2018; Teicher & Samson, 2016). The corpus callosum is the largest white matter tract and plays a critically important role in communication between the right and left hemispheres, particularly between right and left cortical regions.

In our recent large-scale (N = 345) studies of corpus callosum abnormalities in young adults (Ohashi et al., 2022), we observed both gender and sensitive period effects of maltreatment exposure on white matter. In both sexes, the anterior, central, and mid-posterior segments were most significantly affected, which likely play an important role in emotion regulation, cognition, and problem-solving (Luders et al., 2007; Ni et al., 2020). Decrements in callosal white matter tracts that connect right and left hemispheric activity could affect the integration of signals from the two hemispheres. This could also contribute to the observation that some individuals with a history of childhood trauma appear to toggle more completely between left and right hemisphere activation when recalling neutral versus traumatic memories compared to controls (Schiffer et al., 1995).

Lastly, overall severity of maltreatment exposure appears to be associated with reduced white matter integrity in the accumbofrontal 'reward' tract, which interconnects the NAc and the orbitofrontal cortex (DeRosse et al., 2020). This may correlate with reports of a blunted response to reward anticipation and reward receipt, but an augmented response to potent rewards such as drugs of abuse. All of the above, coupled with increased emotional reactivity, may leave some maltreated individuals particularly vulnerable to substance abuse, addictive behaviors of other kinds, and impulsive behaviors.

Alterations in hippocampal and subfield activation

Maltreated individuals, on average, show alterations in hippocampal and subfield volume (Dahmen

et al., 2018; Riem et al., 2015; Teicher & Samson, 2016). Perhaps related to this is an observed tendency for maltreated individuals to display overgeneralized or less specific recall of autobiographical events (McCrory et al., 2017). Specifically, hippocampal areas of the brain activated during recall of autobiographical memories appear to differ for maltreated versus other individuals, specifically for recall of positive versus negative memories. In a study of 67 maltreated children (aged 10–14 years) McCrory et al. (2017) found the left hippocampal regions to be more active during positive compared to negative autobiographical memory recall in the group as a whole. However, when the sample was separated into maltreated and non-maltreated children, different patterns emerged. During cued positive recall prompts, maltreated children showed reduced activation in right hippocampus (extending into the inferior temporal and fusiform gyri) and increased activation in the right middle temporal and parahippocampal gyri. Non-maltreated children showed the reverse pattern. During negative memory prompts, maltreated children showed increased bilateral amygdala activation and greater functional connectivity between the right amygdala and the right middle ACC (typically involved in the salience network), suggesting that negative autobiographical memories hold more salience for maltreated children.

Latent vulnerability factors

In a beautifully formulated review, McCrory et al. (2017) suggest that functional abnormalities often found in maltreated youth (such as either heightened or suppressed threat processing, emotion regulation difficulties, blunted response to anticipated reward, heightened response to receipt of reward, and reduced executive ability to update input, inhibit responses, and shift tasks) indicate there are latent vulnerability factors related to maltreatment exposure. Each is proposed to be associated with underlying neurobiological patterns that distinguish maltreated children from others. Each also represents a measurable behavioral response by which to identify maltreated children with latent vulnerabilities that may render them more likely to develop various forms of psychopathology in the future.

Maltreatment-associated alterations in structural brain network architecture may provide a mechanism to explain the myriad neurobiological and clinical variabilities observed in maltreated individuals. In a network architecture study of 18–25 year-old subjects ($N = 342$), Teicher et al. (Ohashi et al., 2019; Teicher et al., 2020) found those with a history of childhood maltreatment had a sparser small-world brain network with lower connectivity between identified communities of highly interconnected brain regions. However, they had intact connectivity within each of these communities of highly interconnected brain regions. Measures of network architecture identified individuals with maltreatment histories with 90% accuracy, regardless of whether the maltreated participants were psychiatrically asymptomatic or symptomatic. This suggests that maltreated individuals share a common but sometimes latent vulnerability in network architecture.

Further examination identified nine specific brain regions (nodes) with reduced ability to propagate information throughout the network (efficiency) that distinguished the asymptomatic maltreated participants from both the symptomatic maltreated subjects and the unexposed controls. The two regions most affected by reduced efficiency were the right amygdala and the left inferior frontal gyrus (IFG) pars triangularis. Since the right amygdala, on average, is hyperreactive to threats in maltreated individuals (Dannlowski et al., 2012), it makes sense that maltreated individuals with a significantly less connected right amygdala would be asymptomatic more often. In the second region, the IFG pars triangularis, maltreated individuals with high connections or nodal efficiency showed a marked increase in psychiatric symptom scores compared to maltreated subjects with low nodal efficiency. Reduced nodal efficiency in the asymptomatic maltreated individuals was associated with reduced connectivity of this region to the right limbic system and right temporal lobe. The left IFG pars triangularis is a component of Broca's area (a region associated with speech production and semantic processing) and appears to play a critical role in the production of inner speech and intrusive thoughts (Kuhn et al., 2013; Morin & Hamper, 2012). Thus, these investigators hypothesized that psychopathology might emerge in maltreated individuals when a sparse, vulnerable network cannot effectively compensate for abnormalities in one or more nodes. Resilience may thus result from effective compensation that diminishes the impact of specific problematic nodes.

The extent to which maltreatment-related alterations in brain circuits and structures are malleable is unknown. Our studies on resilient and recovered individuals with maltreatment histories suggest that mental wellbeing may not depend on reversing the effects of maltreatment but may result from compensatory alterations. For example, we compared network architecture and nodal efficiency measures in maltreated participants who appeared to be highly resilient (no lifetime history, currently asymptomatic), recovered (positive lifetime history but, currently asymptomatic), and chronic (positive lifetime history with current clinically significant symptoms (Teicher et al., 2020). The highly resilient group had significantly reduced nodal efficiency measures (compared to unexposed controls) in eight of the nine resilience nodes; the recovered group had reduced nodal efficiency in two nodes, and the

chronic group in none. The two regions with reduced nodal efficiency in the recovered group were the right amygdala and the right subcallosal gyrus/olfactory cortex, which are implicated in mood regulation and the risk of depression (Hamani et al., 2011). These findings suggest that reducing connectivity or functional activity in a few brain regions may significantly reduce psychiatric symptoms in maltreated individuals and bring about recovery without reversing the other latent widespread effects of maltreatment on their global network architecture.

Ecophenotypes

In a 2013 review, Teicher and Samson (2013) proposed that maltreated and non-maltreated individuals with the same primary psychiatric disorder were clinically, neurobiologically, and genetically distinct, with the maltreated variant representing a unique ecophenotype. Individuals with the ecophenotype tend to have an earlier onset, more severe symptoms, more comorbid diagnoses, more difficult clinical courses, and a poorer response to standard treatments. Critically, abnormalities in stress-susceptible brain structures are apparent in the ecophenotype but are absent or markedly attenuated in the non-maltreated subtype (Monteleone et al., 2019; Opel et al., 2014; Pechtel et al., 2022; Poletti et al., 2016; Vythilingam et al., 2002). It is likely that these maltreatment-associated neurobiological alterations predated the full emergence of their primary psychiatric disorder and contributed to their preceding latent vulnerabilities.

Clinical toolkit

So, what problematic behavioral presentations might we expect to see in individuals exposed to childhood maltreatment? In a sizeable subset of individuals exposed to maltreatment, we might expect to see symptoms such as functional alterations in threat processing (either heightened or suppressed), diminished conscious awareness of actual environmental threat with preserved unconscious behavioral activation of threat response (fight, flight, or freeze), problems accurately integrating signals from the left and right hemispheres, with possible toggling between states of unemotional recounting of information and affective flooding, as well as negative cognitive mindset, overgeneral memories and difficulty learning from experience, difficulties interpreting social interactions, and poor judgment. We might also expect to see problems with affect regulation and difficulties maintaining relationships (see a discussion of 'social thinning' by McCrory et al. (2022)). Lastly, we might expect to see a diminished response to reward anticipation and reward receipt (anhedonia) but hyperresponsivity to potent rewards such as drugs of abuse or risky rewards.

How to treat these possible behavioral sequelae of exposure to childhood maltreatment? Improved well-being in victims of childhood maltreatment likely does not depend solely on reversing the effects of maltreatment (which may not be possible) but also on introducing compensatory behaviors and skills and neurobiological alterations that address the consequences of maltreatment-induced abnormalities in functioning. Some possibilities are embedded in existing and empirically validated treatments for PTSD, borderline personality disorder, depression, and anxiety disorders. In a recent review, Coventry et al. (2020) suggested treatment of complex trauma by 'using combinations of trauma-focused and skills-based strategies in a flexible manner, depending on symptom presentation, is likely to be advantageous and removes the need for fixed approaches…' Here we present a number of possibilities that could begin to constitute a clinician's toolkit for working with this vulnerable population. The basic clinical presentations listed above are components of a maltreatment-based behavioral profile that can be modified and possibly interrupted to prevent further progression to more severe pathologies.

Tools for overactive threat response system

Daily positive mental health practices that encourage a more resilient baseline and a toolkit of interventions to use as specific problems arise are needed. Foremost is daily sleep hygiene, as quality of sleep relates to the effects of maltreatment on hippocampal and IFG volume (Teicher et al., 2017), the growth and integrity of myelin in the uncinate fasciculus, and likely other developing tracts (Jamieson et al., 2021). Daily structure and minimizing stress exposure will help maintain an optimal level of stimulation. Recommended behavioral practices include paced deep breathing and attention to breath exercises, progressive muscle relaxation, mindfulness training (which at younger ages may function more through distracting attention from worries), physical exercise (shown to improve executive functioning (Mehren et al., 2019)), or yoga. Dialectical Behavior Therapy (DBT) skills training modules (Linehan, 2015) for distress tolerance, emotional regulation, and interpersonal effectiveness are suited for teens and young adults. Training relying on cognitive reappraisal and biofeedback may help older teens gain greater control over amygdala reactivity (Silvers et al., 2017). Some of these tools are outlined in greater detail in several comprehensive clinical protocols and manuals designed for the treatment of adolescent PTSD or complex PTSD (Briere & Lanktree, 2012; Carrion, 2016; Cloitre et al., 2020). For young children, ARC affect modulation exercises as described by Arvidson et al. (2011) may be helpful, and in young adults, skills described by Hopper et al. (2019).

In adults, there is evidence that the structural integrity of the uncinate fasciculus (Ben-Soussan et al., 2020; Piervincenzi et al., 2017; Tang et al., 2012) or the degree of functional connectivity between the amygdala and prefrontal regions (Doll et al., 2016; Gotink et al., 2016) can be strengthened by training in a variety of mindfulness-based techniques. Joss et al. (2020, 2021) reported that mindfulness training also affected relative increases in hippocampal volume that were associated with performance on an episodic memory task as well as stress and depression levels.

Effects on functional connectivity have been reported following real-time fMRI neurofeedback procedures to reduce amygdala reactivity (Herwig et al., 2019; Paret et al., 2016) and following autonomic biofeedback (Nagai et al., 2018). Interestingly, there is also evidence for an association between how often university students utilize cognitive reappraisal techniques for emotion regulation in their daily lives and the integrity of their uncinate fasciculus (d'Arbeloff et al., 2018; Zuurbier et al., 2013), which suggests that cognitive reappraisal training may also help strengthen this connectivity (Hermann et al., 2017). In adolescent studies, it appears that reappraisal techniques can effectively decrease amygdala activation and improve negative mood (Silvers et al., 2017). Of critical importance, while young children (Silvers et al., 2017) can learn cognitive reappraisal and mindfulness techniques, doing so may not attenuate amygdala reactivity but may actually increase amygdala activity due to the coupling between PFC and amygdala, which shifts from positive to reciprocal at about 10 years of age.

Tools to identify the source of activation

A key therapy goal is to identify and manage triggers in the environment. The therapist can ask about the most recent time the patient felt 'normal' and, together with the patient, identify each and all activities (including books, movies, and internet), conversations, thoughts, and exposures that have occurred since that time to help create hypotheses about potential sources of perceived threat. Over time, identifying patterns in content can help the patient (and those who care for them) become more alert to environmental triggers and work on anticipating them. This approach is consistent with Carrion's Cue-Centered Therapy for complex child and adolescent trauma (Carrion, 2016). Discussing triggers can contribute to the construction of an increasingly accurate trauma narrative that will allow the patient more control over memories and flashbacks.

Tools for toggling between verbal/logic and emotional states

One of the most problematic correlates of toggling may be getting triggered into a state of extreme emotional intensity without the ability to access linear thinking and verbal abilities. Patients may become flooded with emotion and find themselves unable to put their experiences into words. Asking a patient to write about their feelings can be a good check on their ability to access verbal logic functions. If they cannot write, they probably need to focus on self-soothing activities using nonverbal methods, similar to the emotion regulation skills outlined in DBT. Modules for fostering emotion regulation skills may also be found in STAIR Narrative Therapy (Cloitre et al., 2020). When the patient is more settled, try to access verbal abilities and introduce activities that involve logic, puzzles, or non-emotional and distracting mental activities. Many patients can feel the shift in affect and describe that the emotional outburst has passed. These rapid shifts in mood may be attributed mistakenly to a bipolar diathesis or borderline features. Using DBT skills language, the goal is to combine emotional and reasonable minds to create 'wise minds.'

Tools for restructuring negative cognitive mindset and learning from experience

Maltreated children, on average, are likely to show fewer detailed autobiographical memories with decreased responsiveness to positive memories and increased attentiveness and response to negative memories. This problem can impair their ability to use past experiences to help navigate future stressors, impair future problem solving, and encourage more negative views of themselves and the world. Specific CBT training for negative thought restructuring can help neutralize negative cognition. Additional therapeutic approaches such as Cognitive Bias Modification interventions, MoL technique, and Memory Specificity Training may also be useful, as described by Dalgleish and Werner-Seidler (2014).

Increasing the ability to learn from experience can be encouraged by constructing a narrative soon after critical events and subsequent reminders when repetitions occur. The construction of a lifeline of critical events may help reduce fragmentation and integrate memories into a cohesive narrative (Ruf et al., 2010; Schauer et al., 2017).

Tools for improving accuracy of perceptions and judgment

As described earlier, trauma-induced modifications to sensory systems and pathways may alter the conscious perception of specific sensory inputs that identify specific environmental threats. Moreover, as a group, maltreated children will likely show fewer detailed autobiographical memories. This would limit their ability to use past experiences to help navigate future stressors and could result in their failure to detect signs of danger in complex social situations. Thus, maltreated individuals may

repetitively place themselves in abusive and dangerous situations. Unpacking these experiences with the goal of identifying missed warning signs could help build a repository of social 'rules' to help prevent future occurrences. Interventions to restore more accurate interpretations of environmental threats can be found in some CBT cognitive restructuring techniques that ask patients (after the fact) to think about alternative explanations for their experiences. Also helpful may be techniques included in mentalization-based therapy (Bateman & Fonagy, 2016). Understanding that the brain can misinterpret signals can help the patient learn to build in a pause before action and consider alternatives.

Tools for affect regulation and problems with relationships

With the myriad of alterations that can occur to structures and systems involved in threat detection and response in maltreated groups, it is no surprise that many of these individuals show dysregulation of affective response and social networks that 'thin' over time (McCrory et al., 2022). In addition to interventions already mentioned, DBT skills training modules for distress tolerance, emotion regulation, and interpersonal effectiveness in teens, social skills training (including cooperative active play groups for younger children and communications groups for teens), and mentalization training (Bateman & Fonagy, 2016) may be helpful.

Tools for diminished response to reward (anhedonia)

Recent successful work with adults suggests possible adolescent approaches might be adapted from modules related to positive affect from Positive Affect CBT (Craske et al., 2016) and modules related to overcontrol from Radically Open DBT (Gilbert et al., 2023; Lynch, 2018; Lynch et al., 2015).

Working alliance

Establishing a consistent and affirming working alliance can lay the foundation for building more positive social expectations. This may be both the most critical and most difficult component of the treatment regimen. Childhood neglect and physical abuse are predictors of adult anxious attachment styles, avoidant attachment, and problems with depression, anxiety, and poor self-esteem (Widom et al., 2018). Some brain areas noted to be altered in maltreated individuals have also been cited as central to social processing in individuals with insecure attachment styles (Perlini et al., 2019). Extensive discussion of relationship models and modules for addressing maladaptive connections may be found in the treatment manual for STAIR Narrative Therapy (Cloitre et al., 2020).

While having some neurodevelopmental explanations for symptoms and problematic behaviors should help decrease blame, it may also feel discouraging to hear that one's brain has been changed by childhood adversity. Explanations should be linked to specific problems the child is experiencing and provided when it is therapeutically appropriate, not all at once. Following the patient's lead in this process will be essential, as attempting to speed up the process through any outside techniques may result in flooding the patient before they are ready or in the 'therapeutic window' (Briere & Scott, 2015). It is unclear to what extent the maltreatment-related alterations in brain circuits and structures are malleable. Whether treatments may reverse some structural or circuit damage or must aim solely to compensate for deficits is yet to be determined.

Pharmacotherapy

Individuals with developmental trauma and psychiatric disorders often receive treatment with virtually all classes of psychopharmacological agents, but many experience little benefit. Even when they experience benefits, the results are rarely sufficient (Williams et al., 2016). In most cases, medications serve more as aids to manage arousal and intolerable affect while patients undergo intensive therapy than as targeted treatments for a long list of comorbid disorders. Clinicians are encouraged to be flexible with their prescribing patterns and add, subtract, decrease, or augment medications as needed to manage the vicissitudes of intensive psychotherapy. In adults with maltreatment histories and depression, there is evidence that dual-action antidepressants are more effective than selective serotonin reuptake inhibitors (Williams et al., 2016) and evidence that ketamine may be more beneficial in those with treatment-resistant depression (O'Brien et al., 2019). Studies are urgently needed to determine how maltreated children differ in response to pharmacotherapies.

Future research

Research on the neurobiological effects of maltreatment is occurring rapidly, with 70 papers published on maltreatment-related alterations in amygdala structure, function, and connectivity in 2022 alone. How can this information be used to effectively treat individuals with maltreatment-associated psychiatric disorders and prevent the emergence of psychopathology in maltreated youths with latent vulnerabilities? First, information on maltreated and non-maltreated subtypes should be integrated into diagnostic nosology, and results from ongoing and future therapeutic trials should be analyzed across disorders to identify potential maltreatment-related differences in therapeutic response (Teicher et al., 2022).

Second, further studies focused on neurobiological alterations associated with resilience and recovery will likely provide novel therapeutic insights. Third, we need to develop a personalized medicine approach that can cost-effectively provide information about childhood maltreatment as a heterogeneous risk factor. Maltreated individuals may vary enormously in which, if any, brain circuits are affected. Identifying more neurobiologically homogeneous subgroups would likely improve efforts to evaluate the effects of targeted somatic or psychotherapeutic interventions. We suspect that components from existing evidence-based protocols found in treatment packages for anxiety disorders, depressive illnesses, PTSD, complex PTSD, substance abuse, borderline personality, narcissistic personality, avoidant personality, and autism spectrum disorders could produce an array of beneficial neurobiological alterations. The task will be to match an individual with the treatment most likely to exert the desired remedial or compensatory effects. Fourth, there is a pressing need to identify latent vulnerabilities throughout childhood and develop preemptive therapeutic interventions to reduce these vulnerabilities (McCrory et al., 2017). Attenuating these latent vulnerabilities may be easier than treating the clinical sequelae that may arise from them. Although these tasks are daunting, research on the neurobiological consequences of childhood adversity provides a vastly enriched biopsychosocial understanding of the developmental origins of health and pathology that will hopefully lead to fundamental advances in clinical psychology and psychiatry.

Conflict of interest statement

No conflicts declared.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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Key points

- Childhood maltreatment is an important preventable risk factor for later psychiatric disorders. Psychiatric disorders emerging in maltreated individuals typically show poorer responses to established treatments.
- Early exposure to maltreatment can alter trajectories of brain development, specifically brain regions and circuits involved in stress response, emotional regulation, interhemispheric integration, and autobiographical memory.
- For the clinician treating survivors of childhood maltreatment, we explain these neurobiological characteristics of some maltreated children.
- We also outline suggested approaches assembled from empirically validated treatment protocols for PTSD, complex PTSD, borderline personality, and depression.
- These approaches allow patients and their clinicians to connect their current challenges to past experiences through explanations that may offer more opportunities for self-compassion and understanding as well as better outcomes.

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