Chapter 4
Developmental Traumatology: Brain Development in Maltreated Children With and Without PTSD

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4.1 Introduction, Goals, and Rationale

The presentation summarized here conveys the emergence and value of research on the impact of maltreatment on child and adolescent neurological development and highlights the advantageous perspective of considering differences between maltreated children who are and are not diagnosed with posttraumatic stress disorder (PTSD). Maltreated children are at a particularly high risk for the development of PTSD; though there are contradictory findings of PTSD prevalence in the literature, select studies show that approximately 40–60% of sexually abused children (Dubner & Motta, 1999; McLeer, Deblinger, Henry, & Orvaschel, 1992), 50% of physically abused children (Green, 1985), and 36% of neglected children exposed to domestic violence (De Bellis, Hooper, Spratt, & Woolley, 2009) have PTSD. These prevalence rates are comparable to those of children exposed to warfare and other deleterious life events. While maltreatment is not the only form of childhood trauma (e.g., loss of a parent), it is known to contribute largely to the presence of PTSD in children.

A developmental traumatology model of child maltreatment (De Bellis, 2001) has been proposed to conceptualize the developmental impact of child maltreatment, particularly through the growth and consequences of attachment disorders;

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J. G. Noll, I. Shalev (eds.), *The Biology of Early Life Stress*, Child Maltreatment Solutions Network, https://doi.org/10.1007/978-3-319-72589-5_4

internalizing disorders such as separation anxiety and major depression; externalizing disorders such as attention deficit hyperactivity, oppositional defiance, and suicide attempts; and cognitive and learning disorders and poor school performance. The role of PTSD in creating or exacerbating the developmental impact of trauma is consequential and should be the focus of further study. Aside from a societal and ethical obligation to disrupt pathways to negative outcomes for maltreated children, research of this kind is also a matter of resource efficiency in the prevention and reduction of other public health issues such as criminality.

Despite the prevalence rates cited above, scientists and clinicians outside the study and practice of trauma work may make the common mistake of assuming that experiences of trauma and the development of PTSD are one in the same, i.e., that all who have experienced trauma (particularly, severe and/or chronic trauma) must have PTSD. To the contrary, there are important differences between individuals in their response to trauma, and likewise, there exist relevant differences between children in their response to maltreatment. Many maltreated children do not develop PTSD, or if they do, PTSD symptoms subsist after a normative period of time; furthermore, many maltreated children do not go on to have poor commonly associated life experiences, such as academic failure. The pathway from maltreatment to poor life outcomes is not deterministic or inevitable. Considering these differences offers an opportunity to identify compounding developmental factors that may deter maltreated children from the path towards negative outcomes.

4.2 Posttraumatic Stress Disorder Diagnosis

Though many individuals exposed to trauma do not develop a mental health diagnosis, the Diagnostic and Statistical Manual (DSM) IV diagnosis of PTSD does require the experience of a trauma event, which involves actual or threatened injury to the self or others. This event must have resulted in intrusive re-experiencing of trauma (cluster B criterion), which could include having ongoing thoughts and reminders of the trauma experience. As an example, a child whose experience of maltreatment involved loud noises (such as domestic violence) may re-experience his or her trauma when a schoolteacher raises his or her voice. As a result of this triggering experience, the child demonstrates further persistent symptoms. For example, he or she may not be able to concentrate in the school environment and may avoid stimuli and/or demonstrate numbing, emotional bluntedness, and/or dissociation (cluster C criterion). The re-experiencing of trauma may also result in heightened physiological arousal and restlessness (cluster D criterion), such as over-stimulation and fidgeting. This is particularly relevant considering that in comparison with other children, children with PTSD are also more restricted in their expression of emotion. Considering the combination of heightened arousal and restricted self-expression allows us to understand why PTSD is sometimes misdiagnosed, for example, as bipolar disorder or schizophrenia. In order to qualify for the PTSD diagnosis, the duration of symptoms must be greater than 1 month and cause clinically significant distress.

In the most recent update to the Diagnostic and Statistical Manual (DSM-V), the PTSD diagnosis in children is distinguished from the PTSD diagnosis in adults to reflect that younger children (less than 7 years old) may have fewer symptoms than adults but qualify for and be similarly impaired by the disorder. PTSD symptomology is also altered in the DSM-V to include the possible presence of dissociative reactions and flashbacks, the addition of a cluster for numbing of responsiveness and negative beliefs about the world, and the clarification that heightened physiological arousal may include reckless or self-destructive behaviors. The research presented in this summary identifies children with the diagnosis of PTSD who would meet diagnostic criteria in both the DSM-IV and DSM-V.

4.3 Normative Childhood and Adolescent Brain Development

An understanding of the neurobiological impact of trauma requires a foundational consideration of normative childhood and adolescent brain development. Human brain development is marked by the acquisition of progressive skills in cognitive, behavioral, emotional, and physical domains and the complementary neurodevelopmental process of myelination in various regions in which neuronal networks increase connectivity (De Bellis & Zisk, 2014). Popular comparative images of white and gray matter in infant and older child brains reflect the significant growth of neural connections that take place in the early years of childhood, though this neuronal development continues through adolescence and into young adulthood (Giedd & Rapoport, 2010). While some areas of the brain (e.g., the hippocampus) continue to regenerate neurons into adulthood, research substantiates that the first 5 years of life involve significant proliferation of neurons and synaptic connections.

While childhood is a time of unique synaptic changes, the neurological developmental emphasis of adolescence involves the pruning of neural connections and associated “fine tuning” of brain development; as a general rule, the connections that are active and in use are maintained, and the connections that go unused are pruned. These connections are maintained or pruned throughout the brain, including the prefrontal cortex, parietal cortex, temporal lobes, and occipital areas, reaching more adult-like levels of structural maturation at different rates. Overall, these neurobiological growth processes support the development of cognitive skills—including improved memory, problem-solving abilities, mental flexibility, planning, behavioral regulation, and emotional regulation—essential abilities in the response and management of traumatic and stressful life experiences, and those abilities that could also be negatively altered by the experience of trauma and development of PTSD.

4.4 Research on Biological Stress Systems and Adverse Brain Development Mechanisms

Extant research indicates that biological stress systems and inflammatory markers can be dysregulated by early experiences of trauma and that these systemic changes impact further neurological development. This research is reflected in studies on the increases of inflammatory markers and risk for auto-immune disease, catecholamine- and glucocorticoid-induced accelerated loss of neurons (Sapolsky, Uno, Reert, & Finch, 1990; Simantov et al., 1996) resulting in a premature aging process, glucocorticoid-induced delays in myelination (Dunlop, Archer, Quinlivan, Beazley, & Newnham, 1997), glucocorticoid inhibition of neurogenesis (Gould, McEwen, Tanapat, Galea, & Fuchs, 1997; Gould, Tanapat, & Cameron, 1997; Gould, Tanapat, McEwen, Flugge, & Fuchs, 1998), and catecholamine-induced abnormalities in the developmentally appropriate or normative pruning process (Lauder, 1988; Todd, 1992). Neurological scientific studies indicate that the impact of trauma is relevant to development and could have long-lasting consequences.

4.5 Research on Maturation and Cognitive Function in Maltreated Children and Adolescents

Technological progress and increased availability of brain imaging equipment has allowed for new directions in the study of neurological development in maltreated children (among several other important areas of developmental neuroscience). Prior to these advancements, research of this nature on the maltreated child population relied primarily on studies of observed and reported cognitive development (Azar, Barnes, & Twentyman, 1988; Augoustinos, 1987; Beers & De Bellis, 2002; Carrey, Butter, Persingler, & Bialik, 1995; Kolko, 1992; Money, Annecillo, & Kelly, 1983; Perez & Widom, 1994; Trickett, McBride-Chang, & Putnam, 1994), for which only one known study (Perez & Widom, 1994) was longitudinal in nature. Study outcomes largely focused on educational outcomes and indicated that maltreated children were more likely than non-maltreated children to have a lower intelligence quotient and lower academic performance. Without undermining the value of this work, it is widely recognized that there are significant gaps in knowledge about maltreated children's developmental experiences, consequences, limitations, and needs.

In addition to the greater opportunities afforded by brain imaging technology, innovative research has focused on maltreated children who experience health and success in adolescence, for example, young people who are medically healthy despite the presence of traumatic stress (De Bellis & Keshavan, 2003). This perspective has allowed for greater consideration of divergent developmental pathways, appreciation of neurobiological contributions to resilience, and identification of intervention opportunities after child maltreatment (even following experiences that are severe in nature).

4.6 Cortical Region Volume of Maltreated Children and Adolescents

Emerging research on brain maturation and impacted neurocognition in maltreated and/or PTSD-diagnosed children and adolescents substantiates the impact of trauma and stress on neural activity and intracranial volume; while some of these studies consider the overall brain size, others focus on the volume (or lack thereof) in individual cortical regions. Relationships between child maltreatment and brain volume have focused on structures such as the hippocampus, cerebellum, and corpus callosum. In a study of children and adolescents with maltreatment-related PTSD and socio-demographically matched healthy control subjects, anatomical findings from Magnetic Resonance Imaging (MRI) scans indicated that subjects with PTSD, in comparison with healthy controls, had smaller intracranial, cerebral, and prefrontal cortex regions, reduced prefrontal cortical white matter, smaller right temporal lobe volumes, and smaller areas of the corpus callosum and sub-regions, including a smaller midsagittal area of the corpus callosum. In comparison with controls, subjects with PTSD also had proportionally larger right, left, and total lateral ventricles, and a greater amount of cerebrospinal fluid (De Bellis et al., 2002). A commonly used image of the brain of an 11-year-old maltreated male depicts larger lateral ventricles (in comparison to a matched control). Such larger spaces are commonly observed in an aging subject with dementia or severe mental illness, which underlines the severity and concerning relevance of such an observation (Fig. 4.1).

De Bellis and Kuchibhatla (2006) conducted a study of maltreated children and adolescents with PTSD, compared with control groups of children with generalized anxiety disorder (no trauma histories) and healthy adolescents (no trauma histories); cerebellar volumes of maltreated children and adolescents with PTSD (including

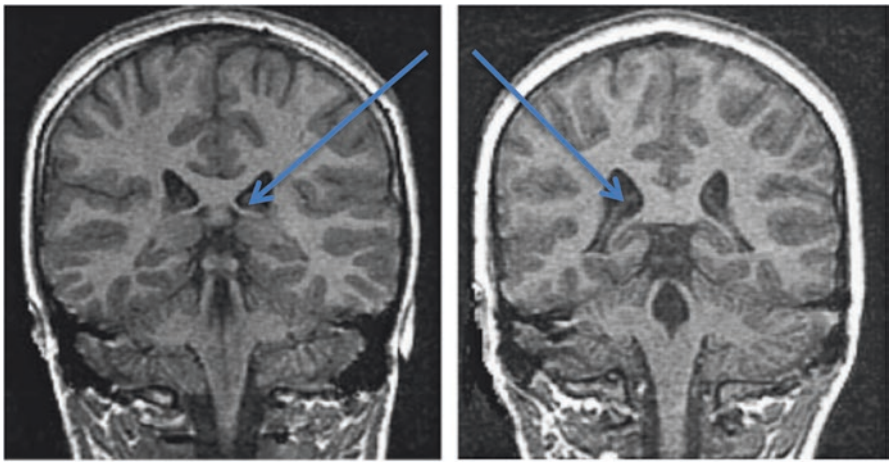

Fig. 4.1 Lateral ventricles in an 11-year-old maltreated male with chronic PTSD (right), compared with a healthy, non-maltreated matched control subject

the left, right, and total cerebellum volume) were significantly smaller. The cerebellum is involved not only in motor movement (the most traditionally recognized functional association), but also increasingly acknowledged for its role in language development, emotional regulation, and reward systems. This region is also known for its significant growth during childhood and adolescence (one of the latest maturing structures, as cited by Giedd and Rapoport 2010) and its relatively low heritability in comparison to other cortical regions (Tiemeier et al., 2010). De Bellis, Keshavan, Clark, et al. (1999) also identified differences between maltreated and non-maltreated children in the corpus callosum, which grows from the interior to the posterior and is also highly involved in attachment and executive functions.

Not all trauma experiences are equal, and as one example of the relevant differences in maltreatment experiences, the *age* at which maltreatment is experienced and the *duration* of the maltreatment experiences appear to play an important role in the neurobiological impact of the trauma. Two studies identified that for maltreated children, brain volumes are positively correlated with the age at onset of maltreatment ($r = 0.40$, $p < 0.05$, De Bellis, Baum, Birmaher, et al., 1999; $r = 0.39$, $p < 0.04$, De Bellis et al., 2002) and negatively correlated with the duration of maltreatment ($r = -0.32$, $p < 0.04$, De Bellis, Baum, Birmaher, et al., 1999; $r = -0.42$, $p < 0.03$, De Bellis et al., 2002). This finding that the earlier a child experiences maltreatment, the smaller their brain size, supports other evidence of the presence of sensitive periods of neurological development. Researchers have also identified a relationship between the years of abuse and intracranial volume in maltreated children with PTSD (De Bellis, Baum, Birmaher, et al., 1999; De Bellis et al., 2002). The aforementioned study of cerebellar volumes (De Bellis & Kuchibhatla, 2006) also substantiates that these volumes are positively correlated with age of onset of trauma leading to PTSD ($r = 0.44$, $p = 0.0005$) and negatively correlated with the duration of trauma ($r = -0.25$, $p = 0.06$).

4.7 Gender Differences

Several studies have indicated that the neurodevelopmental impact for young maltreated males may be greater than for young maltreated females. De Bellis et al. (2002) demonstrated greater lateral ventricle volume increases in male subjects with PTSD than in female subjects with PTSD. De Bellis and Keshavan (2003) compared medically healthy children and adolescents with PTSD to healthy controls, grouped by gender, and found that while all subjects with PTSD had reduced growth in the total corpus callosum compared to non-maltreated subjects, the finding was more prominent in males; furthermore, males with PTSD demonstrated smaller cerebral volumes and rostrum and isthmus areas (corpus callosum regions) in comparison to females with PTSD. De Bellis, Baum, Birmaher, et al. (1999) also found maturational gender differences in the splenium for maltreated boys and girls, with boys' splenium volume more adversely impacted. Other studies have indicated significant gender by PTSD interactions, but there may be no gender differences in the size of the hippocampus or activity of the amygdala for maltreated boys versus maltreated girls. Nonetheless, boys appear to be more vulnerable to developmental trauma disorder.

Prior studies have shown that maltreated males with PTSD show a trend towards more PTSD cluster C symptoms than maltreated females with PTSD; cluster C symptoms represent both avoidant and dissociative behaviors and can be thought of as ways to control painful and distressing re-experiencing of symptoms. Cluster C symptoms can lead to diminished interest in others, feelings of detachment, a restricted range of emotion, and dissociation. Emotional numbing and diminished interest in others, particularly during development, may result in lack of empathy and increased risk for antisocial behaviors. There may be a sociobiological basis to this phenomenon; detachment behaviors during adverse circumstances (such as warfare) would be more beneficial to male than female primitive humans.

4.8 Neurocognitive Function Differences in Maltreated Children With and Without PTSD

A consideration of maltreated children who do not experience adverse brain development has been particularly beneficial to understanding the potentially differing trajectories of maltreated children who do and do not develop PTSD. De Bellis, Woolley, and Hooper (2013) compared maltreated children with PTSD to maltreated children without PTSD and both groups to a control group of healthy, non-maltreated children. This study included children who were previously diagnosed with PTSD but no longer showed signs and symptoms, as well as children who had never been diagnosed despite maltreatment experiences. In order to draw these comparisons, strict clinical inclusion and exclusion methods were utilized. The Kiddie-Sads-Present and Lifetime (K-SADS-PL) assessment for DSM-IV diagnosis of PTSD and other disorders was utilized, and maltreatment was defined and substantiated by child protective services. Included participants lived in a stable home environment, had one non-abusing parent who could cooperate with study protocol, and had access to birth records. Exclusion criteria included participants who used medication with central nervous system effects, had a history of significant medical illness or head injury, experienced obesity or growth failure, had a birth weight under five pounds (or significant prenatal alcohol/drug exposure or birth complications), were diagnosed with anorexia nervosa, autism, pervasive developmental disorder, or schizophrenia, or had a full scale intelligence quotient score of less than 70 for all subjects, or any trauma, maltreatment, or psychiatric illness history for the healthy non-maltreated control subjects.

Interviews with children/adolescents and their parent were conducted in 1 day, including genetic testing of children, cognitive testing of both children and their parents, and mental health interviews of both children and their parents. MRI brain scans for anatomy, Diffusion Tensor Imaging (DTI), Functional Magnetic Resonance Imaging (fMRI), and Magnetic Resonance Spectroscopy (MRS) were completed on separate testing days. Researchers used the Children's Global Assessment Sale (CGAS) and Child Behavior Checklist (CBCL) to document internalizing and externalizing behaviors, as well as measurements of dissociation, total PTSD symptoms, and lifetime summary of maltreatment types, to compare non-maltreated children, maltreated children, and maltreated children with PTSD.

Both maltreated children with PTSD and maltreated children without PTSD performed more poorly than the healthy controls in several areas of cognitive functioning, including intelligence, attention, language, memory, executive functioning, and academic achievement in math and reading. The primary cognitive functioning difference between maltreated children with and without PTSD was on performance of visual-spatial tasks ($F(4, 134) = 4.49$, $p = 0.002$), which has relevance for executive functioning (De Bellis et al., 2013).

In another study grouping maltreated children with PTSD separately from maltreated children without PTSD (and a third group of children without maltreatment experiences), De Bellis et al. (2015) examined anatomical volumetric and corpus callosum DTI measures using MRI scans to find less posterior gray matter volume in children with maltreatment-related PTSD in comparison to maltreated controls. A correlation was identified between total posterior gray matter volumes and the number of PTSD symptoms in maltreated children, such that the greater the number of PTSD symptoms, the lower the posterior gray matter volume ($r = -0.37$, $p < 0.01$). Furthermore, in comparison with the control group, maltreated children without PTSD have a higher volume of cerebellar gray matter, and maltreated children with PTSD have a lower volume of cerebellar gray matter (F2, 113 = 6.7, $p < 0.002$). Similar to the relationship with posterior gray matter, a positive correlation was also found between cerebellum gray matter and PTSD symptoms, such that the greater the number of PTSD symptoms, the smaller the cerebellum ($r = 0.44$, $p < 0.002$). Based on these findings, one might conclude that child maltreatment can lead to "chronic PTSD brain" or "resilience to chronic PTSD brain," differing trajectories that have a substantial impact on the likelihood for further risk.

These findings align with other studies about neurobiological associations of maltreatment-related PTSD, including decreased gray matter, posterior cortex, and cerebellum (including the angular gyrus, cuneus, precuneus, lateral occipital gyrus, superior parietal lobule, posterior cingulate, and visual cortex), and the related functions of visual-spatial processing/decision-making, receptive language, attention and executive functions, the posterior default network, and ventral circuits. Furthermore, gender differences were supported; maltreated males had less gray matter than maltreated females in the left superior prefrontal cortex, a region involved in inhibitory control and risk for impulsivity (De Bellis et al., 2015).

Relevant to these studies is the role of the prefrontal cortex, specifically the ventral medial (or orbital frontal) prefrontal cortex, medial prefrontal (or anterior cingulate) cortex, and the limbic system, including the hippocampus and amygdala. In a third study grouping maltreated children with and without PTSD separately (and including non-maltreated controls), Morey, Haswell, Hooper, and De Bellis (2016) used MRI to demonstrate linear relationships between the ventral medial prefrontal cortex and anterior cingulate cortex volumes; the control group and maltreated children without PTSD were found to have greater volume in these areas than maltreated children with PTSD ($F = 3.6$, $p < 0.03$). Maltreated children without PTSD were also found to have a greater total amygdala volume, particularly larger on the left side, than both maltreated children with PTSD and non-maltreated children ($F = 4.3$, $p < 0.02$). Finally, maltreated children without PTSD were found to have

a greater right hippocampal volume than both maltreated children with PTSD and non-maltreated children ($F = 4.2$, $p < 0.02$). These findings have relevance to the consideration of differences in complex functions that may be modulated by stress and impacted by neurotransmitter activity. These findings may also represent a shared trauma mechanism that leads to PTSD, impulsivity (attention deficit hyperactivity disorder), co-morbidity, and poor outcomes.

4.9 Neurobiology of Hope

The consideration of differing neurobiological trajectories from childhood maltreatment presents an opportunity for intervention. After an initial trauma, most individuals have PTSD symptoms that resolve on their own; for example, it is very common for individuals who experience trauma to have high anxiety or trouble sleeping for several days or several weeks, after which the symptoms dissipate. A pathway exists in which otherwise traumatized individuals can learn and grow through a mechanism called "extinction." For example, though a young male who has experienced physical or sexual abuse by an older male may have initial adverse reactions to the presence of other older males, the healthy and non-threatening presence of a safe older male may allow the traumatized young person to restructure his reaction and replace his associations. This type of restructuring or replacement of unhealthy associations may be supported through the use of cognitive behavioral therapy (CBT), a preferred treatment option; in a review of recent fMRI studies, Porto et al. (2009, as cited in De Bellis & Zisk, 2014) demonstrated that CBT can relieve dysregulation of fear response and negative emotions associated with anxiety. A trauma-focused adaptation of the CBT intervention is particularly relevant. It should be noted that the effectiveness of changing cognitive responses to fear requires an intact ventral medial prefrontal cortex that can inhibit a fear response to the amygdala and interior cingulate cortex (the ventral medial prefrontal cortex is also known to have value in adolescence for the prediction of later drug use, a compounding risk factor). The early identification of PTSD symptoms following early childhood trauma can allow opportunities to prevent and intervene in this pathway while neurobiological potential is still present (De Bellis, 2001).

In addition to the individual use of cognitive behavioral therapy, there is increasing emphasis on evidence-based programming for maltreated children at risk for PTSD and associated negative life outcomes in the family system. Emerging research indicates the amenability of child maltreatment to primary prevention, such as the Nurse-Family Partnership Program, in which expectant mothers in low-income, at-risk families are visited by nurses. Several studies of this program indicate improved later outcomes for children, including greater educational achievement in childhood, decreased internalizing symptoms and decreased substance use in childhood, and decreased antisocial behaviors in young adulthood (Olds et al., 2007; Kitzman et al., 2010; Eckenrode et al., 2010, as cited in De Bellis & Zisk, 2014).

Overall, adverse brain development may be reversible. When rescued from extremely neglectful and abusive environments, some profoundly maltreated children are capable of accelerated rates of catch-up growth, including remission of severe psychopathology and normalization of cognitive function. There is even capacity for neurogenesis in the adult human brain, though this can be inhibited by other environmental stressors, which may be probabilistic for high-risk individuals. Though "rescuing" is not always possible, understanding how and why some maltreated children do not develop PTSD or adverse brain developmental effects allows researchers, clinicians, program developers, and policy makers to focus on the what, where, and when of intervention that may deter more maltreated children from further negative life consequences. The presenter concludes with the importance of support for longitudinal imaging studies of maltreated children and studies that begin prior to the birth of at-risk children, towards the identification of neurobiological sources of protection and resilience.

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