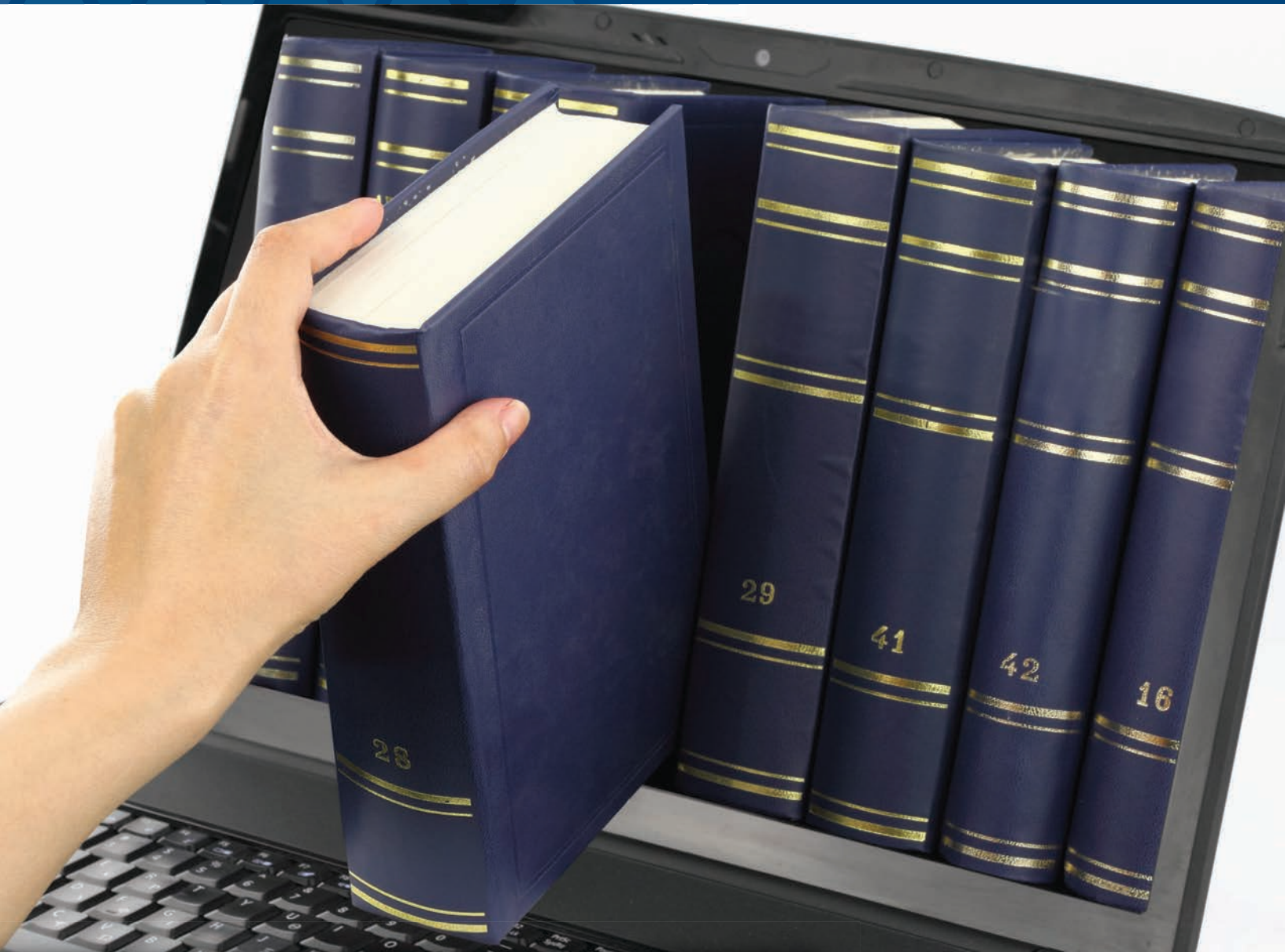


Neurobiological Effects of Child Maltreatment

A Bibliography



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Scope

This bibliography lists English language publications covering the effects of child maltreatment and trauma upon brain and neurobiological development.

Organization

Publications are listed in date-descending order. Links are provided to full text when possible.

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Neurobiological Effects of Child Maltreatment

A Bibliography

Nemeroff, C. B. (2016). [Paradise lost: The neurobiological and clinical consequences of child abuse and neglect](#). *Neuron*, 89(5), 892-909.

In the past two decades, much evidence has accumulated unequivocally demonstrating that child abuse and neglect is associated with a marked increase in risk for major psychiatric disorders (major depression, bipolar disorder, post-traumatic stress disorder [PTSD], substance and alcohol abuse, and others) and medical disorders (cardiovascular disease, diabetes, irritable bowel syndrome, asthma, and others). Moreover, the course of psychiatric disorders in individuals exposed to childhood maltreatment is more severe. Recently, the biological substrates underlying this diathesis to medical and psychiatric morbidity have been studied. This Review summarizes many of the persistent biological alterations associated with childhood maltreatment including changes in neuroendocrine and neurotransmitter systems and pro-inflammatory cytokines in addition to specific alterations in brain areas associated with mood regulation. Finally, I discuss several candidate gene polymorphisms that interact with childhood maltreatment to modulate vulnerability to major depression and PTSD and epigenetic mechanisms thought to transduce environmental stressors into disease vulnerability.

Teicher, M. H., & Samson, J. A. (2016). Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. *Journal of Child Psychology & Psychiatry*, 57(3), 241-266.

Childhood maltreatment is the most important preventable cause of psychopathology accounting for about 45% of the population attributable risk for childhood onset psychiatric disorders. A key breakthrough has been the discovery that maltreatment alters trajectories of brain development. This review aims to synthesize neuroimaging findings in children who experienced caregiver neglect as well as from studies in children, adolescents and adults who experienced physical, sexual and emotional abuse. In doing so, we provide preliminary answers to questions regarding the importance of type and timing of exposure, gender differences, reversibility and the relationship between brain changes and psychopathology. We also discuss whether these changes

represent adaptive modifications or stress-induced damage. Parental verbal abuse, witnessing domestic violence and sexual abuse appear to specifically target brain regions (auditory, visual and somatosensory cortex) and pathways that process and convey the aversive experience. Maltreatment is associated with reliable morphological alterations in anterior cingulate, dorsal lateral prefrontal and orbitofrontal cortex, corpus callosum and adult hippocampus, and with enhanced amygdala response to emotional faces and diminished striatal response to anticipated rewards. Evidence is emerging that these regions and interconnecting pathways have sensitive exposure periods when they are most vulnerable. Early deprivation and later abuse may have opposite effects on amygdala volume. Structural and functional abnormalities initially attributed to psychiatric illness may be a more direct consequence of abuse. Childhood maltreatment exerts a prepotent influence on brain development and has been an unrecognized confound in almost all psychiatric neuroimaging studies. These brain changes may be best understood as adaptive responses to facilitate survival and reproduction in the face of adversity. Their relationship to psychopathology is complex as they are discernible in both susceptible and resilient individuals with maltreatment histories. Mechanisms fostering resilience will need to be a primary focus of future studies.

Glaser, D. (2014). The effects of child maltreatment on the developing brain. *Medico-Legal Journal*, 82(3), 97-111.

Lasting effects of child abuse and neglect are well recognised. Apart from physical effects resulting from injuries and neglect, the effects are on behaviour, emotional well-being, interpersonal relationships and cognitive functioning. These psychological aspects are now known to have their counterparts in brain structure, chemistry and function. The growing knowledge of brain development has shed new light on our understanding of the processes by which especially early abuse and neglect may have a profound effect on the child's later adjustment. The brain undergoes its greatest growth and development in the first years of life, (with a second phase in adolescence). While the sequence of development within the brain is genetically determined, the nature of this development is determined to a considerable extent on the young child's experiences. The absence of some experiences, such as extreme deprivation during sensitive periods of development may mean that certain functions will not develop. For most functions, the nature of experience will

shape brain development. Negative experiences and certain ways of interaction will be incorporated into the brain's connectivity. While learning and new experiences continue throughout life, and their effects continue to be incorporated into brain structure and functioning, previous patterns cannot be erased, only added on to and more slowly. As we know from our adult experiences, learning is far faster in childhood. A further aspect of child maltreatment which has a profound effect on brain development is the significant neurobiological stress which the young, maltreated, child experiences. It is interesting to learn that secure attachment organisation protects the developing brain from the worst effects of the stress response. The effects of the experiences interact with the child's genetic resilience or vulnerability.

Munro, E., & Musholt, K. (2014). Neuroscience and the risks of maltreatment. *Children and Youth Services Review*, 47, 18-26.

Findings from neuroimaging are increasingly being cited in policy debates to strengthen the case for early identification of, and intervention with, children at risk of maltreatment and poor outcomes. While agreeing that neuroscientific research into the risks of maltreatment is a very valuable and exciting area of study, this article challenges the confidence with which these findings are used in policy discussions. It critically discusses the reliability and validity of the relevant findings and the contribution they can currently make to our understanding of the causes and consequences of maltreatment. In addition, it is argued that this type of evidence, which is new in policy debates, is often being used in ways that are problematic. Many participants in the relevant policy debates seem to subscribe either to an implicit version of dualism about the relationship between the mind and the body, or to reductionism — the view that the mental can be reduced to the physical. Such assumptions threaten the way we think about human agency and moral responsibility but it is argued that they are misguided for conceptual reasons. It is concluded that neuroscience has the potential to contribute to our understanding of the causes and effects of maltreatment but cannot do so in isolation from the social sciences. © 2013 Elsevier Ltd. All rights reserved.

Barrera, M., Calderón, L., & Bell, V. (2013). The cognitive impact of sexual abuse and PTSD in children: A neuropsychological study. *Journal of Child Sexual Abuse*, 22(6), 625-638.

Sexual abuse is known to have an impact on both child and adult mental health, but the neuropsychological basis of this effect is still largely unknown. This study compared neuropsychological test results from a group of 76 children, 13 of them sexual abuse victims with symptoms of post-traumatic stress disorder, 26 victims of sexual abuse who showed no symptoms post-traumatic stress disorder, and 37 controls. The groups were matched by age, sex, socioeconomic status, and educational level. Child sexual abuse was associated with reduced ability to inhibit automatic responses measured by the Stroop test regardless of post-traumatic stress disorder status. These findings indicate possible attentional inhibition difficulties in child victims of sexual abuse, which may help explain.

Nemeroff, C. B., & Seligman, F. (2013). [The pervasive and persistent neurobiological and clinical aftermath of child abuse and neglect](#). *Journal of Clinical Psychiatry*, 74(10), 999-1001. *Commentary*

Painter, K., & Scannapieco, M. (2013). Child maltreatment: The neurobiological aspects of posttraumatic stress disorder. *Journal of Evidence-Based Social Work*, 10(4), 276-284.

Childhood trauma due to physical abuse, neglect, or sexual abuse is a serious problem in the United States. Trauma can result in disruption or injury to the developing brain and lead to neurodevelopmental deficits that affect a child's functioning and can result in lifelong problems. Research has provided insight into how early childhood maltreatment affects brain development. This article examines the research on trauma, its effects on the brain, and evidence-based interventions. An overview of normal brain functioning and posttraumatic stress disorder is presented. Implications for social work practice with children who have experienced child maltreatment are discussed.

Hart, H., & Rubia, K. (2012). [Neuroimaging of child abuse: A critical review](#). *Frontiers in Human Neuroscience*, 6, 1-24.

Childhood maltreatment is a stressor that can lead to the development of behavior problems and affect brain structure and function. This review summarizes the current evidence for the effects of childhood maltreatment on behavior, cognition and the brain in adults and children. Neuropsychological studies suggest an association between child abuse and deficits in IQ, memory, working memory, attention, response inhibition and emotion discrimination. Structural neuroimaging studies provide evidence for deficits in brain volume, gray and white matter of several regions, most prominently the dorsolateral and ventromedial prefrontal cortex but also hippocampus, amygdala, and corpus callosum (CC). Diffusion tensor imaging (DTI) studies show evidence for deficits in structural interregional connectivity between these areas, suggesting neural network abnormalities. Functional imaging studies support this evidence by reporting atypical activation in the same brain regions during response inhibition, working memory, and emotion processing. There are, however, several limitations of the abuse research literature which are discussed, most prominently the lack of control for co-morbid psychiatric disorders, which make it difficult to disentangle which of the above effects are due to maltreatment, the associated psychiatric conditions or a combination or interaction between both. Overall, the better controlled studies that show a direct correlation between childhood abuse and brain measures suggest that the most prominent deficits associated with early childhood abuse are in the function and structure of lateral and ventromedial fronto-limbic brain areas and networks that mediate behavioral and affect control. Future, large scale multimodal neuroimaging studies in medication-naïve subjects, however, are needed that control for psychiatric co-morbidities in order to elucidate the structural and functional brain sequelae that are associated with early environmental adversity, independently of secondary co-morbid conditions.

De Bellis, M. D., Spratt, E. G., & Hooper, S. R. (2011). [Neurodevelopmental biology associated with childhood sexual abuse](#). *Journal of Child Sexual Abuse*, 20(5), 548-587.

Child maltreatment appears to be the single most preventable cause of mental illness and behavioral dysfunction in the US. There are few published studies examining the developmental and the psychobiological consequences of sexual abuse. There are multiple mechanisms through which sexual abuse can cause PTSD, activate biological stress response systems, and contribute to

adverse brain development. This article will critically review the psychiatric problems associated with maltreatment and the emerging biologic stress system research with a special emphasis on what is known about victimization by sexual abuse.

Delima, J., & Vimpani, G. (2011). The neurobiological effects of childhood maltreatment: An often overlooked narrative related to the long-term effects of early childhood trauma? *Family Matters*, (89), 42-52.

This paper aims to discuss the concept that some current societal dysfunction may well be an overlooked significant consequence of childhood maltreatment, with its associated trauma effect upon the developing brain. These changes prevent and impair the ability to remediate disadvantage and its effects through purely social policy and justice measures.

Heim, C., Shugart, M., Craighead, W. E., & Nemeroff, C. B. (2010). [Neurobiological and psychiatric consequences of child abuse and neglect.](#) *Developmental Psychobiology*, 52(7), 671-690.

The effects of early-life trauma and its consequences for the treatment of depression are reviewed. The prevalence and clinical sequelae of early sexual and physical abuse, neglect and parental loss are described. An overview of preclinical studies that help guide clinical research and practice is presented. Human clinical studies on the neurobiological consequences of early trauma are summarized. Moderating factors, such as genetic variation and sex differences, are discussed. The few current treatment outcome studies relevant to this research area are described. Guidance for the management of patients with depression and a history of child abuse and neglect are provided. Most patients who have experienced early traumatic experiences are likely best treated with a combination of psychotherapy and pharmacotherapy. This review is dedicated to the memory of Seymour Levine who pioneered the field of early experience research and to a considerable extent inspired the clinical studies described in this review. © 2010 Wiley Periodicals, Inc.

McCrory, E., De Brito, S. A., & Viding, E. (2010). [Research Review: The neurobiology and genetics of maltreatment and adversity.](#) *Journal of Child Psychology & Psychiatry*, 51(10), 1079-1095.

The neurobiological mechanisms by which childhood maltreatment heightens vulnerability to psychopathology remain poorly understood. It is likely that a complex interaction between environmental experiences (including poor caregiving) and an individual's genetic make-up influence neurobiological development across infancy and childhood, which in turn sets the stage for a child's psychological and emotional development. This review provides a concise synopsis of those studies investigating the neurobiological and genetic factors associated with childhood maltreatment and adversity. We first provide an overview of the neuroendocrine findings, drawing from animal and human studies. These studies indicate an association between early adversity and atypical development of the hypothalamicpituitary-adrenal (HPA) axis stress response, which can predispose to psychiatric vulnerability in adulthood. We then review the neuroimaging findings of structural and functional brain differences in children and adults who have experienced childhood maltreatment. These studies offer evidence of several structural differences associated with early stress, most notably in the corpus callosum in children and the hippocampus in adults; functional studies have reported atypical activation of several brain regions, including decreased activity of the prefrontal cortex. Next, we consider studies that suggest that the effect of environmental adversity may be conditional on an individual's genotype. We also briefly consider the possible role that epigenetic mechanisms might play in mediating the impact of early adversity. Finally, we consider several ways in which the neurobiological and genetic research may be relevant to clinical practice and intervention.

Twardosz, S., & Lutzker, J. R. (2010). Child maltreatment and the developing brain: A review of neuroscience perspectives. *Aggression and Violent Behavior*, 15(1), 59-68.

In this article we review neuroscience perspectives on child maltreatment to facilitate understanding of the rapid integration of neuroscience knowledge into the academic, clinical, and lay literature on this topic. Seminal articles from developmental psychology and psychiatry, a discussion of brain plasticity, and a summary of recent reviews of research on stress system dysregulation are presented with some attention to methodological issues. A common theme is that maltreatment during childhood is an experience that may affect the course of brain development,

potentially leading to differences in brain anatomy and functioning with lifelong consequences for mental health. The design of prevention and intervention strategies for child maltreatment may benefit from considering neuroscience perspectives along with those of other disciplines. © 2009 Elsevier Ltd. All rights reserved.

Tyrka, A. R., Price, L. H., Kao, H. T., Porton, B., Marsella, S. A., & Carpenter, L. L. (2010). [Childhood maltreatment and telomere shortening: Preliminary support for an effect of early stress on cellular aging.](#) *Biological Psychiatry*, 67(6), 531-534.

Psychological stress and trauma are risk factors for several medical and psychiatric illnesses. Recent studies have implicated advanced cellular aging as a potential mechanism of this association. Telomeres, DNA repeats that cap the ends of chromosomes and promote stability, shorten progressively with each cell division; their length is a marker of biological aging. Based on previous evidence linking psychosocial stress to shorter telomere length, this study was designed to evaluate the effect of childhood adversity on telomere length. Thirty-one adults with no current or past major Axis I psychiatric disorder participated. Subjects reported on their history of childhood maltreatment and telomere length was measured from DNA extracted from frozen whole blood using quantitative PCR. Participants reporting a history of childhood maltreatment had significantly shorter telomeres than those who did not report a history of maltreatment. This finding was not due to effects of age, sex, smoking, BMI, or other demographic factors. Analysis of subscales showed that both physical neglect and emotional neglect were significantly linked to telomere length. These results extend previous reports linking shortened leukocyte telomere length and caregiver stress to more remote stressful experiences in childhood, and suggest that childhood maltreatment could influence cellular aging.

Neigh, G. N., Gillespie, C. F., & Nemeroff, C. B. (2009). [The neurobiological toll of child abuse and neglect.](#) *Trauma, Violence, & Abuse*, 10(4), 389-410.

Exposure to interpersonal violence or abuse affects the physical and emotional well-being of affected individuals. In particular, exposure to trauma during development increases the risk of psychiatric and other medical disorders beyond the risks associated with adult violence exposure. Alterations in the hypothalamic-pituitary-adrenal (HPA) axis, a major mediating pathway of the

stress response, contribute to the long-standing effects of early life trauma. Although early life trauma elevates the risk of psychiatric and medical disease, not all exposed individuals demonstrate altered HPA axis physiology, suggesting that genetic variation influences the consequences of trauma exposure. In addition, the effects of abuse may extend beyond the immediate victim into subsequent generations as a consequence of epigenetic effects transmitted directly to offspring and/or behavioral changes in affected individuals. Recognition of the biological consequences and transgenerational impact of violence and abuse has critical importance for both disease research and public health policy.

Perry, B. D. (2009). [Examining child maltreatment through a neurodevelopmental lens: Clinical applications of the neurosequential model of therapeutics](#). *Journal of Loss and Trauma*, 14(4), 240-255.

This article provides the theoretical rationale and overview of a neurodevelopmentally-informed approach to therapeutic work with maltreated and traumatized children and youth. Rather than focusing on any specific therapeutic technique, the Neurosequential Model of Therapeutics (NMT) allows identification of the key systems and areas in the brain which have been impacted by adverse developmental experiences and helps target the selection and sequence of therapeutic, enrichment, and educational activities. In the preliminary applications of this approach in a variety of clinical settings, the outcomes have been positive. More in-depth evaluation of this approach is warranted, and is underway.

Andersen, S. L., Tomada, A., Vincow, E. S., Valente, E., Polcari, A., & Teicher, M. H. (2008). [Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development](#). *The Journal of Neuropsychiatry and Clinical Neurosciences*, 20(3), 292-301.

Volumetric MRI scans from 26 women with repeated episodes of childhood sexual abuse (CSA), and 17 healthy women (18–22 years) were analyzed for sensitive periods effects on hippocampal and amygdala volume, frontal cortex gray matter volume and corpus callosum area. Hippocampal volume was reduced in association with CSA at 3–5 years ($\beta=-0.69$, $p<0.0001$) and 11–13 years ($\beta=-0.25$, $p<0.05$). Corpus callosum was reduced with CSA at 9–10 years ($\beta=-0.44$, $p<0.005$),

and frontal cortex was attenuated in subjects with CSA at ages 14–16 ($\beta=-0.48$, $p<0.005$). Brain regions have unique windows of vulnerability to the effects of traumatic stress.

Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ... & Giles, W. H. (2006). [The enduring effects of abuse and related adverse experiences in childhood](#). *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174-186.

Childhood maltreatment has been linked to a variety of changes in brain structure and function and stress-responsive neurobiological systems. Epidemiological studies have documented the impact of childhood maltreatment on health and emotional well-being. After a brief review of the neurobiology of childhood trauma, we use the Adverse Childhood Experiences (ACE) Study as an epidemiological “case example” of the convergence between epidemiologic and neurobiological evidence of the effects of childhood trauma. The ACE Study included 17,337 adult HMO members and assessed 8 adverse childhood experiences (ACEs) including abuse, witnessing domestic violence, and serious household dysfunction. We used the number of ACEs (ACE score) as a measure of cumulative childhood stress and hypothesized a “dose-response” relationship of the ACE score to 18 selected outcomes and to the total number of these outcomes (comorbidity). Based upon logistic regression analysis, the risk of every outcome in the affective, somatic, substance abuse, memory, sexual, and aggression-related domains increased in a graded fashion as the ACE score increased ($P < 0.001$). The mean number of comorbid outcomes tripled across the range of the ACE score. The graded relationship of the ACE score to 18 different outcomes in multiple domains theoretically parallels the cumulative exposure of the developing brain to the stress response with resulting impairment in multiple brain structures and functions.

Gunnar, M. R., & Fisher, P. A. (2006). [Bringing basic research on early experience and stress neurobiology to bear on preventive interventions for neglected and maltreated children](#). *Development and Psychopathology*, 18(3), 651-677.

A major focus in developmental psychopathology is on understanding developmental mechanisms and, armed with this information, intervening to improve children’s outcomes. Translational research attempts to bridge the distance between understanding and intervention. In the

collaborations that have formed the core of our research network on early experience, stress, and prevention science, we have focused on translating basic research on early experiences and stress neurobiology into preventive interventions for neglected and abused children. Our experiences in attempting to move from bench to bedside have led us to recognize the many challenges that face translational researchers. This review provides a brief synopsis of the animal model literature on early experience and stress neurobiology from which we glean several key bridging issues. We then review what is currently known about the impact of childhood neglect and abuse on stress neurobiology in human adults and children. Next, we describe how this work has informed the evaluation of our preventive interventions with maltreated children. Finally, we discuss several considerations that should facilitate a more complete integration of basic research on early experience and stress neurobiology into preventive intervention strategies.

Niehoff, D. (2006). [Invisible scars: The neurobiological consequences of child abuse.](#) *DePaul Law Review*, 56, 847-877.

Wasserman, E. (2005). [Understanding the effects of childhood trauma on brain development in Native children.](#) *West Hollywood, CA: Tribal Law and Policy Institute.*

The information in this article was compiled to assist victim advocates who work with children and their caretakers to understand how the trauma affects the child's development when abuse has occurred – especially when it occurs early in the child's life. This article should also be helpful to Tribes and Tribal agencies seeking to develop programs and services that will promote healing and wellness for Tribal children. This article also provides basic information that will help extended family members, foster parents, teachers and others who are involved with a child that has suffered trauma early in life.

Cellini, H. R. (2004). [Child abuse, neglect, and delinquency: The neurological link](#). *Juvenile and Family Court Journal*, 55(4), 1-14.

Recent research has demonstrated a clear connection between physical, emotional, and sexual abuse and neglect during childhood, and negative changes in a child's neurological development. Abnormal growth and developmental patterns in a child's brain as a result of abuse and neglect can lead to life-long problems with self-control, memory, emotion, judgment, consequential thinking, and moral reasoning, resulting in an increased likelihood of substance abuse, juvenile delinquency, and adult criminal behaviors. This article provides information on the abused child, neurological implications, and recommendations.

Nemeroff, C. B. (2004). Neurobiological consequences of childhood trauma. *The Journal of Clinical Psychiatry*, 65(Suppl1), 18-28.

There is considerable evidence to suggest that adverse early-life experiences have a profound effect on the developing brain. Neurobiological changes that occur in response to untoward early-life stress can lead to lifelong psychiatric sequelae. Children who are exposed to sexual or physical abuse or the death of a parent are at higher risk for development of depressive and anxiety disorders later in life. Preclinical and clinical studies have shown that repeated early-life stress leads to alterations in central neurobiological systems, particularly in the corticotropin-releasing factor system, leading to increased responsiveness to stress. Clearly, exposure to early-life stressors leads to neurobiological changes that increase the risk of psychopathology in both children and adults. Identification of the neurobiological substrates that are affected by adverse experiences in early life should lead to the development of more effective treatments for these disorders. The preclinical and clinical studies evaluating the consequences of early-life stress are reviewed. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

van der Kolk, B. A. (2003). [The neurobiology of childhood trauma and abuse](#). *Child and Adolescent Psychiatric Clinics of North America*, 12(2), 293-317.

Teicher, M. (2002). [The neurobiology of child abuse](#). *Scientific American*, 286(3), 70.

De Bellis, M. D. (2001). [Developmental traumatology: The psychobiological development of maltreated children and its implications for research, treatment, and policy](#). *Development and Psychopathology*, 13(03), 539-564.

In this review, a developmental traumatology model of child maltreatment and the risk for the intergenerational cycle of abuse and neglect using a mental health or posttraumatic stress model was described. Published data were reviewed that support the hypothesis that the psychobiological sequelae of child maltreatment may be regarded as an environmentally induced complex developmental disorder. Data to support this view, including the descriptions of both psychobiological and brain maturation studies in maltreatment research, emphasizing the similarities and differences between children, adolescents, and adults, were reviewed. Many suggestions for important future psychobiological and brain maturation research investigations as well as public policy ideas were offered.

Heim, C., & Nemeroff, C. B. (2001). [The role of childhood trauma in the neurobiology of mood and anxiety disorders: Preclinical and clinical studies](#). *Biological Psychiatry*, 49(12), 1023-1039.

Epidemiologic studies indicate that children exposed to early adverse experiences are at increased risk for the development of depression, anxiety disorders, or both. Persistent sensitization of central nervous system (CNS) circuits as a consequence of early life stress, which are integrally involved in the regulation of stress and emotion, may represent the underlying biological substrate of an increased vulnerability to subsequent stress as well as to the development of depression and anxiety. A number of preclinical studies suggest that early life stress induces long-lived hyper(re)activity of corticotropin-releasing factor (CRF) systems as well as alterations in other neurotransmitter systems, resulting in increased stress responsiveness. Many of the findings from these preclinical studies are comparable to findings in adult patients with mood and anxiety disorders. Emerging evidence from clinical studies suggests that exposure to early life stress is associated with neurobiological changes in children and adults, which may underlie the increased risk of psychopathology. Current research is focused on strategies to prevent or reverse the detrimental effects of early life stress on the CNS. The identification of the neurobiological

substrates of early adverse experience is of paramount importance for the development of novel treatments for children, adolescents, and adults

Kaufman, J., & Charney, D. (2001). [Effects of early stress on brain structure and function: Implications for understanding the relationship between child maltreatment and depression](#). *Development and Psychopathology*, 13(3), 451-471.

Child abuse is associated with markedly elevated rates of major depression (MDD) in child, adolescent, and adult cohorts. This article reviews preclinical (e.g., animal) studies of the effects of early stress and studies of the neurobiological correlates of MDD in adults and children, and it highlights differences in the neurobiological correlates of MDD and stress at various developmental stages. The preclinical studies demonstrate that stress early in life can alter the development multiple neurotransmitter systems and promote structural and functional alterations in brain regions similar to those seen in adults with depression. Preclinical and clinical studies suggest, however, that long-term neurobiological changes associated with early stress can be modified by familial/genetic factors, the quality of the subsequent caregiving environment, and pharmacological interventions. Little is known about how developmental factors interact with experiences of early stress and these other modifying factors. Moreover, in cases of child maltreatment, the effects of early abuse are often exacerbated by failures in the child protection system and repeat out-of-home placements. Given the number of factors that impact on the long-term outcome of maltreated children, multidisciplinary research efforts are recommended to address this problem—with foci that span from neurobiology to social policy.

Perry, B. D. (2001). The neurodevelopmental impact of violence in childhood. In D. Schetky & E.P. Benedek (Eds.), *Textbook of child and adolescent forensic psychiatry* (pp. 221-238). Washington, DC: American University Press.

Kaufman, J., Plotsky, P. M., Nemeroff, C. B., & Charney, D. S. (2000). [Effects of early adverse experiences on brain structure and function: Clinical implications](#). *Biological Psychiatry*, 48(8), 778-790.

Child abuse is associated with markedly elevated rates of major depression and other psychiatric disorders in adulthood. This article reviews preclinical studies examining the effects of early stress, factors that modify the impact of these experiences, and neurobiological changes associated with major depression. Preclinical studies demonstrate that early stress can alter the development of the hypothalamic-pituitary-adrenal axis, hypothalamic and extrahypothalamic corticotropin releasing hormone, monoaminergic, and g-aminobutyric acid/benzodiazepine systems. Stress has also been shown to promote structural and functional alterations in brain regions similar to those seen in adults with depression. Emerging data suggest, however, that the long-term effects of early stress can be moderated by genetic factors and the quality of the subsequent caregiving environment. These effects also can be prevented or reversed with various pharmacologic interventions. Preclinical studies of early stress can provide valuable insights in understanding the pathophysiology and treatment of major depression. They also can provide an important tool to use to investigate interactions between genes and environments in determining an individual's sensitivity to stress. More research is needed to understand how inherent factors interact with experiences of abuse and other psychosocial factors to confer vulnerability to develop depression.

Glaser, D. (2000). Child abuse and neglect and the brain—a review. *The Journal of Child Psychology and Psychiatry and Allied Disciplines*, 41(1), 97-116.

Developmental psychology and the study of behaviour and emotion have tended to be considered in parallel to the study of neurobiological processes. This review explores the effects of child abuse and neglect on the brain, excluding nonaccidental injury that causes gross physical trauma to the brain. It commences with a background summary of the nature, context, and some deleterious effects of omission and commission within child maltreatment. There is no post-maltreatment syndrome, outcomes varying with many factors including nature, duration, and interpersonal context of the maltreatment as well as the nature of later intervention. There then follows a section on environmental influences on brain development, demonstrating the dependence of the orderly process of neurodevelopment on the child's environment. Ontogenesis, or the development of the self through self-determination, proceeds in the context of the nature–nurture interaction. As a

prelude to reviewing the neurobiology of child abuse and neglect, the next section is concerned with bridging the mind and the brain. Here, neurobiological processes, including cellular, biochemical, and neurophysiological processes, are examined alongside their behavioural, cognitive, and emotional equivalents and vice versa. Child maltreatment is a potent source of stress and the stress response is therefore discussed in some detail. Evidence is outlined for the buffering effects of a secure attachment on the stress response. The section dealing with actual effects on the brain of child abuse and neglect discusses manifestations of the stress response including dysregulation of the hypothalamic-pituitary-adrenal axis, and parasympathetic and catecholamine responses. Recent evidence about reduction in brain volume following child abuse and neglect is also outlined. Some biochemical, functional, and structural changes in the brain that are not reflections of the stress response are observed following child maltreatment. The mechanisms bringing about these changes are less clearly understood and may well be related to early and more chronic abuse and neglect affecting the process of brain development. The behavioural and emotional concomitants of their neurobiological manifestations are discussed. The importance of early intervention and attention to the chronicity of environmental adversity may indicate the need for permanent alternative caregivers, in order to preserve the development of the most vulnerable children.

Teicher, M. H. (2000). [Wounds that time won't heal: The neurobiology of child abuse.](#) *Cerebrum*, 2(4), 50-67.