Abstract

Exposure to Adverse Childhood Experiences (ACEs) has been linked to a range of physical health concerns in childhood as well as adulthood, including cardiovascular disease, headaches, autoimmune disease, obesity, chronic lung disease, and generally poor health (Kalmakis & Chandler, 2015). Exposure to any ACEs has been shown to increase the level of everyday life stress. Further, ACE exposure is directly and negatively correlated to adult self-rated physical and mental health and perceived social support (Cameranesi et al., 2019). Violence exposure is one of the most severe sources of human stress and an example of an ACE (Moffitt & Klaus-Grawe 2012). In 2017, there were approximately 123,000 new cases of child abuse, of which 58,000 cases were related to child sexual abuse and 578 fatalities (Rivara et al., 2019). Research suggests that conflict experienced in childhood is more detrimental to adult health than economic hardship (Santini et al., 2021). Exposure to violence often results in the child constantly feeling stressed and interpreting their environment as an unsafe place (Scarpa et al., 2008), and prolonged stress exposure causes damage to the nervous, immune, and endocrine systems, increasing the susceptibility to cardiovascular disease and abnormal brain development (McCrae et al., 2019). Despite many studies establishing the mental health consequences of adverse childhood experiences, few studies focus on the intersection between exposure to ACEs
and physical health consequences. The primary aim of this narrative review is to review and summarize medical and psychological research on the mechanisms linking ACEs to physical health outcomes. Specifically, we focus on the neurobiological and cardiovascular impacts of ACEs on children, increasing their risk for long-term health outcomes like chronic inflammation and obesity (Kalmakis & Chandler, 2015).

**Adverse Childhood Experiences (ACEs)**

ACEs are childhood events that vary in length and severity, often chronic, occurring within a child’s family or social environment that cause harm or distress, thereby disrupting the child’s physical or mental health and development. (Kalmakis & Chandler, 2015). Violence exposure is one of the most severe sources of human stress (Moffitt & Klaus-Grawe 2012), as research suggests that conflict experienced in childhood is more detrimental to adult health than economic hardship (Santini et al., 2021). Childhood trauma, maltreatment, and child abuse are common examples of ACEs (Kalmakis & Chandler, 2015). Child abuse is defined as any form of physical, emotional/psychological, and or sexual act of maltreatment or lack of care that results in emotional harm and or physical injury to a child or youth under the age of eighteen. It includes abuse and the neglect of the child’s physical, emotional, and educational needs, inadequate supervision, and exposure to intimate partner violence (IPV) (Cameranesi et al., 2019). It is increasingly recognized that IPV exposure is not limited to direct witnessing but often includes a family atmosphere of fear, control, impaired parenting behavior by caregivers, and an increased risk of other stressors like maltreatment or neglect (Gartland et al., 2021). Furthermore, one in four adults has been physically abused as a child (Cameranesi et al., 2019). Also, one in five women and one in thirteen men report having been sexually abused as a child (Cameranesi et al., 2019). It is essential to highlight that exposure to any ACEs has been shown to increase the level
of everyday life stress and is directly and negatively correlated to adult self-rated physical and mental health and self-perceived social support (Cameranesi et al., 2019).

There are gender differences in the rates and the impacts of exposure to child abuse. On average, women have a higher exposure to childhood sexual abuse, domestic violence, and sexual assault, while men are more likely to be exposed to natural disasters, motor vehicle accidents, and physical assault (Wamser-Nanney & Cherry, 2018). In 2018, it was estimated that 14.1% of males, compared with 20.4% of females, experienced childhood sexual abuse, while 24.3% of males, compared with 21.7% of females, experienced childhood physical abuse (Rivara et al., 2019). Women are also more likely to experience symptoms of PTSD, internalizing disorders, and somatic complaints, while men are more likely to experience symptoms of externalizing disorders (Wamser-Nanney & Cherry, 2018). Additionally, girls exposed to ACEs are more likely to exhibit intrusive thoughts, hyperarousal, sexual anxiety, and an overall perception that the world is unsafe, while boys exposed to ACEs are more likely to display higher levels of aggression (Wamser-Nanney & Cherry, 2018). Following early exposure to ACEs, boys are more likely to demonstrate externalizing problems earlier and a faster decline in symptomology than girls, who are more likely to exhibit internalizing problems (Wamser-Nanney & Cherry, 2018). For girls, exposure to childhood physical and or sexual abuse increases the probability of exposure to physical, sexual, and or psychological IPV as an adult (Sanz-Barbero et al., 2019). The chronicity and social context in which trauma occurs may help explain gender differences in trauma exposure, as girls are more likely to experience PTSD symptoms in socially gendered roles (Wamser-Nanney & Cherry, 2018).

Research supports a cumulative effect of ACEs on a person’s health, with more adverse experiences leading to an increase of significant effects on physical and mental health (Kalmakis & Chandler, 2015). Unfortunately, children who are victims of one violent incident are more
likely to be exposed to re-victimization and poly-victimization (Moffitt & Klaus-Grawe 2012). For example, children victimized in one incident of physical abuse are likely to suffer subsequent incidents of physical abuse and other forms of victimization (e.g., verbal and sexual abuse) (Moffitt & Klaus-Grawe 2012). In addition to the effect of accumulation and severity of ACEs, the timing of the adverse event is significantly associated with health outcomes (Kalmakis & Chandler, 2015). Studies have shown that, apart from infants, children and youth in developmental states have a greater probability of developing complex health concerns, with four or more ACEs serving as an indicator of significant and complex health outcomes for these age groups (McCrae et al., 2019). Exposure to violence can result in the child constantly interpreting their environment as an unsafe place (Scarpa et al., 2008), and prolonged stress in childhood can cause changes to the nervous, immune, and endocrine systems, increasing the susceptibility to disease and abnormal brain development in the absence of protective factors (McCrae et al., 2019).

Neurobiological Impact

ACEs are believed to cause an over-stimulation of the body’s stress response system, impairing the neuro-regulatory system (McCrae et al., 2019) and the nervous, immune, and endocrine systems (Sheikh, 2017). Over time, impairment of these systems results in significant consequences during critical periods of brain development, often leading to reduced volume of the hippocampus, prefrontal cortex, and amygdala (McCrae et al., 2019). The hippocampus is known for its role in cognitive function, primarily involving learning processes and memory. Along with the parahippocampus, the size of the hippocampus has been positively correlated with accuracy, memory, executive function, performance speed, and the ability for abstract thought (Aas et al., 2012). Studies show that hippocampal volume is smaller in adults reporting a history of ACEs but not in maltreated children, leading to a hypothesis that exposure to ACEs
may cause abnormal hippocampal development that only becomes apparent in a mature brain (Moffitt & Klaus-Grawe 2012). Structural neuroimaging studies have also found deficits in general volume and gray and white matter in the amygdala, hippocampus, corpus callosum, and the dorsolateral and ventromedial prefrontal cortex among victims of ACEs (Barrios et al., 2015). The prefrontal cortex involves working memory (the ability to keep things in mind) and goal-directed, self-regulatory, and social behavior (McEwen & Morrison, 2013). The prefrontal cortex development is slower and more prolonged than other brain structures (McEwen & Morrison, 2013), making it especially vulnerable to early stress (Moffitt & Klaus-Grawe, 2012). Deficits in the prefrontal cortex have also been associated with multiple brain disorders like attention deficit disorder, PTSD, schizophrenia, Alzheimer’s disease, and depression (McEwen & Morrison, 2013). Additional studies demonstrate structural abnormalities in the prefrontal cortex in maltreated adolescents (Moffitt & Klaus-Grawe 2012), contributing to various behavioral and cognitive problems (Barrios et al., 2015) like adult psychopathology, anxiety, depression, and bipolar disorder (Pusalkar et al., 2016). The amygdala is a critical structure in emotional processing, and recently, its role in higher cognitive functions like working memory and executive control in humans has been the focus of research studies (Aas et al., 2012). The amygdala’s volume has been linked to worse performance on immediate and delayed verbal recall in patients with schizophrenia, as well as acoustic and visual attention in patients with affective disorders. Childhood trauma has been associated with significantly a smaller amygdala and hippocampal volume, consequently playing an essential role in regulating the stress response systems (Aas et al., 2012).

The hypothalamic-pituitary-adrenal (HPA) axis and Autonomic Nervous Systems (ANS) are two primary physiological stress systems used to regulate our stress response. Childhood trauma has been shown to influence the HPA axis affecting the medial temporal volumes and
cognitive function (Aas et al., 2012). In 2015, a study of 104 women between the ages of 18 – 25 recruited at three schools for health care and social work in Basel, Switzerland, measured biological responses to stress by taking saliva and heart rate measurements before and after stress induction to examine the association of duration and age of ACE occurrence on stress reactivity. The study concluded that when ACEs repeatedly occur and are chronic, significant alterations in stress reactivity in adulthood make the person more susceptible to later mental or physical disorders (Voellmin et al., 2015). The same neural circuitry regulates the ANS as the HPA axis, yet the ANS has a faster response to stress, making it a faster physiological response system and more likely to affect cognitive and behavioral responses to environmental stress (Oosterman et al., 2019). During a stressful situation, the ANS facilitates a rapid response to stress by suppressing the parasympathetic nervous system and activating the sympathetic nervous system to help initiate physiological arousal (increased heart rate and blood pressure). When stress demands are low, the parasympathetic nervous system is activated to reduce physiological arousal and promote homeostasis (Oosterman et al., 2019). The experience of multiple chronic ACEs has been shown to overstimulate the ANS and dysregulate the HPA axis (Kalmakis & Chandler, 2015). The integrated model of sympathetic and parasympathetic functioning states that low basal levels of parasympathetic activity and low reactivity of the parasympathetic nervous system during stress reflect dysregulation of emotional processes in adults and children (Oosterman et al., 2019). In support of the allostatic load theory, a shift away from homeostasis, which states that ACEs may permanently alter the neurobiological stress management systems (Sheikh, 2017), prolonged overstimulation and dysregulation of HPA and ANS systems have been shown to cause abnormal brain development and stress system disorders (Kalmakis & Chandler, 2015). Disruptions to these systems promote a cascade of physiological, neurochemical, and hormonal changes, leading to alterations in brain structure (Barrios et al.,
for example, changes to the brain’s white and gray matter, its volume and functional connectivity, altered neurotransmitter metabolism, changes to the neuroendocrine stress response, impaired glucose metabolism, and chronic inflammation (Rivara et al., 2019).

**Cardiovascular Impact**

Adverse childhood experiences have been associated with stress dysregulation, immune dysfunction, and, ultimately, inflammation (Sheikh, 2017). Inflammation is a part of the immune response, a defense mechanism specializing in recognizing foreign antigens and triggering a rapid immunological response against them. Inflammation inducers become chronic with an unsuccessful inflammatory response, and the resolution phase cannot occur. Studies have found that children exposed to maternal rejection and other forms of ACEs are twice as likely as those of non-maltreated children to show impairment in their immune response and elevated clinically significant biomarkers for inflammation. Chronic inflammatory states often lead to significant tissue damage and age-related diseases like diabetes, dementia, increased risk of psychopathology (Moffitt & Klaus-Grawe 2012), and cardiovascular disease (CVD) (Su et al., 2015). Despite medical advancements, CVD remains the number one cause of death for men and women in the United States, with the direct and indirect cost of CVD projected to increase from $579 billion in 2012 to $1.2 trillion by 2030 (Su et al., 2015). A growing body of evidence shows that exposure to ACEs disrupts normal development and increases vulnerability to CVD through behavioral, mental, emotional, and physical health problems (Su et al., 2015). A study by Women’s Health Across the Nation reported that women with a history of childhood sexual abuse presented greater carotid intima-media thickness (IMT), a subclinical measure of CVD risk, suggesting that early exposure to ACEs is correlated to the long-term development of atherosclerosis, calcification of the arteries. Also, exposure to ACEs increases the probability of an infant developing risk factors like obesity, high blood pressure, and cholesterol (Su et al.,
2015). Studies have shown a clear link between ACEs and obesity, defined as body fat deposition that results from a disturbance of energy homeostasis, as child abuse is associated with a 36% higher risk of adult obesity and an odds ratio of 1.36 (Alhalal, 2018, Su et al., 2015). Potential pathways in which ACEs may lead to obesity include high cortisol levels from chronic stress, disturbed hormonal levels (Alhalal, 2018), as well as negative affect (depression, anger, stress), disordered eating, and low-activity levels, as studies show that children who were sexually abused often avoid engaging in physical activity with peers (Su et al., 2015).

A 23-year longitudinal cohort study examining the long-term effect of exposure to ACEs on blood pressure found that compared to those without a history of ACEs, individuals exposed to ACEs had an elevated risk of developing hypertension at earlier ages (Su et al., 2015). The number of ACEs a child is exposed to has been associated with attenuated cortisol and heart rate responses to stress (Voellmin et al., 2015). Vagal tone is a cardiovascular function and a measure of the parasympathetic nervous system that facilitates a person’s adaptive response to environmental change and control over heart rate (McLaughlin et al., 2015). By measuring continuous cardiac and hemodynamic measures in a community-based sample of 168 adolescents between the age of thirteen and seventeen, a study examined whether vagal tone can interact with child exposure to psychosocial stress to predict psychopathology in adolescents. Results from the study found that low vagal tone is correlated with internalizing psychopathology in adolescents exposed to high levels of stress, and a low resting vagal tone is associated with major depression in adults (Oosterman et al., 2019, McLaughlin et al., 2015). The study provides novel evidence that low vagal tone is a potential marker of adolescent stress sensitivity associated with internalizing psychopathology after exposure to ACEs (McLaughlin et al., 2015). Furthermore, a study of forty children between ages seven and thirteen reporting exposure to community violence was assessed for the influence of heart rate (HR) and HR
variability (HRV) on the correlation between exposure to community violence and proactive and reactive aggression in children (Scarpa et al., 2008). The study found that violence victimization is correlated with increased proactive aggression in children with low levels of resting HR and decreased proactive aggression in children with high levels of resting HR. Likewise, child exposure to community violence is related to increased aggression in children with high resting HRV and decreased reactive aggression in children with low levels of HRV. Though the study emphasizes the need for further research into the subject, they speculate that low HR may reflect an impulsive personality that could place the child at greater risk of aggressive socialization, and high HRV may also reflect disinhibited temperament (Scarpa et al., 2008).

Discussion

Each year, more than 30% of children in the United States experience ACEs (Cameranesi et al., 2019). Regarding IPV alone, it is estimated that the average child exposed to intimate partner violence costs the national economy $50,000 throughout their lifetime, with an approximate total of $55 billion for all children exposed to IPV in the United States. The cost includes increased use of social services, health care utilization, educational outcomes, workforce productivity, and criminal behavior (Carlson et al., 2019). ACEs cost the United States $124 billion annually, with individual lifetime costs equal to or higher than the economic burden of diabetes or stroke (McCrae et al., 2019). Identifying the mechanisms responsible for the onset of physical diseases in adult survivors of ACEs is critical to planning and implementing intervention programs to help reduce the associated adverse health outcomes (Cameranesi et al., 2019) and help decrease the negative impact on the US economy. The dynamic interconnection of symptoms is evident. Exposure to ACEs can cause children to interpret their environment as unsafe, causing them to live in a chronic state of stress, prolonging the release of stress hormones, leading to chronic inflammation, and affecting the immune, neurological, and
cardiovascular systems in children (Scarpa et al., 2008). Chronic inflammation has been shown to cause heart tissue damage (Moffitt & Klaus-Grawe, 2012), increasing the risk of CVD (Su et al., 2015), as well as leading to irregular vagal tone (McLaughlin et al., 2015), heart rate and heart rate variability (Scarpa et al., 2008). These mechanisms are related to a higher risk of psychopathology, increased aggression in childhood, and depressive disorders in adulthood, thus increasing the potential for further development of CVD (Scarpa et al., 2008, McLaughlin et al., 2015). Neurologically, ACEs have been found to over-burden the body’s stress response system during crucial development periods, often affecting brain development by reducing the volume of brain structures like the prefrontal cortex, amygdala, and hippocampus (McCrae et al., 2019). Reduced volume in these brain structures is correlated with learning processes (Aas et al., 2012), working memory, goal-directed, self-regulatory, social behavior (McEwen & Morrison, 2013), as well as overburdened HPA and ANS stress systems (Aas et al., 2012), causing further abnormal brain development and further increasing the risk for stress system disorders (Kalmakis & Chandler, 2015). ACEs are also believed to increase the risk of other chronic diseases like arthritis, ulcers, migraines, gastrointestinal disorders, cancer, pain disorders, asthma, allergy, sleep problems, bronchitis, hypothyroid, and psychiatric disorders in later life (Sheikh, 2017, Gartland et al., 2021, Cameranesi et al., 2019, Rivara et al., 2019), though more research is needed to establish the specific mechanisms associated with the development of these diseases.

This study comes with limitations. Narrative reviews are different from a meta-analysis in that the procedure is less standardized; thus, the conclusions drawn are subjected and dependent on the reviewer’s knowledge and expertise. Because one person conducted this narrative review, the way studies were analyzed, the conclusions drawn, and the scope of research were limited by the time and resources available. Consequently, there is a higher risk of unconscious bias during the selection process and the interpretation of findings. Finally, future
research should focus on other social determinants of health, like family and community risk and protective factors, to deepen our understanding of the effects of ACEs on adult physical health (Cameranesi et al., 2019).

This body of research has several important clinical implications. Efforts to prevent one type of violence can prevent other types of violence (Carlson et al., 2019), lowering the incidence of re-victimization and poly-victimization. Though not the focus of this review, it is vital to highlight that a growing body of evidence demonstrates that additional social support for under-resourced families could protect against developing physical and psychopathological symptoms in individuals exposed to ACEs (Cameranesi et al., 2019). Transition-to-fatherhood programs engaging new and expecting fathers that focus on IPV prevention and gender equity can help promote positive gender and sexual-social norms and healthy, non-violent child care practices (Carlson et al., 2019). From a healthcare perspective, due to the negative physical health consequences of ACEs, the management of victims should include the facilitation of access to health care (Rivara et al., 2019). Despite growing evidence supporting the negative health consequences of ACEs, primary care providers continue to treat patients with many physical health problems without clearly understanding their childhood history (Kalmakis & Chandler, 2015). Consequently, additional training is encouraged for healthcare workers to help them address the patient’s history of ACEs, current IPV, PTSD symptoms, and depressive symptoms (Alhalal, 2018). The primary aim of this narrative review was to review and summarize medical and psychological research on the mechanisms linking ACEs to physical health outcomes. Our conclusions support the consensus that exposure to adverse childhood experiences significantly increases the risk of negative physical health outcomes in adulthood. There is a need to develop research and programs preventing early adversity and promoting positive child development (Su et al., 2015).
References


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