The effects of Early Life Stress on brain and behavior

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Abstract

The prenatal period and the first postnatal years are very important for a child's development. Exposure to harmful external factors in this period can have lasting effects on this development. Unfortunately, many children experience a form of stress like maltreatment or abuse in their early childhood. Given this prevalence of forms of early life stress and the effects it can have on the important development which takes place in that period, early life stress poses a serious health problem. This paper aims to provide a review of some of the literature on early life stress (ELS) and in particular the long-term effects it has on those who suffer from it. I will focus mainly on the neurological and physical effects and the effects on social and emotional behavior. I will also discuss a few of the factors determining the resilience of the victims and some potential methods of prevention or treatment. I hope to show that ELS and child abuse are major health issues that can have an impact lasting long after childhood. There are many studies about ELS that have found significant negative consequences of it. To summarize, stress during early years of development, pre- or postnatal, has noticeable effects on the development of the brain. It leads to an increased risk for psychiatric disorders, smaller hippocampi, and hyperreactive ventral striatum resulting in memory deficits, cognitive defects, higher chances of depression and addiction, and even higher chances of various physical health problems. It also has a significant effect on behavior such as increased problematic behavior and reduced social behavior, deficits in emotion recognition and regulation, and increased chances of depression. Females seem to be more resilient to some of these negative effects, like the structural, behavioral and memory effects but not to the anxiety and mood related effects. Prevention and treatment have shown promising effects, especially when implemented as early on as possible. Even though, much research still needs to be done into prevention and treatment of these effects especially treatment implemented during later life stages like adolescence or adulthood. More research into this matter could be very beneficial to reducing the prevalence of some of the most prevalent physical and mental health problems in the world.

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Introduction

The prenatal period and the first postnatal years are very important for a child's development. In these years many neurological and behavioral developments take place (Dawson et al., 2000). With this in mind, it makes sense that exposure to harmful external factors in this period can have lasting effects on this development. An example of a harmful external factor is stress. Research has indeed shown that experiencing stress during these sensitive periods (prenatal, postnatal, and early childhood) can have damaging consequences for the development of biological systems and behavior (Anda et al., 2006; Dawson et al., 2000). Unfortunately, many children experience a form of stress like maltreatment or abuse. In the Netherlands, it is estimated that 26 – 37 per 1000 children are victims of maltreatment, 46% of these cases being in the context of domestic violence (Figure 1) (van Berkel et al., 2020). Given this prevalence of forms of early life stress and the effects it can have on the neurological development which takes place in that period, early life stress poses a serious health problem.

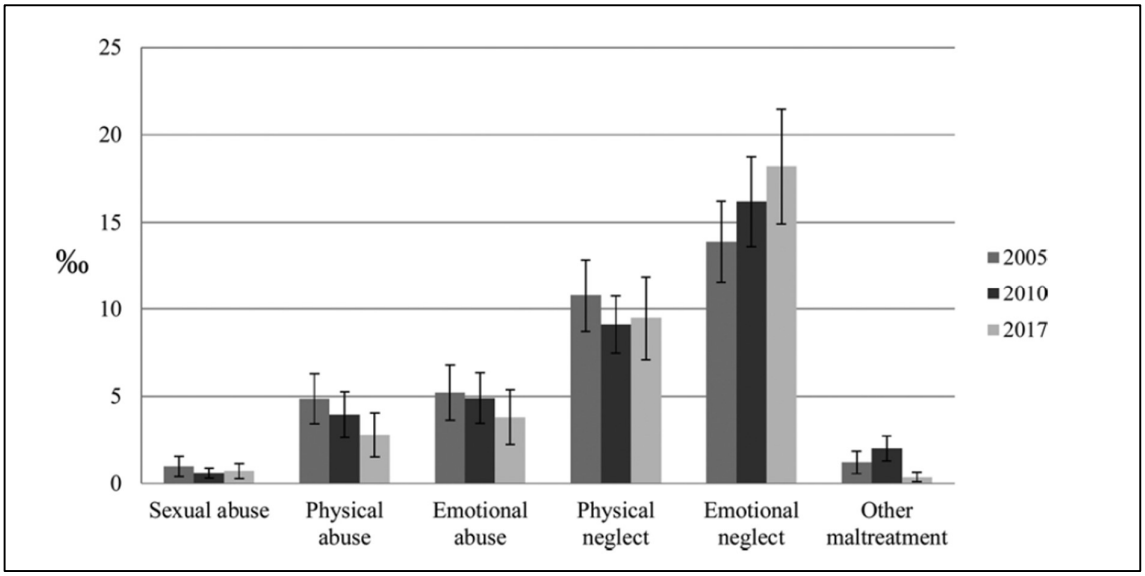

Figure 1. Prevalence estimates of the different types of child maltreatment in the Netherlands 2005, 2010 and 2017 (van Berkel et al., 2020).

This paper aims to provide a review of some of the literature on Early life stress (ELS) and in particular the long-term effects than can be seen in animal models and those who suffer from it. I will focus mainly on the neurological and physical effects and the effects on social and emotional behavior. I will also discuss a few of the factors determining the resilience of the victims and some potential methods of prevention or treatment. Unfortunately, given the time and word limits, the scope of this paper is limited and, on some occasions, I cannot go as deep into the specifics as I would like. Through this paper, I hope to show that ELS and child abuse are major health issues that can have detrimental consequences long after childhood.

As suggested by the title of the paper the main question I will try to answer in this paper is:

What are the effects of ELS on the brain and behavior of those who suffer from it?

I have divided the literature part of this paper into 4 sections each discussing a different subtopic:

- The physiological and neurological effects of ELS
- The effects of ELS on social and emotional behavior

- The important factors involved in individual differences in susceptibility to negative consequences of ELS
- The reversibility and prevention of the effects of ELS

After I have discussed my findings in the literature, I will summarize my findings and draw a conclusion. Before I dive into my findings, I will first clarify some of the terms that will be frequently used in this paper.

Frequently used terms explained

Early Life Stress (ELS) can be best described as exposure to stress during the early years of an individual's life. Stress can broadly be defined as "a state of real or perceived threat to homeostasis that may challenge an organism's well-being" (Smith & Vale, 2006). In this paper, we will look at two different types relating to early life specifically: (maternal) deprivation and maltreatment. According to Gonzalez and Wekerle, Child maltreatment can be defined as: "All forms of abuse or neglect committed by adults against minors that result in actual or potential harm to the child. There are five main classifications of Childhood Maltreatment: physical, sexual, and emotional abuse, neglect, and exposure to intimate partner violence" (Gonzalez & Wekerle, 2016). In stress studies on rats **maternal or paternal deprivation** is often used, defined as the absence of expected cognitive and social inputs from the mother or father respectively (Machlin et al., 2019). According to the encyclopedia of behavioral neuroscience An example of how maternal deprivation is achieved in a test is to separate the pups from their mother after birth, leave them alone and without food and water for a certain period on a heating pad to avoid hypothermia, and then reunite them with the mother (Kentrop et al., 2018). According to the encyclopedia of behavioral neuroscience: "These procedures vary greatly among various research groups, ranging from a single 24-h separation to repeated episodes of separation lasting 12, 6, or 3 h and administered on Postnatal days 1–2 through 14–21" (Kalinichev & Francis, 2010). When discussing **prenatal stress**, studies refer to stress experienced by the mother, maternal stress, during the pregnancy. This is known to potentially lead to miscarriages, early births, cognitive deficits, and birth defects (Mulder et al., 2002; Weinstock, 2005). In studies on rats, the most popular stressor used to replicate this is restraining the pregnant rats for periods ranging from only 5 minutes to up to 3 weeks depending on the study (Buynitsky & Mostofsky, 2009). Studies about ELS, sensitive periods, and early life in general look at several different specific periods. The first period encountered frequently in the literature is the **prenatal** period. This period can be defined as the developmental period up to the birth of the individual. **Postnatal** refers to the first weeks immediately after birth. In humans, when looking at the period starting immediately after birth and ending with puberty, around the age of 10-12, the term **Childhood** is most commonly used. In rats, this is usually referred to as the **Juvenile** period and it ends with puberty at 34 postnatal days for females and 45 for males (McCutcheon & Marinelli, 2009). Starting with puberty comes **adolescence**, which is usually not considered early life but is mentioned here and there in this paper when discussing the effects of ELS. Adolescence is considered to roughly be between 12 and 18 years after which follows the **adult** period. In rats, adolescence is considered to be between 34 (females) or 45 (males) and 63 days after birth (McCutcheon & Marinelli, 2009). As said before the Prenatal, perinatal, childhood, and juvenile periods are considered early life.

Neurological and physiological effects of ELS

As mentioned in the introduction, stress during these sensitive periods (prenatal, postnatal, and early childhood) can have damaging consequences for the development of biological systems and behavior (Anda et al., 2006; Dawson et al., 2000). These effects range from increased chances to develop psychopathologies to a reduction of learning capacities and even effects involving the cardiovascular system.

Effects on psychopathology

Many studies have shown that ELS can lead to an increased risk for anxiety, mood, and personality disorders in adult life (Raymond et al., 2018). Childhood maltreatment survivors also show a higher prevalence of depression, substance abuse, eating disorders, suicidal symptoms, and psychosis as well as diminished cognitive functioning (Teicher & Samson, 2016). Post-traumatic stress disorder is also a common and chronic finding among maltreated youths (Morey et al., 2016). One study calculated that ELS is responsible for as much as 45% of all childhood-onset psychiatric disorders and 26-32% of late-onset disorders, making it the leading important preventable risk factor of psychopathologies like mental illness or substance abuse (Green et al., 2010; Teicher et al., 2016). A research review by Teicher and Samson showed that witnessing or being the victim of violence or verbal or sexual abuse has a significant effect on the development of specific brain regions involved in the processing and conveying of that aversive experience. These morphological alterations are seen in the anterior cingulate, dorsal lateral prefrontal and orbitofrontal cortex, corpus callosum, and hippocampus of victims of ELS, areas involved in a wide range of cognitive functions, some of which we will discuss below. They also found that maltreatment is associated with an enhanced response to threat in the amygdala and a diminished striatal response to anticipated reward, which will be discussed more in the paragraph on social behavior and emotional behavior (Teicher & Samson, 2016).

Effects on the hippocampus and memory capacities

As mentioned above ELS also affects the morphology of the hippocampus, which is heavily involved in the formation of new long-term memories. As to be expected this has a negative impact on one's memory and learning capacities. In mice, the study of Naninck et al. shows the effect ELS has on the developing brain, especially areas related to memory. Limiting the nesting and bedding material in early postnatal mice (2 to 9 days after birth) was shown to cause differences in the structure and function of the hippocampus (Naninck et al., 2015). These changes were seen, for instance in the dentate gyrus (DG) structure of the hippocampus. This structure is strongly associated with forming new episodic memories, among other important functions (Amaral et al., 2007). The mice used in the study had lasting reduced DG volumes (figure 2). They also showed reduced survival of neurons born during development in both sexes. Only in the males, a reduction was also seen in the survival of adult-born neurons, hindering their ability to form new memories and impairing their performance in memory and learning tasks (Naninck et al., 2015). Interestingly, in females this effect on memory and learning was less noticeable and the effects on neurogenesis were only seen during the early development (0-15 postnatal days). During adulthood (150 postnatal days), the females showed no lasting changes and less prominent cognitive impairments. This suggests that male individuals are affected differently by ELS than their female counterparts and might be more susceptible to certain negative effects of ELS (Naninck et al., 2015). I will discuss this suggested effect of sex on susceptibility to ELS more in the paragraph on factors involved in susceptibility.

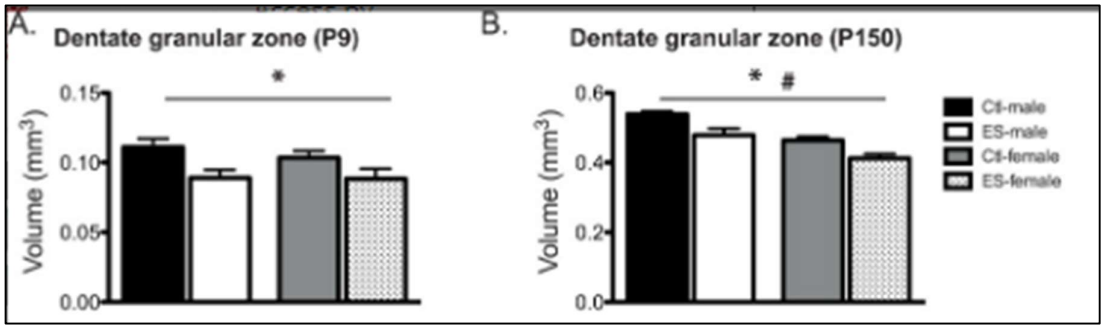

Figure 2. Volume of the granular zone is reduced and developmental neurogenesis is increased by chronic ES exposure. A: At P9, ES had caused a significant reduction in dentate granular zone volume (: main effect of condition, $F_{1,22} = 9.470$; P = 0.006), B: At P150, dentate granular zone volume was significantly reduced by exposure to ES (*: main effect of condition, F1,29 = 13.990 P < 0.001) and significantly different between males and females: (#: main effect of sex, F1,29 = 22.115; P = 0.001). (Naninck et al., 2015).*

These effects on the hippocampus and memory capacities are not exclusive to mice. In humans, Goodman, Freeman, and Chalmers found in their research review that ELS leads to a reduction in working memory capacity and phonological and visuospatial working memory task performance in test subjects (Goodman et al., 2019). Other studies have also shown the disruptive effect ELS has on hippocampal plasticity and long-term potentiation believed to cause cognitive and affective disorders and playing a role in memory decline (Cui et al., 2006; Foster, 1999).

Effects on the HPA-Axis

The HPA-axis, hypothalamic-pituitary-adrenal axis, is a key stress response system. It consists of a cascade of central and peripheral events resulting in the release of cortisol from the adrenal gland mediating the long-term effects of stress (Smith & Vale, 2006). Besides the stress response, the HPA-axis is involved in regulating the cardiovascular and metabolic systems, immune functions, behavior, and reproduction (Joseph & Whirledge, 2017). Maladaptation of the HPA-axis' functional maturation, as a result of chronic stress, may result in altered stress susceptibility in later life. The development of the HPA-axis and the regulatory brain regions takes place both pre- and postnatally and stress in those periods of early life can thus lead to maladaptation (Van Bodegom et al., 2017). In their review of studies about the causes of the ELS-induced alterations in the structural and functional development of the HPA-axis and its regulatory brain regions (amygdala, hippocampus, and prefrontal cortex) van Bodegom et al. found that multiple different forms of ELS typically result in hyper-reactivity of the HPA-axis in adulthood. This same hyper-reactivity is found in individuals suffering from major depression. They name increased corticotrophin-releasing hormone signaling and impaired glucocorticoid receptor-mediated negative feedback, which plays an important role in the regulation of the HPA-axis, as causes of this hyper-reactivity (Gjerstad et al., 2018; Van Bodegom et al., 2017). Several other studies also found hyper-reactivity of the HPA-axis as a result of ELS (Maniam et al., 2014; Tofoli et al., 2011). Interestingly, other studies suggest that ELS leads to HPA-axis hypo-reactivity instead (Gunnar et al., 2009; Puetz et al., 2017; Zhang et al., 2019). As

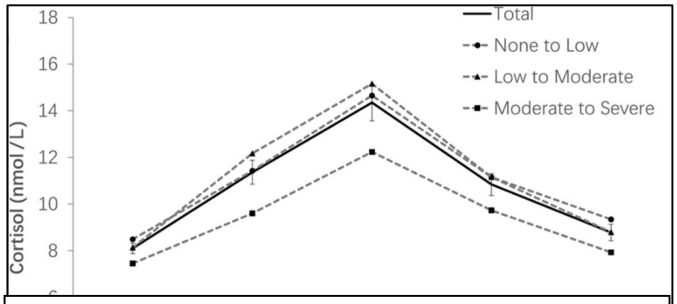

Figure 3. Cortisol (nmol/L) response pattern before and after the Trier Social Stress Test (TSST). The black line refers to the total. The grey lines refer to three subgroups according to the level of childhood trauma (Zhang et al., 2019).

seen in figure 3, Zhang et al. found that her subjects exposed to moderate to severe ELS had a lower baseline cortisol level and a blunted cortisol response after a Trier Social Stress Test. Looking into these conflicting results I found two studies addressing the issues and providing possible explanations. King et al. looked into the differences between elevated and blunted patterns of cortisol regulation in children and adolescents exposed to ELS. They concluded that the determining factor was age. Specifically, they found that in the subjects that were in early puberty ELS was associated with a blunted cortisol awakening response (a peak in cortisol levels roughly 30 minutes after waking). In subjects in later stages of puberty they found ELS to be associated with a heightened cortisol awakening response (King et al., 2017). Since the Van Bodegom, Maniam, and Tofoli studies all looked at the HPA reactivity in adults and the Gunnar and Puetz studies looked at children aged 10-12 and 10.6 ± 1.75 years respectively this explanation could explain some of the conflicting results. It does not however explain the results found by Zhang et al who looked at subjects aged 22.6 ± 1.8 years and found hyper-reactivity. A different explanation is provided by Goldman-Mellor et al. They describe that "adults exposed to early-life adversity have dysregulated cortisol reactivity trajectories, but that the pattern of those trajectories differs based on their history of psychological distress during adulthood" (Goldman-Mellor et al., 2012). They found in older ELS-exposed adults that those with a history of psychological distress during adulthood showed blunted cortisol responses and those without showed heightened responses compared to non-ELS-exposed adults (Goldman-Mellor et al., 2012).

Effects on brain connectivity and emotional stability

In their above-mentioned study, Puetz et al. also found that maltreated children showed significant reductions in global and local connectivity strength in the brain. These reductions were associated with the reductions in cortisol secretion and also with higher levels of internalizing and externalizing behaviors. The lower connectivity strength was seen especially in the ventromedial prefrontal cortex, an area of the brain associated with the regulation of our emotions. This suggests that childhood maltreatment can have an effect on the emotional stability of individuals that can last far beyond childhood (Puetz et al., 2017).

Effects on physical health

Besides the slightly more obvious neurological effects, ELS can also have lasting effects on the rest of the body. It has been shown to be associated with musculoskeletal and respiratory problems, cardiovascular disease, and gastrointestinal and metabolic disorders (Wegman & Stetler, 2009). Also, higher rates of inflammation, metabolic syndrome, arthritis, heart disease, cancer, and shortened telomeres, associated with lower life expectancy, are seen in survivors of childhood maltreatment (Teicher & Samson, 2016). These results show that ELS can have a profound effect on many aspects of the health of ELS survivors both mental and physical.

Effects of ELS on social and emotional behavior

The above-mentioned alterations in brain circuitry are reflected in various types of behavior such as social behavior, emotional behavior, reward processing, depression, and addiction.

Social behavior

When looking at problematic behavior two broad types of behavior can be distinguished, externalizing behavior and internalizing behavior. Externalizing behavior refers to lashing out at one's environment or at other people, symptoms being aggression, delinquent behavior, hyperactivity, and attention problems. Alternatively, internalizing behavior refers to taking your feelings out on yourself, showing

internally focused symptoms like anxiety, fear, depression, and social withdrawal (Willner et al., 2016). Numerous studies have shown that children exposed to ELS in the form of abuse or neglect show an increased risk of both internalizing and externalizing behavior later in life (Busso et al., 2017; Jaffee, 2017). ELS has been frequently linked to social withdrawal, difficulties in the regulation of emotions, sustaining social relationships, and other internalizing behaviors (Fareri & Tottenham, 2016). The difficulties in the regulation of emotions are discussed more extensively below. This effect on social behavior is seen in both animals and humans. For instance, studies on social behavior in rhesus monkeys and institutionalized humans have shown that infants who were not raised by their parents show less social behavior and have reduced performance in social cognitive tasks (Kraemer, 1997; Rutter et al., 2001). Turner et al. found similar results in a study in the sixties on chimpanzees. They concluded that animals that spent their first three years socially and perceptually deprived, in a covered bare crib without seeing or touching a caretaker, were prone to avoid social situations and contact. They were also less likely to mate (Turner et al., 1969). In rodents, it is also widely reported that maternal stressors can lead to increases in behaviors associated with anxiety, depression, and schizophrenia in humans and to deficits in social behavior, spatial learning, and memory (Weinstock, 2017).

Emotions

Recognition of emotions is also affected in several ways in maltreated youths. They are for instance less accurate in recognizing emotions when matching emotions in a story to pictures of someone expressing that emotion (Pollak et al., 2000). When shown pictures of prototypical emotions they are also less likely to correctly name which emotion is being expressed (During & McMahon, 1991). These results reveal that maltreatment can leave youths with a deficit in emotion recognition, making it harder to react appropriately to the emotions of other people, reducing their chances of successful social interactions. Predicting how other people will react to their negative reactions might also be more difficult because of this, further reducing the chances of successful social interactions (Jaffee, 2017).

Reward processing and Depression

As mentioned in the previous paragraph, Teicher and Samson found a diminished striatal response to anticipated reward in victims of ELS such as witnessing or being the recipient of violence or verbal or sexual abuse (Teicher & Samson, 2016). A review by Novick et al. also found that ELS leads to a deficit in reward responsiveness functions associated with the ventral striatum and that this effect is strongest when the stress is experienced early in development, for instance during the first 2 years (Novick et al., 2018). Many other studies also conclude that there is a negative association between ELS and reward response later in life (Birn et al., 2017; Boecker et al., 2014; Herzberg & Gunnar, 2020; Matthews & Robbins, 2003). In a review by McCrory et al. of studies on children and adolescents exposed to various forms of early neglect and/or maltreatment and the effect this had on, among other things, their ability to regulate their emotions it was found that the subjects exposed to ELS showed a blunted neural response to (anticipation of) rewards, especially in the ventral striatum. The researchers even concluded that the observed patterns are associated with symptoms seen in cases of depression (McCrory et al., 2017). And indeed it is well known that stress is a risk factor for depression, especially stress during childhood (Heim et al., 2010). This makes ELS very relevant to society today, as depression is a very common and major public health concern. According to a report published by the World Health Organization (WHO), depression is a leading cause of disability and suicide worldwide, with an estimated 4.4% of the world's population suffering from it, which is roughly 322 million people (figure 4) (World Health Organization; 2017). Matthew and Robbins found in their study on rats that neonatal (between 5 and 20 days after birth) maternal separation leads to anhedonic

behavior resembling human depressive psychopathology (Matthews & Robbins, 2003). These results and the depression-associated neural patterns found by McCrory, as described above, indeed suggest a strong association between ELS and depression. In her review of the relationship between maltreatment and mental health problems, Jaffee tries to explain the mechanisms behind this association. She found that studies show that individuals that were maltreated in their childhood are less responsive to reward, especially the anticipation of it, when compared to non-maltreated peers. When comparing their neural circuitry involved with (anticipation of) reward, a difference can be seen in the activation in maltreated individuals. Jaffee concludes that this reduced responsivity combined with a deficit in their ability to learn from positive experiences can partly explain the increased risk of depression in adults with a history of maltreatment (Jaffee, 2017). Since depression is an important mental health problem in the world and ELS seems to be a significant contributor, more research into this association and possible methods of prevention or treatment could be very beneficial.

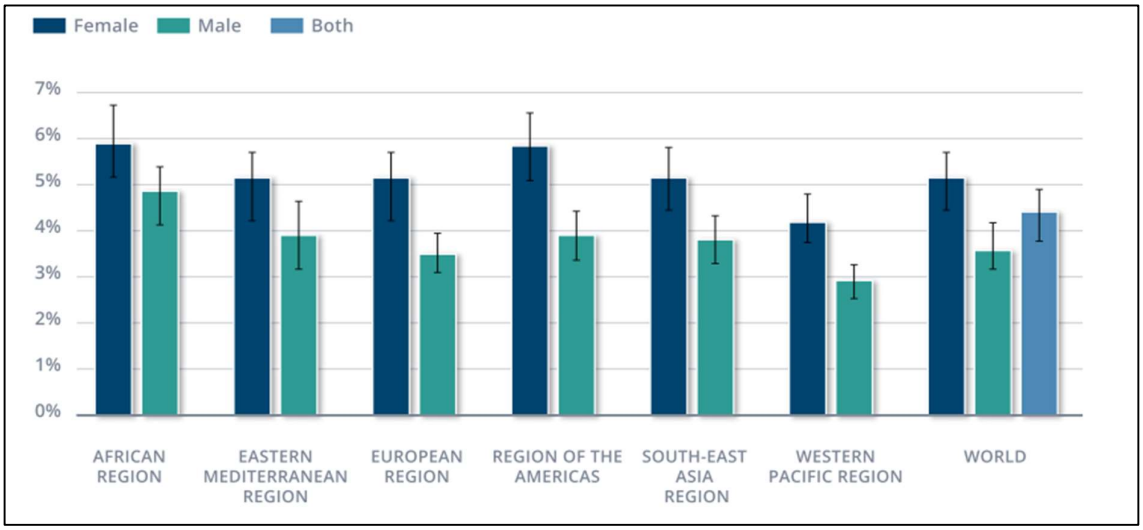

Figure 4. Prevalence of anxiety disorders (% of population), by WHO Region (World Health Organization, 2017).

Addiction

Lastly, ELS has a noticeable effect on the likelihood of adults becoming addicted during their adult life. As mentioned above ELS is responsible for 45% of all childhood-onset psychiatric disorders, making it the most important preventable risk factor of psychopathologies like mental illness or substance abuse (Green et al., 2010; Teicher et al., 2016). In a review, Mary-anne Enoch concluded that maltreatment and stressful life events in early childhood were associated with alcohol and drug dependence in early adulthood. She found that a blunted response to stress and reward as a result of ELS may indicate vulnerability to addiction (Enoch, 2011). She also mentions studies suggesting that this effect can be worsened or prevented by genetic and environmental factors, which we will discuss further in the paragraph on prevention and treatment. Gondré-lewis et al. describe the neurological changes behind this increased vulnerability to addiction in their study. They found that, in mice, maternal separation led to increased impulsivity in the test subjects, which is a key risk factor for excessive alcohol drinking. They also found evidence that impulsivity and binge drinking could be effectively reversed through medication. They used the Corticotrophin-releasing factor 1 (CRF1) receptor antagonist antalarmin and the novel $GABA_A$ a2 subunit ligand 3- PBC to manipulate the CRF and GABA signaling in the central amygdala and medial prefrontal cortex and found that this was effective in reversing both impulsivity and binge drinking. These results suggest that alteration and subsequent malfunctioning of the CRF

and GABA receptors caused by ELS could be the cause of this vulnerability to addiction and show a potential method of treatment (Gondré-Lewis et al., 2016).

The important factors involved in individual differences in susceptibility to negative consequences of ELS

Even though research has clearly shown the negative consequences ELS can have, among those who experience ELS, even in severe forms, a large portion of children never develop psychopathologies (Enoch, 2011). So which factors are involved in determining the susceptibility to the negative consequences of ELS? The factors seem to differ depending on the negative effects being researched. For instance, in a review of studies about the underlying causes of the ELS-induced alterations in the development of the HPA-axis and its key external regulators in both humans and animals several factors were found that appeared to strongly affect the effect of ELS. These factors were the developmental time window in which the ELS took place, the sex of the offspring, and in which developmental time window the effects were assessed (Van Bodegom et al., 2017). However, in her study on the role of ELS as a predictor for alcohol and drug dependence, as mentioned in the previous chapter, Enoch concludes that in this case the gene-environment interactions and relationships with family and peers are important factors leading to resilience instead (Enoch, 2011). Sex seems to be an influential factor with many studies having found results indicating that males are less resilient to the effects of ELS (Loi et al., 2017; Naninck et al., 2015; Schroeder et al., 2013). For instance, as mentioned in the chapter on physiological effects Naninck et al. found in their study that only in the male mice there was a reduction in the survival of adult-born neurons and their ability to form new memories. They also showed impaired performance in both memory and learning tasks. These changes were less prominent in the female test subjects. The effects on neurogenesis even disappeared completely in the females after development, showing no lasting changes. These results give a strong indication that females are indeed less susceptible to certain negative effects of ELS (Naninck et al., 2015). An extensive literature review by Loi et al. draws a similar conclusion. Female and male animals that suffered from ELS showed similar results in anxiety-related tasks but in hippocampus-dependent learning tasks the females showed a lack of structural and behavioral differences. They conclude that their results agree with recent findings in studies on humans that females appear to be relatively resilient to structural and hippocampal effects of maltreatment, but not to anxiety and mood-related effects (Loi et al., 2017). Even in the case of prenatal stress, the sex of the subject can have a significant effect. In a study on the behavioral effects of prenatal stress on two different strains of rats (WKY and control Wistar rats). In the control rats, prenatal stress led to weight loss, hyperactivity, and an increase in risk-taking behavior. This was again most notable in the male rats (Schroeder et al., 2013). Clearly, several factors are at play to determine the resilience of children to ELS, most prominent of which is the sex of the victim. Unfortunately, most of these factors are outside of the control of the child or anyone else and are thus not viable methods of prevention.

Preventability of the negative effects of ELS

ELS can have a devastating effect on the mental and physical health of those who have experienced it. The literature on the effects of adversity on children in institutional, foster care, and normal settings shows that interventions, consisting of training and support for the caregivers and child, were successful in attenuating some of the effects of ELS, most notably the effects on brain development. Timing is often mentioned as a key factor in determining the effectiveness of the intervention, the

earlier the better. Nurturing traits in the parents or caregivers also seem to have a positive effect on the intervention (Purewal Boparai et al., 2018). Timing does indeed seem to be an important factor at play. Dawson et al. also note in their review of literature on the effects of early experience on child development and psychopathology that prevention and early intervention methods are the most effective in the early years of development and should, if possible, begin during the prenatal and infant-toddler stage. The promotion of optimal prenatal and toddler development can minimize or even avoid some or all of the negative long-term consequences of early experiences (Dawson et al., 2000). Of course, in most cases, this is simply not possible, especially when the ELS takes place in a later life stage. But besides coaching, what are other potential methods of intervention? In their study, Morley-fletcher et al. looked at the degree of reversibility of the effects of prenatal stress on social play and HPA hyperreactivity. They found that the reduction in social play behavior and increased reactivity of the HPA axis shown by the stressed rodents was noticeably reduced by environmental enrichment in their adolescence. This enrichment consisted of larger cages and objects to play, explore and hide. Their results showed that giving rodents an enriched environment could effectively treat the negative effects of prenatal stress on social behavior and the HPA-axis (Morley-Fletcher et al., 2003). Other studies have found similar results, one stating that an enriched environment completely overcame the effects of postnatal stress in rats like impaired spatial learning, memory, and increased depressive-like behavior (Cui et al., 2006). These findings suggest that the negative effects of stress in different stages of early life are reversible/treatable by applying the right stimuli in later life stages. Further research into this and whether or not a similar approach could work in humans is needed though. Another study found that presenting rats with their maternal odor reversed social behavior deficits and depressive-like behavior as a result of abuse during childhood. Interestingly, this was even the case when it was the mother that was abusive (Raineki et al., 2015). Whether this could be the case in humans has to this day not been researched. Something that was found in humans is, as discussed in the paragraph on neurological and physiological effects, the finding that CRF and GABA signaling in the central amygdala and medial prefrontal cortex was effective in reversing both impulsivity and binge drinking as a result of ELS (Gondré-Lewis et al., 2016). These results are promising and suggest that a potential treatment for alcoholism and possibly other addictions through medication could become a possibility. To summarize, there is evidence that (some of) the negative effects of ELS can be prevented or reversed. The efficacy of the prevention is determined by multiple factors. Starting the prevention as early as possible seems to be a crucial factor. The evidence found so far is promising, however a lot more research is still needed.

Conclusion

This paper aimed to provide a review of some of the literature on Early life stress (ELS) and in particular the long-term effects it has on the brain and behavior of those who suffer from it. Through this paper, I hope to show the readers that ELS and child abuse are major health issues that can have an impact lasting long after childhood. As discussed above, there are many studies about ELS that have found significant negative consequences of it. To summarize, stress during the early years of development, the pre- or postnatal and juvenile periods, has noticeable effects on the development of the brain. It leads to an increased risk for psychiatric disorders, smaller hippocampi, and hyperreactive ventral striatum resulting in memory deficits, cognitive defects, higher chances of addiction, and even of various physical health problems. It also has a significant effect on behavior such as increased problematic behavior and reduced social behavior, deficits in emotion recognition, and increased chances of depression. Females seem to be more resilient to some of these negative effects, like the structural, behavioral and memory effects but not to the anxiety and mood related effects. Prevention

and treatment have shown promising effects, especially when implemented as early on as possible. Even though, much research still needs to be done into prevention and treatment of these effects especially treatment implemented during later life stages like adolescence or adulthood.

In conclusion, I believe the literature surrounding ELS shows that ELS has a serious lasting physical, neurological, and mental effect on its victims. Given the prevalence of child maltreatment as discussed in the introduction, ELS should be considered a serious health problem. As of yet, there is still a lot unknown when it comes to potential treatments and preventions. More research into this matter could be very beneficial to reducing the prevalence of some of the most prevalent physical and mental health problems in the world.

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