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Persistent biological alterations after child maltreatment: is there any hope to counteract it?

Childhood maltreatment - including neglect and psychological, physical, and sexual abuse - has well-documented long-term psychological and biological effects. Individuals exposed to maltreatment are at higher risk of antisocial behavior, substance addiction, dysfunctional parenting, and stress-related disorders such as depression and PTSD. Maltreatment can also cause lasting biological changes, including altered stress hormones, inflammation, and persistent changes in brain structure and function. The article explores whether the timing of maltreatment affects outcomes, whether these effects persist or are transmitted across generations, and whether they can be reversed through interventions, with a specific focus on brain-related consequences.

The long-lasting psychological consequences of various forms of childhood maltreatment, including neglect, psychological, physical and sexual abuse, are well documented. Indeed, individuals who have experienced maltreatment in childhood often present a wide range of alterations once adults, such as an increased risk

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of antisocial behaviour and of dysfunctional parenting, a heightened likelihood of developing addictions (to nicotine, cannabis, alcohol, and even «hard» drugs), and a higher incidence of stress-related disorders such as major depression and post-traumatic stress disorder, to name just a few. Furthermore, child maltreatment might induce enduring biological modifications, including altered stress hormone levels, presence of inflammatory markers, and changes in brain morphology and function persisting up to adulthood. This rises several questions. For example: does maltreatment in early childhood produce the same outcomes as maltreatment during adolescence? Do these effects persist over time, fade with age, or might even be passed on to the next generation. And, to introduce a note of hope - are these biological consequences reversible? In other words, can interventions attenuate or counteract them? These are some of the crucial questions this article will seek to address, drawing on scientific studies published in recent years. Given the scope of the topic, our focus will be limited to the brain-related consequences of childhood maltreatment.

The brain can be assessed in different way and scales: one can measure the volume of different areas or focus on its functioning for example. To start with, we focus on the size of different brain areas. This can be measured using various techniques, such as in vivo brain imaging methods like Magnetic Resonance Imaging (MRI). The advantage of these approaches is that they have no effect on the brain itself and can therefore be used in living subjects, including measurements that can be repeated over an individual's lifetime, allowing researchers to track developmental trajectories. These methods are considered non-invasive, as they do not harm the participant, whose only requirement is to undergo an MRI scan.

Most studies recruit groups of adults who either have or have not experienced childhood maltreatment. These measurements are particularly informative because they shed light on whether alterations observed in children persist into adulthood. To determine whether participants have experienced maltreatment, researchers often use retrospective questionnaires assessing childhood experiences.

What do such studies reveal? Some have exa-

mined the morphology of brain regions involved in processing sensory information. When a child experiences maltreatment, information regarding the traumatic event reaches the brain through sensory channels: hearing (in cases of verbal abuse), vision (when witnessing violence), or the genital area (in cases of sexual abuse). Researchers have therefore investigated whether sensory processing areas of the brain are altered, and whether these alterations are linked to the specific type of maltreatment experienced (for review, see Teicher M.H. et al., 2016). For example, one study examined the auditory cortex volume in individuals exposed to psychological abuse such as humiliation – a form of verbal maltreatment. As young adults, these individuals showed increased grey matter volume in part of the auditory cortex. Moreover, the size of the left arcuate fasciculus – a bundle of nerve fibers connecting Broca's area (language production) to Wernicke's area (language comprehension) – was reduced, which may be associated with difficulties in understanding language. In another study, witnessing interparental violence was linked to a reduction in the volume of certain visual cortical areas and in a fiber tract connecting the visual cortex to regions involved in processing emotional information. These effects were especially pronounced when exposure occurred between the ages of 7 and 13, suggesting a possible window of heightened sensitivity. Finally, research on sexual abuse has shown that, in adulthood, survivors exhibited reduced volume in both the visual cortex and in a region of the cortex responsible for body representation - specifically, the subregion linked to the representation of the genital area. In summary, alterations in sensory brain areas tend to be specific to the sensory modality involved in the maltreatment. Children exposed to psychological abuse displayed changes in auditory and language-related areas but not in visual or somatosensory cortices; those who suffered sexual abuse showed changes in somatosensory and visual regions but not in auditory areas; and those who witnessed violence exhibited changes in visual but not auditory or somatosensory regions. These findings point to a striking sensory-specific pattern of brain alterations following childhood maltreatment.

Once information is processed by the sensory



areas, it is relayed in parallel to three other brain regions involved respectively in emotions, memory, and higher cognitive functions: the amygdala, the hippocampus, and the prefrontal cortex. Do adults who experienced childhood maltreatment show alterations in the volume of these regions? Once again, findings depend on the type of maltreatment (for a review, see Teicher M.H. et al., 2016). A reduction in amygdala volume has been reported in adults who experienced physical abuse as well as neglect during childhood. However, similar changes are also observed in children exposed to other forms of early adversity, such as poverty. The same applies to the hippocampus, whose volume is reduced not only after physical abuse and neglect, but also in cases of poverty and sexual abuse - particularly when these occur before the age of 13. Finally, reduced prefrontal cortex volume has been observed following physical abuse, neglect, and sexual abuse. Overall, different forms of maltreatment appear to induce volume alterations in brain regions involved in emotion regulation, memory, and decision-making. It is also noteworthy that poverty - while not a form of maltreatment - produces similar effects, and when combined with maltreatment, leads to even greater alterations.

A further question is whether these volume changes are linked to cellular-level modifications in the brain regions concerned. Research (Murthy S. and Gould E., 2020) indicates that (a) childhood maltreatment affects neuronal populations in several brain regions, particularly the prefrontal cortex, amygdala, hippocampus, and areas within the brain's reward circuitry (including the nucleus accumbens and ventral tegmental area); and (b) these cellular effects vary depending on the region. In the prefrontal cortex, the number and size of neurons are generally reduced, whereas the opposite pattern is seen in the amygdala. Since traumatic memories engage these networks, such structural changes may help explain why these memories become so deeply embedded.

As we have seen, childhood maltreatment alters the morphology of multiple brain regions - but what about brain function? Research has focused mainly on two areas: the amygdala and the striatum, the latter being involved in reward processing and the anticipation of pleasurable events. While

the volume of these two regions is not consistently altered by maltreatment, their activity is strongly affected, a finding replicated across numerous studies. The amygdala shows markedly increased activation in maltreatment survivors, particularly when they are shown images of human faces expressing emotions (Hein T.C. and Monk C.S., 2016). This hyperactivity likely reflects an enhanced ability to detect threats: danger is identified more rapidly in individuals with a maltreatment history, regardless of the specific type of abuse experienced. Conversely, striatal activity is reduced (Novick A.M. et al., 2018) both during the experience of pleasure and when anticipating rewarding events.

As we have seen, childhood maltreatment leads to cognitive and emotional consequences that can persist throughout life and are associated with brain alterations. However, not all individuals respond to maltreatment in the same way: some are highly vulnerable and develop severe impairments, while others are resilient, meaning that despite their history of maltreatment, they maintain cognitive and brain functioning within the normal range. Some even experience what is known as «post-traumatic growth», whereby adversity fosters positive changes such as increased optimism, improved emotional regulation, greater empathy, and enhanced compassion toward others. Along similar lines, the «match-mismatch» or «stress inoculation» theory proposes that low levels of stress, experienced at certain points in life (for example, during childhood), can later protect an individual from the harmful effects of more severe stress - functioning somewhat like a vaccine. Whatever the framework, the question arises: what factors support these adaptive outcomes? Such factors may be psychosocial or biological. Studies have shown that resilience or post-traumatic growth can be promoted by social support from caregivers, friendships during adolescence, and engagement in spirituality.

Are biological factors involved in resilience as well? The answer is clearly yes. Some factors directly induce resilience or vulnerability because they are present before exposure to adversity; these are termed induction factors, as they are causally involved. Others are not causally linked but serve as markers associated with resilience or vulnerability.

One of the primary induction factors is genetic. In the face of adversity, certain individuals carry protective genetic variants that buffer against harmful consequences, while others have variants that increase risk. One landmark investigation into this topic comes from the Dunedin Cohort in New Zealand - a longitudinal study of 1,037 individuals born between 1972 and 1973, followed from birth into adulthood for physical development, mental health, behavioral traits, genetic makeup, family environment, and life events. This cohort remains active today, with participants now over 50 years old. Data on childhood maltreatment were collected when participants were between 3 and 11 years old. The first influential study, published in 2002 (Caspi A. et al., 2002) when participants were young adults, examined the link between variants of the Monoamine Oxidase A (MAO-A) gene and vulnerability or resilience to childhood maltreatment. MAO-A is an enzyme that breaks down neurotransmitters implicated in conditions such as depression, post-traumatic stress disorder, and addiction. Depending on the genetic variant, these neurotransmitters are degraded more or less efficiently. Findings showed that adults who had experienced childhood maltreatment and carried the low-activity MAO-A variant exhibited antisocial behavior and heightened aggressiveness, whereas those with the high-activity variant did not show such antisocial traits, even when maltreated as children. This demonstrates that the genetic factor conferred resilience to the effects of maltreatment. Notably, individuals carrying the «vulnerability» variant but not exposed to maltreatment did not develop antisocial behaviors-highlighting a gene \times environment interaction. Subsequent studies have identified additional protective genetic factors. Caution is warranted, however, with research focusing on single genetic variants: such studies magnify the role of one factor while overlooking the complex network of interacting influences. Nevertheless, despite these limitations, they provide valuable insights.

Another question that arises at this stage is whether there are brain regions whose volume or functional activity could protect against the effects of maltreatment or serve as markers of resilience. Studies investigating brain regions whose volume or function might play a role in inducing

resilience are particularly difficult to conduct in young children, as they would require MRI data collected prior to the experience of maltreatment – an impossible prerequisite. However, there are a few studies on brain markers of resilience and vulnerability – that is, on the neural «signature» of resilience/vulnerability. These studies are easier to carry out because they can be based on comparing the brains of individuals who experienced childhood maltreatment but who are either vulnerable or resilient.

Overall, findings show that: (a) resilience is an active process, meaning it involves brain changes that help an individual adapt optimally to adverse circumstances; and (b) the neural circuits of resilience and vulnerability are not simple mirror images of each other, as each is associated with its own specific brain changes. The most significant human study to date (Burt K.B. et al., 2016), involving 1,870 adolescents, found that resilient functioning was associated with a larger volume in part of the prefrontal cortex. This structural feature may support improved cognitive performance, better academic outcomes, and enhanced emotional regulation. The latter could facilitate more effective adjustment to stressful situations in adulthood, thereby offering protection against certain stress-related psychopathologies, such as depression, post-traumatic stress disorder, and addiction.

In conclusion, biological factors can either induce resilience or vulnerability to childhood maltreatment – most notably genetic factors – or be associated with these states. In the latter case, they reflect active changes that enable the individual to adapt to their environment, either in an adaptive or maladaptive way.

It has been observed that the consequences of childhood maltreatment persist over the long term, in that not only do survivors show alterations that endure into adulthood, but these psychological and psychopathological consequences can also be found in subsequent generation(s). Indeed, the descendants of individuals who survived childhood maltreatment often display psychopathological alterations similar to those of maltreatment victims, even though they themselves were not subjected to abuse as children. One possible explanation is that this occurs through psychological mechani-



sms, particularly attachment deficits: the idea here is that maltreatment induces changes in survivors' parenting behavior, such that when they have children, their behavior does not foster attachment – even if it is not abusive. However, this hypothesis remains far from universally accepted.

A further question is whether descendants of maltreatment survivors who themselves were not abused also show biological alterations, in addition to the psychological effects just described. Studies suggest that this is indeed the case: certain behavioral and biological alterations observed in individuals exposed to maltreatment and violence during childhood are transmitted to the next generations – that is, to the children and grandchildren of these individuals. For example, in the case of stress hormones, research has shown a correlation between children's cortisol levels (measured in hair samples) and their mothers' maltreatment scores: the higher the mother's maltreatment score, the lower the offspring's cortisol level (Broeks C.W. et al., 2023). Other studies have examined brain morphology using MRI to compare the brain anatomy of children whose parents were or were not maltreated, revealing differences in prefrontal cortex connectivity (Lugo-Candelas C. et al., 2023).

Human studies, however, face significant limitations. For ethical reasons, it is not permissible to induce maltreatment in humans to study its effects, and the generational interval of 20–30 years makes it impossible to track the transmission of biological traits over multiple generations within a feasible research timeframe, especially given that scientific funding is usually limited to short periods. Animal experiments overcome these constraints: since mice reach sexual maturity at about seven weeks, researchers can examine the effects of transmitting a biological alteration across multiple generations in a relatively short time. Some teams have developed protocols to address this question – for example, applying social stress to «infant» mice, then tracking outcomes over 4–6 generations. Such studies (van Steenwyk et al., 2018) have shown behavioral sequelae transmitted across five generations, and in some traits, up to six. It is unlikely that these effects were due to altered parenting behavior, as the transmission occurred via fathers and, under laboratory conditions, mouse pups are almost entirely cared for by

mothers, with minimal contact with fathers. This effectively rules out dysfunctional parenting as the mechanism of transmission. On the biological side, research has focused on DNA methylation as a potential mechanism. Indeed, methylation changes in various genes have been observed across multiple generations.

Another mechanism involves a fascinating molecule: oxytocin. This substance is linked to attachment, empathy, social memory, and parental behaviors. Some popular science authors have sensationally labeled it the «love hormone», though this is a highly simplified, reductive, and inaccurate description. What is clear is that oxytocin levels are markedly reduced in adults who survived childhood maltreatment. Oxytocin acts by binding to oxytocin receptors, and research has shown that DNA methylation of the genes encoding these receptors is altered in survivors (Gouin J.P. et al., 2017), indirectly reducing receptor expression. Interestingly, this methylation effect is not only found in survivors themselves but also in their children – who were never directly maltreated. This represents yet another example of the transgenerational transmission of a biological marker of childhood abuse.

The body of work on this subject is dizzying. One cannot help but think of violent family environments, or war zones where children are often victims, and how cycles of violence can perpetuate themselves from generation to generation – threatening the social cohesion of communities in an endless loop.

As we have seen, childhood maltreatment can produce enduring psychopathological and behavioral consequences, as well as biological alterations that last into adulthood and, in some cases, are passed on to subsequent generations. At first glance, this might seem hopeless. Yet there is reason for optimism: research also shows that certain interventions – such as placement in foster families, adoption, or specific psychotherapies – can mitigate the behavioral and cognitive impacts of maltreatment. This raises an important question: do such interventions also reduce or counteract the biological consequences? Several studies have addressed this point.

One particularly striking investigation, which attracted considerable public attention, was con-

ducted in Romania on children subjected to extreme neglect. From birth or early infancy, these children were placed in institutions that turned out to be profoundly abusive. In the early 1990s, thousands were found staring blankly, confined to barred cribs. They had suffered severe emotional deprivation, growing up in orphanages without ever meeting the warm, attentive gaze of an adult. Lacking the necessary sensory, emotional, and social stimulation for healthy development, they displayed significant delays across multiple domains: language, motor skills, cognition, and emotional growth. Attachment patterns were a focal point of this research. In a typical attachment assessment, a young child plays with their mother in a room, shows distress when she leaves, and seeks comfort when she returns – hallmarks of secure attachment. By contrast, the institutionalized Romanian children almost never exhibited normal patterns. Many displayed «insecure-avoidant» attachment, marked by emotional detachment; others had «insecure-ambivalent» attachment, characterized by instability; and many showed disorganized attachment, with contradictory behaviors. These findings were widely publicized, as the images of these children were deeply shocking. Some eventually found placement in nurturing foster families, but many did not. Research was conducted on a cohort of children as part of a project called the Bucharest Early Intervention Project (BEIP). In this study, researchers recruited 136 children aged between 6 and 31 months. Some of them had been living in Romanian orphanages since infancy, while others had been placed in foster care. These two groups were compared with children who had never been institutionalized (the control group). Several aspects of the children's development were assessed through tests, including attachment style, cognitive functions, and mental health. Brain development was also evaluated using neuroimaging. Because these measurements were repeated over time, researchers were able to track developmental trajectories and assess the impact of a nurturing foster family on these trajectories. The findings showed that placement in foster care could reverse some of the cognitive impairments – measured through IQ – as well as antisocial behaviors and attachment disorders. The effects on IQ and attachment were particularly strong,

but they depended on the child's age at placement. Children placed before the age of two almost fully caught up, whereas those placed later only partially recovered. The degree of recovery was closely linked to age at placement: the later the placement, the less recovery occurred (Humphrey K.L. et al., 2022). This suggests the existence of a «critical period» during which social relationships are especially crucial. However, because beneficial effects were still observed even with later interventions – albeit to a lesser extent – the study indicates that recovery is always possible and it is never too late. When the children were between 8 and 11 years old, MRI scans were conducted (Almas A.N. et al., 2012). These revealed that children who had always lived in institutions had a marked reduction in cortical grey matter volume compared with controls, while institutionalized children placed in foster care had intermediate volumes. At age 16, EEG recordings measured brain wave patterns. For some brain rhythms, foster care children had recovered fully; for others, the recovery was only partial (Debnath R. et al., 2019). Thus, foster care not only supported emotional and cognitive recovery but also promoted brain-level recovery. This aligns with the fact that young children's brains are highly malleable, making recovery easier.

These results had a major impact on the scientific community, reinforcing the idea that affection and human interaction in childhood are not luxuries but fundamental needs – just as essential as food. Taken together, these findings deliver a dual message: children's brains and behaviors have a remarkable capacity for recovery when placed in supportive conditions early in life, yet certain scars – especially biological ones – can endure. The Romanian orphanage case stands as both a testament to resilience and a powerful reminder of the profound, lasting costs of early deprivation.

Other research has explored different forms of intervention, such as psychotherapy. There are several types, and for example, trauma-focused cognitive-behavioral therapy is known to be effective in treating post-traumatic stress disorder, including in survivors of childhood maltreatment. A recent study looked not only at the improvement of symptoms after treatment but also at brain changes (Gonzalez-Alemay E. et al., 2024). This research was conducted not in adults but in children

aged 7 to 12 years, since effective therapies are available for this age group. The study found that grey matter alterations in the brain caused by maltreatment were reversed by therapy—particularly in specific brain regions involved in emotion regulation, memory consolidation, attention, processing of pleasurable experiences, motor coordination, and self-representation. Given the functions of these brain regions, it is reasonable to suggest a causal relationship between the normalization of brain anatomy and the therapeutic benefits.

Another recent study (Winter A. et al., 2023) examined the beneficial effects of social support on brain connectivity. As seen earlier, survivors of childhood maltreatment often show disrupted patterns of connections between brain regions. It is also well established that perceiving strong social support from one's environment (family, friends, colleagues, neighbors etc.) can lessen the psychological and behavioral consequences of maltreatment. This raises the question of whether perceived strong social support could also mitigate brain connectivity disruptions caused by maltreatment. The study showed that this is indeed the case: social support not only has a direct positive effect, but it also reduces the brain's physical connectivity alterations seen in adult survivors especially in frontal and temporal areas, which are key for cognition and emotion. This finding underlines the importance of providing strong support to survivors of childhood maltreatment.

The various studies described in this article show that childhood maltreatment can lead to long-lasting brain effects in adulthood, which may even be passed on to the next generation. However, it is essential not to adopt a reductionist interpretation of these findings. Despite the presence of brain alterations, some individuals go on to lead remarkable lives. One well-known example is that of American neuroscientist James Fallon, who discovered through neuroimaging that he had reduced activity in his prefrontal cortex a pattern typically seen in psychopaths. Yet despite this brain difference, he displayed entirely normal behavior. His explanation: the exceptionally nurturing maternal care he received in childhood had protected him. This is a striking illustration of the profound importance of relational and environmental context.

SUMMARY

Il maltrattamento infantile – inclusa trascuratezza e abuso psicologico, fisico e sessuale – ha effetti psicologici e biologici a lungo termine ampiamente documentati. Le persone che hanno subito maltrattamenti sono maggiormente a rischio di sviluppare comportamenti antisociali, dipendenze da sostanze, genitorialità disfunzionale e disturbi legati allo stress, come la depressione e il disturbo da stress post-traumatico. Il maltrattamento può inoltre provocare cambiamenti biologici duraturi, tra cui alterazioni degli ormoni dello stress, processi infiammatori e modifiche persistenti della struttura e del funzionamento del cervello. L'articolo analizza se il momento in cui avviene il maltrattamento influenzi gli esiti, se tali effetti persistano nel tempo o possano essere trasmessi alle generazioni successive e se possano essere reversibili attraverso interventi mirati, concentrandosi in particolare sulle conseguenze a livello cerebrale.

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