How trauma-induced epigenetic changes mediate the link between early-life adversity and the development of anxiety, and their implications for treatment

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Abstract

This paper examines how early-life exposure to severely unsafe environments, including war, chronic violence, and instability, shapes the developing brain through the interaction of environmental stress, genetic susceptibility, and epigenetic regulation. It focuses on fear and anxiety as outcomes of altered neural circuitry, especially within the amygdala, hippocampus, prefrontal cortex, and stress-related neurotransmitter systems such as glutamate, norepinephrine, and dopamine. The paper argues that toxic stress during periods of high neuroplasticity can modify the expression of genes involved in the HPA axis, including FKBP5, leading to long-term changes in emotion processing and stress regulation. These changes may increase the risk of anxiety and trauma-related psychopathology in adolescence and adulthood. At the same time, the paper highlights the potential of safe, enriched, and trauma-informed environments, together with therapeutic interventions, to support fear extinction, restore healthier neurobiological functioning, and promote resilience.

Methodology

The methodology for this paper was based on a qualitative literature review and guided exploration of existing educational materials. During my Polygence pod sessions, I used established Canva presentations from the topic “Neuroscience of Emotions: How internal states are generated and shaped” as a structured framework for organizing key concepts. To deepen and verify my understanding, I also consulted a range of scientific articles, the book “Behave” by Robert Sapolsky, and “Brain Facts”, which my mentor Rahul Patel provided as a useful source in our shared documents for the pod. These materials were used to compare perspectives, identify recurring themes, and build an interdisciplinary understanding of how emotional states emerge from interactions between neural, genetic, and environmental factors. This approach allowed me to synthesize scientific evidence into a coherent discussion of fear, stress, and neurodevelopment.

Lastly, generative AI tools were used to assist in designing some of the causal and conceptual diagrams in this paper. Specifically, “Biorender” as well as “Figure Lab” were used on July 30th and 31st 2026 to generate initial diagram layouts from text prompts. All scientific content, variable selection, causal directions, and interpretations were determined by the author. The AI was not used to generate or analyze empirical data.

Introduction

The question of how complex the human brain is can generally be answered by means with the intricate neural and synaptic network that allows fast and effective communication but shouldn’t only be. Since the brain doesn’t function within a vacuum. Human beings live, breathe, create and replicate themselves within environments they adapt to. This poses a crucial parallel to be considered in this
process as the brain mechanisms couldn’t function without initial stimuli, without a surface on which to project the expressions of behaviour or emotions.

An important pillar of the environmental interaction of the human organism can also be made out on the genetic level which plays an important role in examining how the brains develop depending on the environment. Epigenetics serves as the critical biological mediator bridging genetic vulnerability, environmental quality, and neurodevelopmental trajectories. It acts as an biochemical interface where experiential inputs regulate gene expression without altering the underlying DNA sequence. The fact is that prolonged exposure to specific stimuli, for example toxic stress, triggers epigenetic modifications that permanently alter the molecular architecture of the brain.

While learning about the concept and following the global news I made the observation that many children living under fragile conditions are constantly exposed to those aversive impulses and structures.

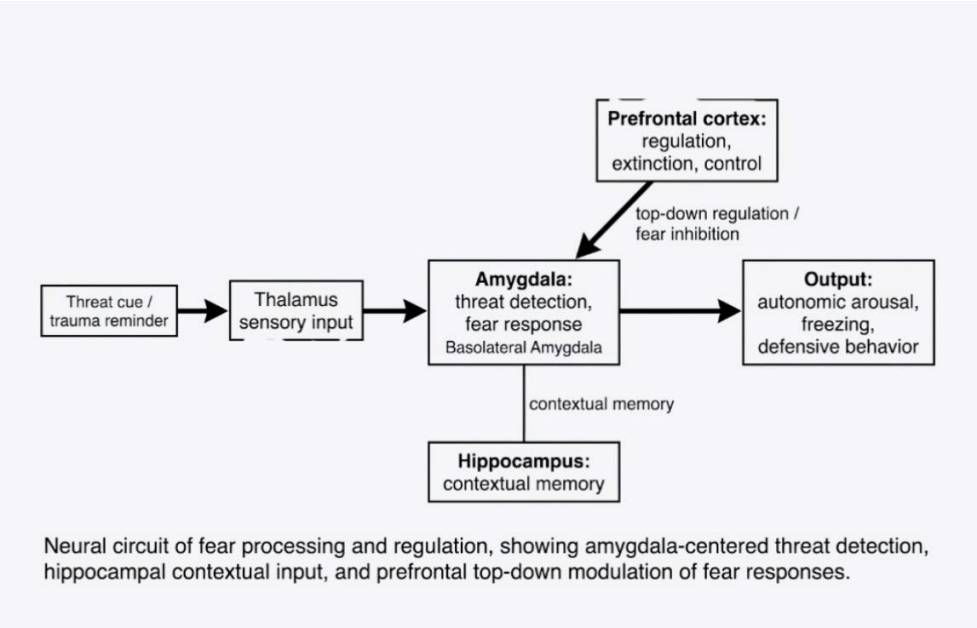
This was the premise of the abstraction I constructed over the course of working on this research paper. I wished to examine in more detail how environmental, genetic and neural factors interact with and influence each other to create a continuous living experience. As this

living experience differs for all individuals (in the sense of emotional presence, brain development, neuroplasticity, etc) and since trends can be detected as to what environment might produce which brain products I seek to examine how specifically how early-life exposure to severely unsafe environments (e.g., war, chronic violence, or instability) induces specific epigenetic modifications in genes regulating the stress response and emotion processing (such as those in the HPA axis and limbic system) in times of higher neuroplasticity. Furthermore, this essay seeks to investigate how that alters the development and connectivity of fear- and anxiety-related neural circuits in children, leading to increased risk for anxiety and trauma-related psychopathology in adolescence and adulthood.
I believe this is a question we all should ask ourselves not just as scientists or researchers but as human beings with the same origin living distributed b it still interconnected across cultures. I hope to be able to contribute to this interdisciplinary discussion and societal surface by furthermore proposing mechanisms that can inform preventive societal structures and targeted therapeutic interventions in affected populations.

Results

Fear is a psychological, physiological and behavioural state induced by a thread to well-being or survival. It can either be actual or potential, meaning that the emotion might be a response to an actually threatening or aversive stimulus or what merely to a perceived one. As for internal responses and mechanisms, Fear as well as anxiety is linked to increased arousal, expectancy and autonomic and neuroendocrine activation. That is that first and foremost the amygdalar neural system is in action processing and examining the Impulses in order to produce emotional reactions.
In evolutionary history, fear is positioned as a facilitator of coping with adverse or unexpected situations by providing an appropriate adaptive response.
Speaking about fear, we do need to decide to what extent we can differentiate the phenomenon of pure fear from the one that is anxiety as both concepts are closely related and almost identical to some, nonetheless, by some key factors, clearly distinguishable to others.
Ethologists stated that anxiety is the motivational state aroused by specific stimuli giving rise to defensive behaviour. It is furthermore argumented, that anxiety centers more increasingly around the idea of learned fear, innate fear or fear of novelty, thus depicting a certain habituation being more internalised than the fear-driven reaction that is imminent and present in a known and sole situation of arousal. Moreover, anxiety can be perceived as being connected with other motivational aspects, such as perfectionism or uncertainty essentially mirroring internal conflicts. Hence, anxiety can be slightly more individual and intricate in its interconnectivity and therefore rather increase a sense of uncontrolability making coping more difficult.
To be now able to identify the neural circuitry underlying fear and anxiety symptomatics, we can invoke the development of specific experimental paradigms. Typically, during such processes, an aversive stimulus is paired with a neutral stimulus which results in the neutral stimulus becoming a signal of imminent threat. This then enabled researchers to make out several key

structures that are linked to the generation and modulation of fear responses to the conditioned threat signal - the locations are basically the areas where the receptors are situated to which typical neurotransmitters linked to fear responses bind to. Generally and firstly, the thalamus integrates sensory input from the primary sensory cortices and sends according output to the amygdala. The amygdala, especially its basolateral structures, in turn process aversive signals and send output to the hypothalamus and brainstem to produce defensive behavioural mechanisms. An important aspect associated with this pathway is the regulation of the amygdalar activity, as hyperactivity of the latter could cause an “Amygdala Hijack" where the emotional centers override the ability to think rationally. The hippocampus thereby plays the crucial role to contextualise the threat cue whereupon the medial prefrontal cortex that receives the input from hippocampus and thalamus to project to the amygdala in order to modulate fear behaviour on the basis of complex environmental information.



Neural circuit of fear processing and regulation, showing amygdala-centered threat detection, hippocampal contextual input, and prefrontal top-down modulation of fear responses.

This schematic was created in BioRender (https://www.biorender.com) with assistance from the BioRender AI layout tool. The initial layout was generated from the prompt “[create a conceptual diagram of the neural circuit involved in fear responses consisting of the thalamus, amygdala, hippocampus and PFC]” and then manually edited, labeled, and verified by the author for scientific accuracy.

As with every emotion contributing to a continuous life experience, fear invokes a neurotransmitter as well as a receptor system, that can not only assist in understanding where fear stems from exactly within the brain lobes but also, how brain mechanisms are directly linked to according behavioural outcomes, e.g. overreaction due to an overly activation and release of a specific chemical messenger. Understanding this neural circuitry with all its components and concepts (such as neuroplasticity or neuroanatomy of fear/anxiety) allows us to properly understand how and why emotions are created, shaped and expressed.
Glutamate, as the principal and most abundant excitatory neurotransmitter involved in the neural fear and anxiety network drives rapid depolarisation and thus high frequency neuronal firing

enabling the signalling of active threat detection between the basolateral amygdala and PFC. Moreover, norepinephrine (noradrenaline) broadcasts vigilance and physiological arousal signals across the brain during acute stress to prioritise evaluation. Being a Monoamine neurotransmitter and stress hormone, it triggers the classic „fight-or-flight“ autonomic response amplifying the consolidation of emotionally charged fear memories. Another neurotransmitter is dopamine, which encodes motivational salience as well as the emotional significance of environmental cues as either dangerous or safe while driving the active prefrontal and amygdala signaling necessary for fear extinction. Logically, then, in children exposed to chronic, severe trauma, neuroscientists observe a phenomenon known as frontal hypodopaminergia meaning that dopamine levels drop significantly or become deeply blunted in the PFC.
Through synaptic transmission, the process where, after the neurotransmitters are synthesised inside the presynaptic neuron, they are then stored in vesicles to be
released through the synaptic cleft to the postsynaptic neuron. In some cases however, such as with dopamine that originates in the midbrain but is, as we know, important in the PFC in fear situations, the neurotransmitters are transported via the axonal transport enabled by the long axon structure of the neurons constructing specific pathways towards the locations of the complementary receptors (e.g. basolateral amygdala).
Those can be either presynaptic or postsynaptic, in that their function differs whether they are located on the sending or the receiving neuron around the synaptic cleft.
In fear conditioning, glutamate receptors are those that glutamate binds to - hence enabling synaptic plasticity and long-term-potentiation in the amygdala opening calcium channels upon binding. Dopamine receptors modulate behavioural flexibility and emotional gating. Its D1- and D2-like receptors contribute to increasing fear assessment by. the PFC. Lastly, there are the adrenergic receptors. Its Beta-Receptors are bound by norepinephrine and then activate the Gs-protein&adenylyl cyclase pathway, drastically spiking cyclic AMP and intracellular calcium. This chemical cascade forces rapid neuronal firing. In war zones or refugee journeys, a child’s locus coeruleus continuously blasts norepinephrine into the basolateral amygdala, altering the local structural plasticity. As a result, the amygdala is turned into a hyperactive alarm system firing intensely at the slightest trigger.
Generally, one can state that genetics have effects on the susceptibility of specific neural circuitries, rather than the destiny, meaning that genetic factors can determine the intensity of emotional activation and arousal, but not the distinct emotion itself necessarily. Most anxiety-related traits are polygenic meaning that many genetic variants contribute a small effect while interacting with life experiences. This idea is closely linked to the thought that our genetic basis remains the same and stable throughout life, however, that, as human beings, we develop and change in accordance with the mutable environments we are in. As a result, our identity or emotional personality stays dynamic and never static. The greater part (by up to 80%) of the variation in General Anxiety Disorders for instance is explained by environmental influences and gene-environment interactions. The function of the fear related circuits can then again be modified through epigenetic regulation induced by trauma for example.

Concretely, genetics in fear and anxiety related contexts manages to influence how reactive different parts of the circuit are, whether that targets the Regulation of serotonin, dopamine or the stress response System.
One example is the FKBP5 gene responsible for regulating the glucocorticoid receptor (GR): When cortisol binds to the GR, FKBP51 binds to this complex and reduces the receptors sensitivity to cortisol acting as a brake to the stress response (HP axis).

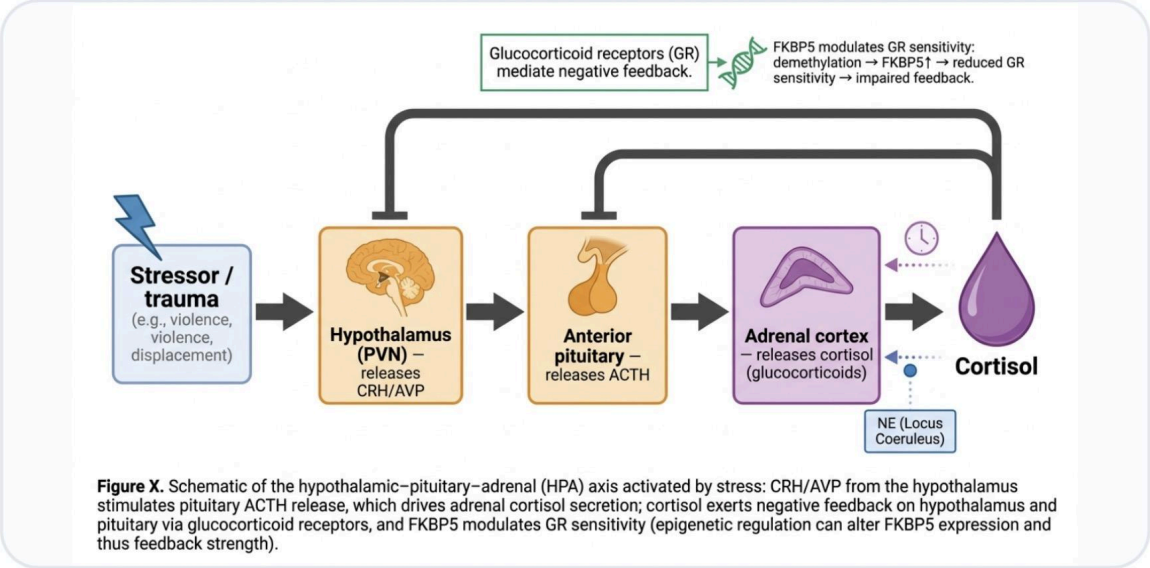
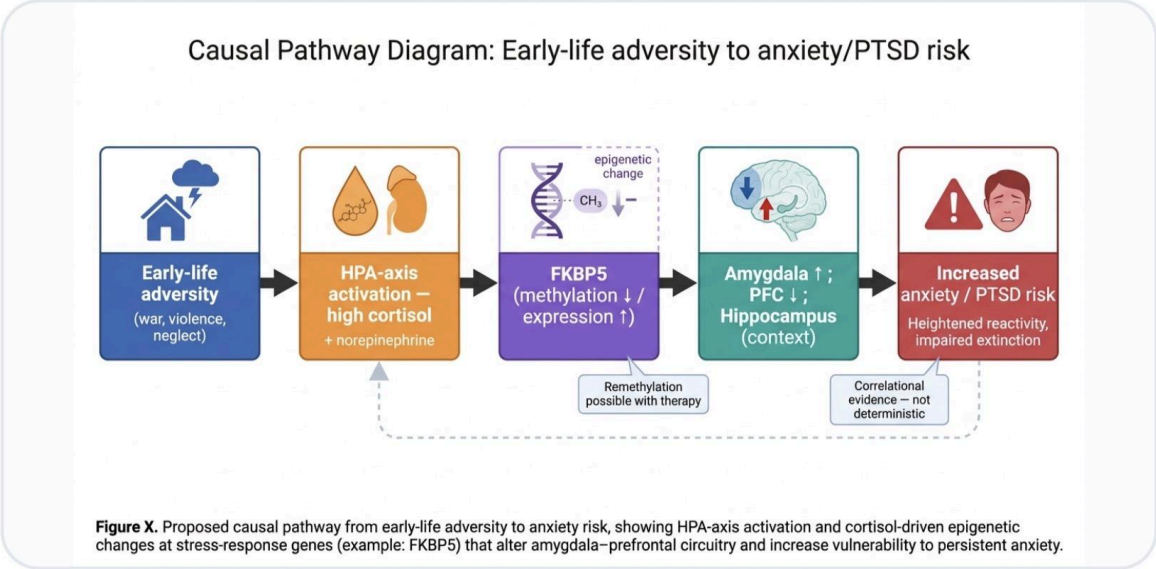


Figure X. Schematic of the hypothalamic–pituitary–adrenal (HPA) axis activated by stress: CRH/AVP from the hypothalamus stimulates pituitary ACTH release, which drives adrenal cortisol secretion; cortisol exerts negative feedback on hypothalamus and pituitary via glucocorticoid receptors, and FKBP5 modulates GR sensitivity (epigenetic regulation can alter FKBP5 expression and thus feedback strength).

This conceptual diagram was drafted using the AI-assisted design tool FigureLabs (https://figurelabs.ai) using the prompt "[create a diagram of the HPA-axis responsible for the production of the fear response throughout the hypothalamus, pituitary gland and adrenal cortex]". The initial layout was vectorized and subsequently manually refined, labeled, and verified by the author to ensure scientific accuracy.

Our actual DNA sequence (the A, C, T, G code) cannot be changed by the environment. However, the environment can drastically change how our body reads that code. This is the science of epigenetics. In children surviving war, refugee flight or ongoing trauma, the continuously high level of cortisol within the brain causes a chemical reaction to the child's DNA called demethylation. Normally, the body placed tiny methyl groups on certain genes. Those act like a tape, covering the gene to keep it off or quiet. The intense storm of cortisol then strips away the methyl tags from the FKBP5 gene leading to it being exposed and stuck in the ON position. It then begins to overproduce proteins that impair the brain's internal brakes, leaving the child in a permanent high-anxiety state.



This conceptual diagram was drafted using the AI-assisted design tool FigureLabs (https://figurelabs.ai) using the prompt “[create a causal pathway depicting the combination of environmental and biochemical factors leading up to anxiety development risk later on]”. The initial layout was vectorized and subsequently manually refined, labeled, and verified by the author to ensure scientific accuracy.

Through the exposure to war or physical assault, neutral cues become terrifying as the brain pairs them with a traumatic event, which is called fear conditioning and one of the most central environmental effects on the brain. This learned fear can also translate into cultural fear or social modelling, when e.g. a parent or a peer reacts with intense panic to a specific stimulus, which teaches the child to fear it. But also physical and macro environmental stressors can play a significant role in fear intensity and expression. Severe sleep deprivation or poor air pollution when living through extreme weather or high levels of urban noise and crowing biologically lowers the brain's threshold for panic. Through epigenetics those factors can be linked to specific genetic structures, as described above.

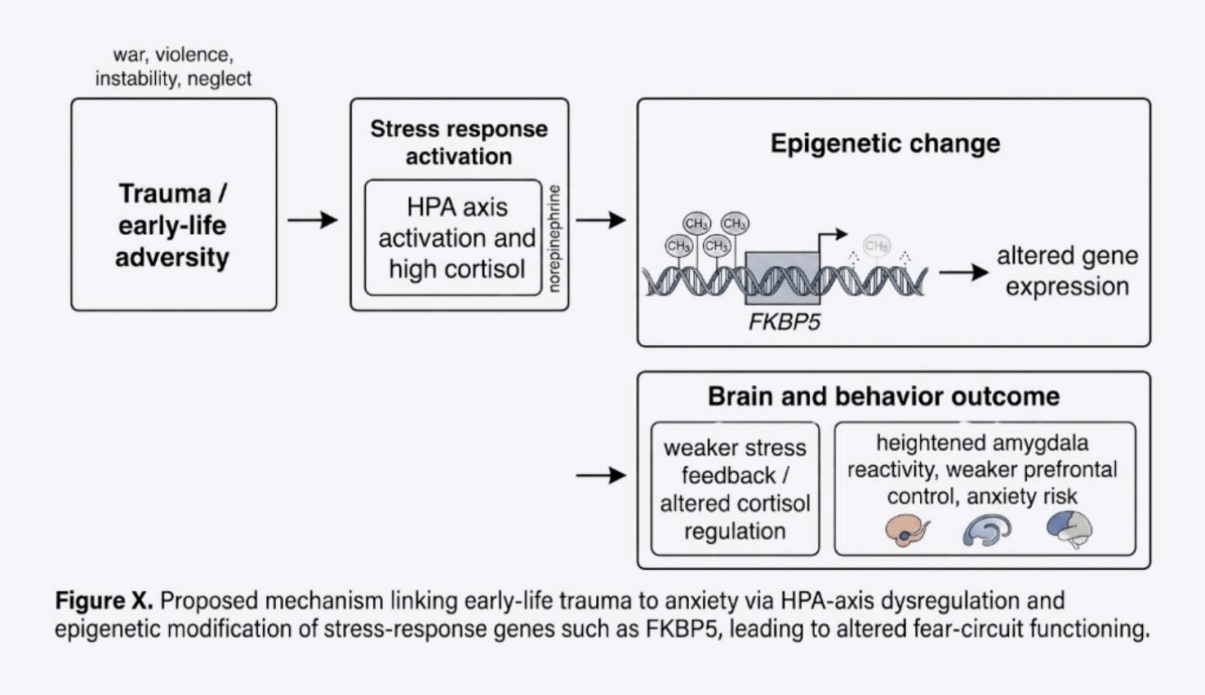


Figure X. Proposed mechanism linking early-life trauma to anxiety via HPA-axis dysregulation and epigenetic modification of stress-response genes such as FKBP5, leading to altered fear-circuit functioning.

This schematic was created in BioRender (https://www.biorender.com) with assistance from the BioRender AI layout tool. The initial layout was generated from the prompt "[create an HPA-axis pathway depicting the aspect of epigenetic change in trauma]" and then manually edited, labeled, and verified by the author for scientific accuracy.

Discussion

The question that should be subsequently asked here is how an examination in the change of the environmental aspect a child is confronted with can also change target fear conditioning or the body's threshold to cope with panic. In other words, how constructive, enriched environments can actively reverse the neurobiological damage of trauma. A safe environment can generally be achieved through elements such as trauma-informed classrooms or culturally sensitive Community clinics that focus on psychotherapy for example. An answer, then, to the treatment of fear conditioning is the rewriting of fear memories, the promotion of fear extinction. In a safe environment, a person is exposed to harmless triggers triggering dopamine in the PFC that then signals extinction learning. It physically forces the NMDA receptors in the amygdala to rewrite the old memory code, through which a new, dominant memory path is created. In General, restoring healthy dopamine levels helps the PFC to regain the top-down inhibitory control over the emotional center, which reverses hypodopaminergia.

Without the constant threat of danger, the brainstem stops overproducing norepinephrine which allows the overworked alpha-2 adrenergic receptors to upregulate. As a result, the biological brakes needed for fear regulation are re-installed.

In those enriched environments, when trauma-focused psychotherapy and absolute safety alter the body's neurochemistry, they activate specific internal enzymes that physically place the chemical tape back onto the DNA, e.g. on the FKBP5 gene. This process is called "methylation" reversing demethylation leading to increased fear responses.

First, approaches like Trauma-Focused Cognitive Behavioural Therapy (CBT) can lead to the hypothalamic-pituitary-adrenal (HPA) axis to finally stop hyper-secreting cortisol. The drastic drop of intracellular fluid no longer being saturated with high toxic stress markers sends a signal into the nucleus of the neuron. This awakens a specific family of enzymes called DNA Methyltransferases that maintain and repair the epigenome. Those enzymes then harvest methyl groups floating within the cell that are navigated to the exposed, unmethylated sections of the stress genes. After binding, the toxic overproduction of stress-chaperone proteins stops and the brain's natural cortisol feedback loop is restored, lowering the child's physiological panic response to reverse the biological baseline of PTSD (as the neurobiological disorder where the environmental trauma causes those structural epigenetic modification and severe chemical imbalances).

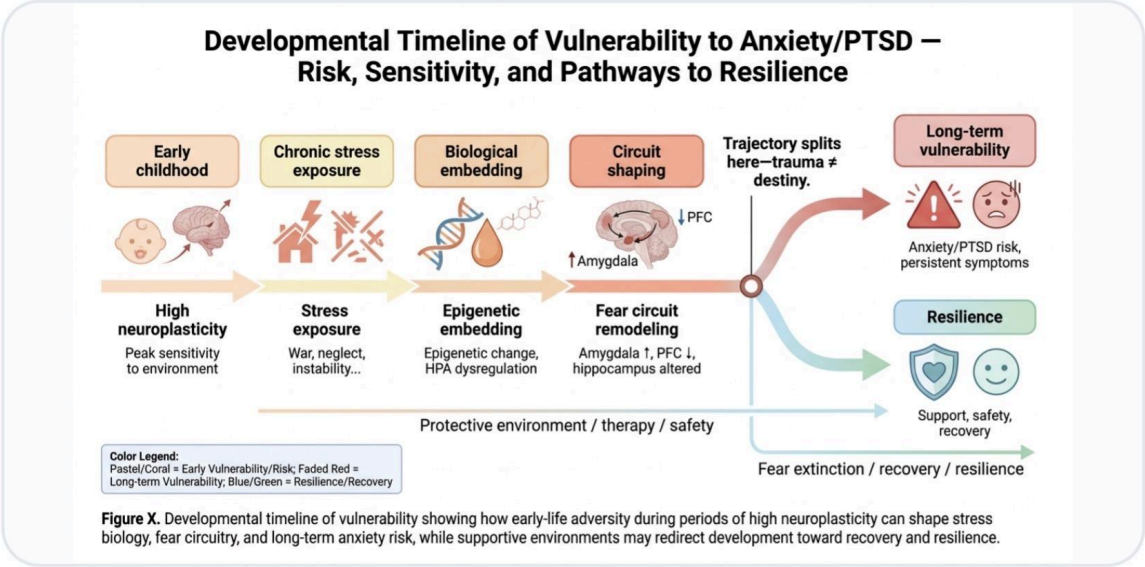


Figure X. Developmental timeline of vulnerability showing how early-life adversity during periods of high neuroplasticity can shape stress biology, fear circuitry, and long-term anxiety risk, while supportive environments may redirect development toward recovery and resilience.

This conceptual diagram was drafted using the AI-assisted design tool FigureLabs (https://figurelabs.ai) using the prompt "[create a digram showing a vulnerability timeline that includes the development of a childs brain with the distinct outcomes of effects of experiences of adversity in either safe or unsafe environment]". The initial layout was vectorized and subsequently manually refined, labeled, and verified by the author to ensure scientific accuracy.

Building upon those examinations, we need to invoke the current realities of research as well, though:

Current studies mostly show a link between epigenetic changes and PTSD, but cannot definitely prove whether the trauma caused the biological change or if pre-existing biological profiles made the individuals more vulnerable. Future research thus aims to target the longitudinal tracking of children before, during and after displacement to isolate exact cause-and-effect timelines. Moreover, the human brain tissue cannot be safely sampled in living children, which is why researchers must rely on peripheral blood which may not perfectly depict what happens in the brain's emotional centers. Advancing neuroimaging-epigenetic mapping is an approach in future examination.

Conclusion

The reality reflects that many children and young people experience high levels of trauma, stress and uncertainty in the context of wars, immigration or domestic abuse.

The complex neural network responsible for integrating, processing and externalising fear underlies a genetic influence but can be wired through those environmental stressors via the concept of epigenetics. A hyperactivity in those circuits is a direct result also produced through a neurotransmitter imbalance depicting e.g. a suppression of dopamine and an increase in cortisol or norepinephrine that both lead to more intense fear reaction and expression. Children learn to fear and feel unsafe, which states a central problem mechanism in today's world as regional or global conflicts involving violence, physical and psychological harm are since long numerous and long lasting. Understanding neuropsychology as an idea to combine the environmentally induced changes in the brain chemistry, as a depletion in dopamine, is crucial to be able to navigate psychotherapy - the fostering of safe environments enabling a spike in dopamine levels again. Observing the behaviours of those children in how they express their fear, as in fear conditioning circumstances, is a first step to be able to target those intricate mechanisms for which treatments to exist. Scientists, but also politicians promoting social institutes and communities are in charge in this context to further make this necessary development possible in our society.

The continuity of human beings opens many new perspectives on the question of how we treat science and the way our brains work. We especially observe this when working with the ability of the brain to rewire itself through producing new neurons or strengthening synaptic connections that is especially rapidly possible within the brains of children, as those brains are yet characterised by high cellular flexibility and a lack of structural stabilisation (socialising, etc.). This leaves us with the realization that children, and also those in war zones, are logically more prone to be affected with trauma, but also with the fact that the reversing processes can take place similarly fastly, which is also so important.

Because understanding this neuroplasticity and epigenetics that both demonstrate how we, as humans, necessarily and permanently interact with our environments and hence develop behaviours and thinking patterns, we are able to not just elevate in science and research but also to gain more cultural awareness on the pathway of comprehending who we are and can be for each other.

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