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Review Article

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Epigenetic Reprogramming: Evolutionary Synergies for the Prevention of Emerging Diseases

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Abstract

From the perspective of systems theory, human health results from a dynamic balance between environmental, biological, and behavioral factors [1]. The interaction between endocrine-disrupting chemicals (EDCs), sedentary lifestyles, ultra-processed food consumption, and disconnection from natural stimuli disrupts circadian rhythms, metabolism, and brain functions, generating a state of neuroendocrine dysregulation and systemic inflammation [1,2]. Exposure to EDCs compromises hormonal and neurochemical regulation, with transgenerational effects that increase the risk of psychiatric and metabolic disorders in future generations, exacerbated by the role of adipose tissue as a bioaccumulator of toxins [3,4]. Emerging diseases, once exclusively associated with viral infections (such as COVID-19 and the Zika virus), now also include metabolic, neurodegenerative, and psychiatric disorders that are rapidly increasing due to circadian disruption, chronic inflammation, and loss of environmental variability [3,5,6]. These factors operate systemically, leading to neurochemical imbalances, hormonal dysfunctions, and impaired adaptive responses [7]. To counteract these effects, a systemic approach is necessary, based on circadian rhythm regulation, exposure to nature and cold, neurofeedback, functional nutrition, and hormonal balance [8]. In this context, epigenetic reprogramming emerges as a key mechanism to modulate gene expression without altering DNA, enabling the reversal of environmental damage *through targeted interventions in lifestyle, diet, and neuroprotection [9].*

These strategies represent a new frontier in the prevention and treatment of neuroendocrine dysfunctions and emerging diseases, laying the foundation for an integrated therapeutic paradigm adapted to the needs of modern society.

1. Introduction

In recent decades, advances in neuroscience have highlighted how our biology, psyche, and behaviors are deeply influenced by environmental and hormonal factors. Among these, endocrine-disrupting chemicals (EDCs) represent one of the most insidious threats, interfering with the regulation of hormonal systems, metabolism, and brain function. Chronic exposure to these substances, now widespread on a global scale, has been associated with an increase in psychiatric disorders, not only in directly exposed individuals but also in subsequent generations due to transgenerational epigenetic effects [3,4]. Recent studies have demonstrated that EDCs can alter gene expression in neural circuits involved in mood regulation, increasing vulnerability to disorders such as anxiety, depression, and cognitive dysfunctions.

At the same time, there has been a significant increase in adipose tissue in the population, particularly among younger generations, which exacerbates the effects of EDCs. Body fat is not merely an energy store but acts as a true bioaccumulator of toxins and environmental pollutants, retaining lipophilic substances such as bisphenol A (BPA), phthalates, dioxins, and polychlorinated biphenyls (PCBs) [3,4]. This accumulation has a direct impact on hormonal and metabolic regulation, affecting the production of cortisol, insulin, testosterone, and thyroid hormones, all of which are crucial for mental and physical health. One of the most critical aspects of this dynamic is the transgenerational transmission of pollutants. Pregnant mothers transfer EDCs and bioaccumulated toxins to the fetus through the placenta and breast milk, predisposing newborns to endocrine imbalances, neurodevelopmental alterations, and greater vulnerability to psychiatric disorders [10]. Recent studies have shown that fetal exposure to EDCs can modify brain architecture and dopaminergic and serotonergic circuits, increasing the risk of mood disorders, autism, and ADHD.

To further worsen this scenario, several dysfunctional habits of modern society contribute significantly. Chronic sedentarism, which reduces the production of essential neurotransmitters such as dopamine and serotonin, excessive consumption of junk food, which promotes inflammation and gut microbiota alterations, directly impacting the gut-brain axis, disconnection from nature, depriving the body of ancestral stimuli necessary for optimal psychophysiological function, and lack of exposure to natural thermal variations [6]. This last factor, due to a life spent in constantly climate-controlled environments, prevents the activation of thermoregulation mechanisms and adaptive responses to cold and heat, negatively affecting metabolism and stress resilience [11].

If EDCs compromise the homeostatic balance of our bodies, it is essential to counterbalance their effects through integrated strategies acting at multiple levels. Our body and brain possess extraordinary adaptability and self-regulation capabilities, but to activate these mechanisms, it is necessary to provide the right stimuli, aligned with our evolutionary biology. Scientific evidence suggests that a systemic and synergistic approach can restore psychophysiological balance, going beyond the simple pharmacological management of symptoms. Strategies such as biofeedback and neurofeedback, circadian rhythm regulation, cold exposure, peptide integration, hormonal balancing with low-dose testosterone, targeted physical activity, and functional nutrition can offer a biological counteraction to the detrimental effects of EDCs, restoring the body's natural resilience. This article aims to explore how these methodologies can synergistically interact to counteract imbalances induced by endocrine disruptors, improving mental health, emotional regulation, and cognitive performance. This science-based analysis seeks to redefine the concept of well-being, considering the body as a dynamic system in continuous adaptation. To address this scenario, it is essential to adopt an integrated intervention model, taking into account the interaction between these factors and promoting strategies based on circadian rhythms, nature exposure, neurofeedback, cold exposure, and hormonal modulation. Only a systemic and preventive approach can ensure the restoration of neuroendocrine balance and overall well-being.

1.1 Health as a Complex System: Interaction between Biological, Environmental, and Behavioral Factors

Systems theory, developed by Ludwig von Bertalanffy, describes living organisms as open systems that constantly interact with their environment [1]. This approach recognizes health as the result of a dynamic balance between biological, environmental, and behavioral factors, moving beyond the reductionist view that analyzes disorders in isolation [2,7]. Any imbalance in one of these domains can trigger cascading effects throughout the entire organism, altering metabolism, hormonal regulation, and neurocognitive function [12]. From a biological perspective, the human body is regulated by complex systems, including the central nervous system (CNS), the hypothalamic-pituitary-adrenal (HPA) axis, and the endocrine system. These circuits ensure homeostasis, the ability to maintain an internal balance despite external variations. However, chronic exposure to EDCs disrupts these mechanisms, compromising the production of neurotransmitters and key hormones such as dopamine, serotonin, cortisol, and testosterone [3,4]. The decline in testosterone and neuroprotective peptides such as BDNF has been associated with reduced neuroplasticity, increased stress vulnerability, and diminished emotional resilience.

Environmental factors directly influence the body's biological regulation. Exposure to electromagnetic radiation, atmospheric pollutants, and circadian rhythm disruptors alters energy metabolism and sleep quality. The modern urban environment, characterized by limited natural light exposure, high sedentarism, and absence of natural temperature fluctuations, has reduced the body's adaptive capacity. Lack of exposure to cold or heat, for instance, impairs adaptive thermogenesis, decreasing the body's ability to respond to environmental stimuli and increasing the risk of metabolic dysfunctions [11]. Moreover, disconnection from nature has been correlated with higher stress levels and HPA axis dysregulation [13]. Behavioral factors play a crucial role in health regulation. Modern diets, high in sugar and ultra- processed foods, alter gut microbiota and the gut-brain axis, contributing to chronic inflammation and neurochemical dysfunctions [6]. Sedentarism reduces BDNF production and neuronal adaptability, increasing the risk of mood disorders [14]. On the other hand, strategies such as gratitude and mindfulness have demonstrated neuroprotective effects, improving amygdala regulation and increasing dopamine and oxytocin release, with positive effects on emotional resilience.

1.2 Impact of Endocrine-Disrupting Chemicals (edcs): Hormonal, Neurochemical, and Metabolic Alterations with Transgenerational Effects

Endocrine-disrupting chemicals (EDCs) are synthetic compounds that interfere with the endocrine system by altering hormone production, release, and metabolism. These chemicals, found in plastics, pesticides, cosmetics, and industrial products, have been linked to hormonal, neurochemical, and metabolic dysregulations, significantly impacting both mental and physical health [3,4]. One of the primary mechanisms of action of EDCs is their interference with hormone receptors, either mimicking or blocking the action of natural hormones such as estrogens, androgens, thyroxine, and glucocorticoids. Bisphenol A (BPA), for example, binds to estrogen receptors, disrupting the normal androgen-estrogen balance in both men and women, affecting fertility, emotional regulation, and cognitive function. Phthalates, on the other hand, reduce testosterone production, leading to decreased neuroplasticity, lower motivation, and impaired stress management.

At the neurochemical level, chronic EDC exposure has been linked to alterations in key brain neurotransmitters, including dopamine, serotonin, and GABA, affecting both behavior and mental health. Some studies indicate that accumulation of dioxins and PCBs (polychlorinated biphenyls) increases the risk of anxiety and depression, through their modulation of amygdala and prefrontal cortex activity. Furthermore, chronic brain inflammation induced by EDCs has been correlated with neurodegenerative disorders and a reduced ability of the brain to respond to neurogenesis stimuli [6]. From a metabolic perspective, EDCs contribute to hypothalamic-pituitary-adrenal (HPA) axis dysfunction and increased systemic inflammation. This manifests as an increase in visceral adipose tissue, which serves as a bio accumulator of toxins, exacerbating insulin resistance and chronic low- grade inflammation. Reduced production of adiponectin and leptin, two key hormones regulating appetite and metabolism, has been observed in individuals with high EDC exposure, leading to metabolic dysfunctions and chronic fatigue [10].

The effects of EDCs are not limited to directly exposed individuals but can be transmitted to subsequent generations through epigenetic mechanisms. During pregnancy and lactation, fetuses and newborns can absorb maternal EDCs, directly affecting their neurological development and metabolism. Recent studies demonstrate that prenatal exposure to PCBs and phthalates can influence synaptic connection formation in the fetal brain, increasing the risk of autism spectrum disorders, ADHD, and anxiety in future generations [15]. Moreover, epigenetic modifications induced by EDCs can alter gene expression related to HPA axis regulation, further amplifying the intergenerational transmission of stress vulnerability and neuropsychiatric disorders. The accumulation of EDCs in maternal adipose tissue is particularly concerning, as during pregnancy and breastfeeding, these compounds are released into the bloodstream and transmitted to the fetus through the placenta and to the newborn via breast milk [3]. This suggests that the environmental toxic burden of previous generations may influence the neuroendocrine development of new generations, predisposing them to metabolic diseases, hormonal imbalances, and mental health disorders.

1.3 Decline in Testosterone and Neuroprotective Peptides: Correlation between edcs, Modern Lifestyle, and Reduced Neuroplasticity

Over the past few decades, there has been a significant decline in testosterone levels and neuroprotective peptides in the general population. This reduction has been attributed to a combination of environmental factors, including exposure to endocrine-disrupting chemicals (EDCs), sedentary behavior, inadequate diet, and chronic stress [3,4]. The deficiency of these key elements has direct consequences on metabolic health, cognitive function, and emotional regulation, leading to an increase in disorders such as anxiety, depression, neuroinflammation, and early cognitive decline.

1.3.1 Reduction in Testosterone: Effects on Mental and Metabolic Health

Testosterone, beyond its critical role in sexual function and muscle mass development, is also essential for neuroplasticity, motivation, and stress resilience. Recent studies have shown that chronic reduction in testosterone levels is associated with:

- Increased stress vulnerability: Testosterone modulates the activity of the amygdala and prefrontal cortex, regions involved in anxiety regulation and emotional responses [3]. Its deficiency promotes excessive activation of the HPA axis, leading to cortisol overproduction and mood imbalances [4].
- Decline in motivation and cognitive function: Testosterone regulates dopamine, the key neurotransmitter for motivation and reward processing. Reduced testosterone levels are linked to lower initiative, apathy, and depressive symptoms.
- Increase in adipose tissue and reduction in muscle mass: Testosterone is essential for lipid metabolism. Low levels promote visceral fat deposition, which in turn acts as a bio

accumulator of toxins and EDCs, amplifying their negative effects on hormonal regulation [10].

1.3.2 Impact of edcs on Testosterone Production

Chronic exposure to endocrine-disrupting chemicals (EDCs) is one of the primary causes of declining testosterone levels in the modern population. Compounds such as phthalates, bisphenol A (BPA), dioxins, and PCBs interfere with testosterone biosynthesis and regulation through various mechanisms:

- Inhibition of testosterone synthesis: EDCs disrupt the activity of Leydig cells in the testes, which are responsible for testosterone production.
- Increased conversion of testosterone into estrogens: Certain chemical compounds enhance the activity of aromatase, an enzyme that converts testosterone into estradiol, reducing its availability and altering hormonal balance [4].
- Transgenerational effects: Prenatal exposure to EDCs can reduce testosterone production capacity from the earliest stages of development, with consequences persisting across generations.

1.3.3 Neuroprotective Peptides and Declining Neuroplasticity

In addition to testosterone decline, there has been a decrease in the production of neuroprotective peptides, such as brain-derived neurotrophic factor (BDNF), insulin-like growth factor-1 (IGF-1), and delta sleep-inducing peptide (DSIP). These peptides are critical for brain health, sleep regulation, and stress resilience [9].

- BDNF and neuroplasticity: BDNF is essential for neuron survival, learning, and memory. Its reduction has been linked to an increased risk of depression, anxiety, and early cognitive decline [14]. Studies show that sedentarism, an inflammatory diet, and lack of exposure to nature all contribute to lower BDNF production [6].
- IGF-1 and neural regeneration: IGF-1 supports brain cell growth and repair. Its decline, often associated with reduced physical activity and excess body fat, has been linked to an increased risk of neurodegenerative diseases such as Alzheimer's and Parkinson's.
- DSIP and sleep regulation: DSIP modulates the sleep-wake cycle and promotes recovery from oxidative stress in the brain. Lower levels have been observed in individuals exposed to environmental pollutants and those suffering from chronic sleep disorders.

1.3.4 Impact of Modern Lifestyle

Beyond EDCs, various modern lifestyle factors have contributed to the decline in testosterone and neuroprotective peptides. Specifically:

- Reduced physical activity: Exercise, particularly resistance training, stimulates the production of testosterone and BDNF. Chronic sedentarism has been linked to a significant reduction in both [14].
- Limited natural light exposure and circadian rhythm disruption: Testosterone and BDNF regulation are influenced by circadian rhythms. Constant exposure to artificial light and reduced natural light-dark cycles impair their production [16].
- Inflammatory and hypercaloric diet: A diet rich in sugars and saturated fats decreases testosterone synthesis and BDNF production, increasing systemic inflammation and altering insulin signaling [6].
- Chronic stress and hyperactivation of the HPA axis: Excessive stress increases cortisol production, which in turn reduces testosterone and BDNF synthesis, negatively impacting psychophysical resilience [12].

The combination of EDC exposure, sedentarism, circadian disruptions, and dysfunctional diet has contributed to an unprecedented decline in testosterone levels and neuroprotective peptides in the modern population. These changes have had a profound impact on mental, metabolic, and cognitive health, predisposing individuals to mood disorders, increased body fat, and early neurodegenerative decline. Understanding these mechanisms is essential for developing targeted strategies to restore neuroendocrine homeostasis, including physical activity, circadian rhythm regulation, nature exposure, and targeted hormonal modulation.

2. Effects of EDCs and Modernity on Health

2.1 Neurochemical and Hormonal Dysregulation: Interference with Dopamine, Serotonin, and GABA

Endocrine-disrupting chemicals (EDCs) significantly impact the brain's neurochemical regulation, interfering with key neurotransmitters such as dopamine, serotonin, and gamma-aminobutyric acid (GABA). These neurotransmitters are essential for cognitive function, mood regulation, and stress response. Chronic exposure to EDCs alters their production and metabolism, increasing susceptibility to mood disorders, anxiety, depression, and cognitive dysfunction [3,4].

2.1.1 Effects on Dopamine and Motivation

Dopamine is a key neurotransmitter involved in motivation, reward processing, and executive function. EDCs such as bisphenol A (BPA) and phthalates have been shown to disrupt dopaminergic circuits, reducing activity in reward-related brain regions such as the striatum and nucleus accumbens. These effects have been associated with:

- Reduced motivation and initiative, leading to apathy and difficulty in pursuing long-term goals.
- Increased vulnerability to addiction: Impaired dopamine activity has been linked to a higher propensity for impulsive behaviors and addictions, including food, substances, and technology dependence [4].
- Attention deficits: Dysregulation of the dopaminergic system contributes to the rise in ADHD cases among younger generations.

2.1.2 Serotonin Interference and Increased Vulnerability to Depression

Serotonin (5-HT) plays a crucial role in mood regulation, anxiety control, and sleep cycles. Research has demonstrated that polychlorinated biphenyls (PCBs), pesticides, and dioxins can disrupt serotonin availability in the brain, leading to:

- Increased depressive and anxious symptoms, caused by reduced serotonergic neurotransmission in the prefrontal cortex [15].
- Sleep disturbances: Serotonin is a precursor to melatonin, and its deficiency contributes to insomnia and circadian rhythm dysregulation.
- Higher stress vulnerability: Serotonin plays a role in the regulation of the hypothalamic- pituitary-adrenal (HPA) axis; its depletion results in a hyperactive stress response and increased cortisol production [3].

2.1.3 GABA Dysregulation and Increased Nervous System Hyperactivity

GABA is the primary inhibitory neurotransmitter in the brain and is essential for controlling neuronal excitability. Exposure to EDCs has been associated with reduced GABAergic transmission, leading to:

- Increased anxiety and emotional reactivity, as GABA normally reduces excitability in the amygdala, the brain region responsible for fear responses.
- Higher predisposition to anxiety spectrum disorders, including panic attacks and post- traumatic stress disorder (PTSD).
- Deficits in concentration and behavioral regulation, particularly observed in children exposed to BPA and phthalates during pregnancy [3].

The cumulative neurochemical disruptions caused by chronic exposure to EDCs highlight how these compounds significantly impair mental well-being, increasing the risk of psychiatric and cognitive disorders in exposed populations.

2.2 Toxin Accumulation in Adipose Tissue: Bioaccumulation of edcs and its Impact on Metabolism and Inflammation

Adipose tissue is not merely an energy reservoir but a metabolically active organ that regulates the production of hormones and cytokines. Endocrine-disrupting chemicals (EDCs), being lipophilic, tend to accumulate in body fat, where they can persist for years, altering metabolism and endocrine regulation [10]. This phenomenon, known as bioaccumulation, is particularly relevant in individuals with excessive adipose tissue, as fat serves as a toxin reservoir that gradually releases contaminants into the bloodstream, exacerbating metabolic and neuroendocrine dysfunctions [3].

2.2.1 Bioaccumulation of EDCs in Body Fat

The most commonly accumulated EDCs in adipose tissue include:

- Dioxins and PCBs from plasticizers and industrial pollutants, which disrupt the hypothalamic-pituitary-adrenal (HPA) axis and increase systemic inflammation [4].
- Phthalates and BPA, found in plastic containers and canned foods, which interfere with lipid metabolism and insulin sensitivity.
- Organochlorine pesticides, which inhibit thyroid function and disrupt glucose metabolism.

2.2.2 Impact of Bioaccumulation on Metabolic Regulation

The accumulation of EDCs in adipose tissue has direct consequences on metabolic regulation, including:

- Increased insulin resistance – EDCs interfere with insulin signaling, promoting visceral fat accumulation and type 2 diabetes risk.
- Dysregulation of leptin and adiponectin – Leptin regulates satiety, while adiponectin enhances insulin sensitivity. EDC exposure reduces both, leading to weight gain and chronic fatigue [10].
- Chronic inflammation – Adipose tissue exposed to EDCs releases inflammatory cytokines (TNF-α, IL-6), contributing to immune dysfunction and higher risk of neurodegenerative diseases.

2.2.3 Effects of EDC Release During Weight Loss

One often-overlooked aspect of bioaccumulation is that weight loss leads to the release of stored EDCs into the bloodstream, temporarily increasing plasma concentrations and causing:

- Temporary endocrine dysfunction, with hormonal fluctuations and increased oxidative stress [4].
- Effects on the central nervous system, including fatigue, irritability, and cognitive difficulties, as toxins are processed by the liver and nervous system.

These effects emphasize the need for a targeted detoxification strategy, including liver support, inflammation regulation, and hormonal balance, to minimize the adverse effects of EDC mobilization from adipose tissue during weight loss [3].

2.3 Circadian Rhythm Disruptions: Artificial Light Exposure and Sleep-Wake Cycle Dysregulation

Circadian rhythms are biological cycles regulated by the light-dark alternation, influencing numerous physiological processes such as hormone production, metabolism regulation, and cognitive function. Their disruption has been associated with sleep disorders, increased stress levels, and neuroendocrine dysfunctions [5].

One of the primary disruptors of circadian rhythms is excessive exposure to artificial light, particularly blue light emitted by electronic devices and LED lighting. The retina contains photoreceptors sensitive to blue light, which regulate melatonin production—the key hormone for sleep regulation. However, overexposure to artificial light inhibits melatonin release, leading to:

- Delayed sleep onset and reduced sleep quality.
- Increased evening cortisol levels, causing sympathetic nervous system hyperactivation and greater stress vulnerability.
- Dysregulation of serotonin and dopamine secretion, altering mood stability and promoting anxiety and depression [5].

Circadian rhythm disruptions not only impact emotional regulation but also affect metabolism. Chronic sleep deprivation has been linked to increased insulin resistance and higher ghrelin production (the hunger hormone), contributing to weight gain and type 2 diabetes risk [6].

Moreover, lack of exposure to natural morning light further desynchronizes the biological clock. The circadian system is regulated by a group of neurons in the hypothalamic suprachiasmatic nucleus (SCN), which respond to sunlight to regulate the sleep-wake cycle and the secretion of hormones like

cortisol and testosterone [8].
Reduced morning sunlight exposure leads to:

- Decreased alertness and productivity during the day.
- Alterations in energy metabolism, predisposing individuals to fat accumulation.
- Mood and cognitive impairments, increasing the risk of seasonal affective disorder (SAD).

The combination of evening artificial light exposure and reduced morning sunlight exposure is one of the primary causes of circadian misalignment, leading to sleep disorders, hormonal imbalances, and increased susceptibility to metabolic and psychiatric conditions [5].

2.4 Disconnection from Nature and Loss of Environmental Stimuli: Reduced Neuroplasticity and Increased Stress

Humans evolved in an environment rich in natural sensory stimuli, including sunlight, direct contact with the earth, and natural sounds. However, modern urbanization and lifestyle changes have drastically reduced the amount of time spent in nature, leading to environmental disconnection that negatively impacts neuroplasticity and stress management [13].
Exposure to nature has been linked to:

- Reduced amygdala activity, improving emotional regulation and decreasing anxiety [17].
- Increased dopamine and serotonin production, enhancing psychological well-being and stress resilience [13].
- Improved heart rate variability (HRV), reflecting better autonomic nervous system self- regulation [18].
- One of the primary mechanisms through which nature influences health is grounding, which involves direct physical contact with the earth, allowing the transfer of electrons from the Earth's surface into the human body. This process has been associated with:
- Reduced oxidative stress and systemic inflammation [18].
- Improved sleep and cortisol regulation.
- Beneficial effects on circulation and muscle tension reduction.

Additionally, contact with natural environments stimulates the release of phytoncides and terpenes, volatile compounds emitted by trees, which have demonstrated neuroprotective and immune-boosting properties [17]. The loss of natural stimuli and constant exposure to artificial, sterile, and overstructured environments diminish neuroplasticity and increase chronic stress, contributing to the rising prevalence of depression and anxiety disorders in modern society [13].

2.5 Effects of Sedentary Behavior and Ultra-Processed Diets: Systemic Inflammation and Gut-Brain Axis Dysregulation

The combination of a sedentary lifestyle and ultra-processed food consumption is a major driver of low-grade chronic inflammation and dysregulation of the gut-brain axis [6].

2.5.1 Effects of Physical Inactivity on Brain and Metabolic Health

A lack of regular physical activity leads to:

- Reduced BDNF (Brain-Derived Neurotrophic Factor) production, impairing neuroplasticity and increasing the risk of neurodegeneration [14].
- Higher risk of insulin resistance and chronic inflammation, contributing to accelerated brain aging.
- Dysregulated cortisol secretion, increasing stress vulnerability and reducing recovery capacity.

2.5.2 Ultra-Processed Diets and Gut Microbiota Alteration

Ultra-processed foods, rich in refined sugars, trans fats, and chemical additives, disrupt the composition of the gut microbiota, promoting a pro-inflammatory state that directly impacts mental health [6]. Some key effects include:

- Reduced bacterial diversity, impairing the production of neurotransmitters like serotonin and GABA.
- Increased intestinal permeability, allowing toxins to enter the bloodstream, contributing to neuroinflammation [3].
- Dysregulation of the gut-brain axis, increasing the risk of anxiety, depression, and cognitive dysfunctions [6].

The combination of sedentary behavior and industrialized diets is having an unprecedented impact on global health, fueling the rise of psychiatric, neurodegenerative, and metabolic disorders, emphasizing the need for a systemic and integrative lifestyle approach (Mendelson et al., 2023).

3. Neuroendocrine Rebalancing Strategies

Neuroendocrine rebalancing is essential to counteract the negative effects of endocrine disruptors (EDCs), sedentary lifestyles, and the disconnection from natural biological rhythms. To restore homeostasis, interventions must target multiple levels, including circadian rhythm regulation, cognitive function optimization via neurofeedback and biofeedback, and stress response management [16].

3.1 Circadian Rhythms and Natural Light: Regulation of Melatonin and Metabolism through Sunlight Exposure and Time-Restricted Feeding

Circadian rhythms are 24-hour biological cycles that regulate key physiological functions, such as sleep, metabolism, and hormone secretion. Their proper function depends on the alternation between natural light and darkness, which modulates melatonin, cortisol, and testosterone production. However, excessive exposure to artificial light, reduced sunlight exposure, and disrupted eating patterns have contributed to widespread circadian dysregulation in modern populations, negatively impacting metabolic, cognitive, and psychiatric health [16].

3.1.1 Natural Light Exposure and Melatonin Regulation

One of the most effective methods for restoring circadian rhythms is morning sunlight exposure, which stimulates serotonin and cortisol production, promoting wakefulness and mental well-being. Sunlight acts as a primary regulator of the suprachiasmatic nucleus (SCN) in the hypothalamus, the brain region responsible for synchronizing the biological clock with the light-dark cycle [8].
The benefits of natural light exposure include:

- Improved sleep quality due to increased evening melatonin production.

- Regulation of cortisol, supporting a natural cycle of morning activation and evening relaxation.
- Optimization of dopamine and serotonin synthesis, enhancing mood and motivation [5].
- Metabolic benefits, leading to better energy utilization and improved body weight regulation.

Conversely, excessive exposure to artificial light at night, especially blue light from smartphones and LED screens, suppresses melatonin production, disrupting the sleep-wake cycle and increasing the risk of sleep disorders and metabolic dysregulation [16].

3.1.2 Time-Restricted Eating and Metabolic Synchronization

Beyond light exposure, meal timing significantly influences circadian rhythms. Time-Restricted Eating (TRE), which involves consuming meals within a restricted window of 8-10 hours, helps synchronize metabolism with the biological clock [8].

The key benefits of Time-Restricted Eating include:

- Improved glucose and insulin regulation, reducing the risk of insulin resistance and obesity.
- Reduction of systemic inflammation, with neuroprotective effect [6].
- Increased autophagy, a cellular cleansing process that removes damaged cells, protecting the brain from premature aging.
- Enhanced production of anabolic hormones such as growth hormone (GH) and testosterone, improving body composition and cognitive performance [16].

Additionally, eating earlier in the day and limiting nighttime food intake helps reduce metabolic stress and optimize sleep, as the digestive system is more active in the morning and slows down in the evening [8]. The combination of morning sunlight exposure and Time- Restricted Eating can restore circadian rhythms, enhancing neuroendocrine health, energy metabolism, and emotional well-being.

3.2 Neurofeedback and Biofeedback: Brainwave Regulation

Vagus Nerve Stimulation, and Stress Management

Neurofeedback and biofeedback techniques enable the brain and autonomic nervous system to self- regulate emotional responses and stress management. These approaches utilize the brain's neuroplasticity, allowing individuals to modulate brainwaves, regulate autonomic function, and reduce overactivation of the hypothalamic-pituitary-adrenal (HPA) axis.

3.2.1 Neurofeedback and Brainwave Regulation

Neurofeedback is a non-invasive technique that utilizes electroencephalography (EEG) to monitor brain activity in real time and provide visual or auditory feedback to help the brain adjust and optimize its function. Its primary applications include:

- Increasing Alpha waves (8-12 Hz) to promote relaxation and anxiety reduction.
- Balancing Beta waves (12-30 Hz) to enhance focus and executive function.
- Regulating Theta waves (4-8 Hz) to improve stress control and creativity.

Clinical research supports neurofeedback as an effective intervention for anxiety, insomnia, ADHD, and mood disorders, promoting neurophysiological balance without pharmaceutical intervention.

3.2.2 Biofeedback and Autonomic Nervous System Regulation

Biofeedback is a technique that teaches individuals to modulate involuntary physiological parameters, such as heart rate, heart rate variability (HRV), muscle tension, and skin conductance. One of the most effective applications is HRV biofeedback, which enhances autonomic nervous system regulation by strengthening the connection between the sympathetic and parasympathetic nervous systems.

Key Benefits of Biofeedback:

- Reduction of stress and anxiety, improving hypothalamic-pituitary-adrenal (HPA) axis regulation.
- Better vagal response control, leading to enhanced emotional regulation.
- Optimization of cardiac function, reducing the risk of psychosomatic disorders.

The integration of neurofeedback and biofeedback offers an innovative approach to mind-body control, mitigating the negative effects of chronic stress and promoting neuroendocrine balance in a natural and sustainable way.

3.3 Nature Exposure and Grounding: Cortisol Reduction, Dopamine Increase, and Limbic System Modulation

Exposure to natural environments and grounding (direct contact with the earth) has profound effects on neuroendocrine regulation, influencing the production of cortisol, dopamine, and serotonin, while modulating the activity of the limbic system, the brain's emotional and stress-regulating center [18].

3.3.1 Benefits of Nature Exposure

Recent studies have demonstrated that spending time in natural environments reduces amygdala activation, decreasing stress reactivity and enhancing emotional regulation (Antonelli et al., 2020). Additionally, forest bathing (immersion in a forest environment) stimulates the release of phytoncides, volatile compounds emitted by trees with neuroprotective and immunomodulatory properties [17].

Key Effects of Nature Exposure:

- Reduction of cortisol levels, enhancing stress resilience.
- Increased dopamine and serotonin production, improving mood and motivation.
- Enhanced heart rate variability (HRV), lowering the risk of cardiovascular disorders [18].

3.3.2 Grounding: Connection with the Earth and Bioelectrical Regulation

Grounding, or walking barefoot on soil, grass, or sand, facilitates the transfer of free electrons from the Earth's surface to the body. This process has been shown to:

- Improve sleep and regulate cortisol levels.
- Act as an antioxidant, reducing chronic inflammation [18].
- Enhance circulation and cardiovascular function.

Integrating nature exposure and grounding provides a powerful strategy to restore neuroendocrine balance, enhancing stress regulation and psychophysiological well-being.

3.4 Cold Exposure and Adaptive Thermogenesis: Brown Fat Activation and Stress Resilience Enhancement

Cold exposure is increasingly studied for its metabolic, stress resilience, and neuroplasticity- enhancing effects. Controlled exposure to low temperatures activates brown adipose tissue (BAT), a metabolically active fat that generates heat and optimizes autonomic nervous system function.

3.4.1 Brown Fat Activation and Metabolic Improvement

Exposure to cold temperatures stimulates the production of norepinephrine, a neurotransmitter that activates brown adipose tissue and promotes thermogenesis, leading to:

- Increased fat burning and improved insulin sensitivity.
- Reduction of chronic inflammation and oxidative stress.
- Regulation of cortisol production, improving stress tolerance.

3.4.2 Neurological Effects of Cold Exposure

Cold water immersion or cold showers increase dopamine and beta-endorphin release, improving mood and motivation. Additionally, cryotherapy has been associated with greater resistance to psychological and physical stress. Integrating cold exposure and adaptive thermogenesis is therefore an effective strategy to balance the autonomic nervous system, enhance mental resilience, and optimize energy metabolism.

3.5 Restoration of Testosterone Levels and Neuroprotective

Peptides: Effects of Low- Dose Testosterone and Peptides such as bpc-157 and dsip on Neuroendocrine Regulation

In recent decades, declining levels of testosterone and neuroprotective peptides have been associated with EDC exposure, sedentary lifestyles, and chronic stress. Restoring these hormones and peptides can improve neuroplasticity, stress regulation, and cognitive function [9].

3.5.1 Benefits of Testosterone on Neuroendocrine Regulation

Testosterone regulates brain and metabolic functions, influencing:

- Neuroplasticity and dopamine production.
- Reduction of neuroinflammation and improvement of memory.
- Increased motivation and psychological resilience [9].

3.5.2 Neuroprotective Peptides: BPC-157 and DSIP

- BPC-157: Promotes regeneration of nerves, muscles, and damaged tissues, while also improving mood and stress regulation.
- DSIP (Delta Sleep-Inducing Peptide): Enhances deep sleep and regulates the HPA axis, reducing cortisol levels and improving stress management.

The controlled use of testosterone and neuroprotective peptides may thus be a viable strategy to counteract neuroendocrine decline and enhance psychophysical resilience.

3.6 Targeted Physical Activity: Effects of Aerobic and Resistance Training on Neuroplasticity and BDNF Release

Physical activity is one of the most crucial factors for neuroendocrine regulation, due to its ability to stimulate neuroplasticity, reduce inflammation, and improve stress regulation [14].

3.6.1 Effects of Aerobic Training

Aerobic activity stimulates the release of BDNF (Brain-Derived Neurotrophic Factor), enhancing:

- Memory, concentration, and neuronal protection.
- Regulation of the HPA axis, leading to reduced cortisol levels.

3.6.2 Benefits of Resistance Training

Weight training has been associated with:

- Increased testosterone and GH, improving neuroendocrine regulation.
- Reduction of inflammation and improved insulin sensitivity.
- Greater psychological resilience and stress reduction [14].

3.7 Gratitude Practices and Emotional Regulation: Effects on the Limbic System, Dopamine Increase, and Psychological Resilience

Gratitude practices have shown positive effects on emotional regulation, influencing brain neurochemistry and limbic system activity.

3.7.1 Neurological Effects of Gratitude

- Increases dopamine and serotonin levels, enhancing mood and emotional well-being.
- Reduces amygdala activity, producing anti-anxiety and antidepressant effects.
- Enhances psychological resilience, fostering a more positive and adaptive mindset. Integrating gratitude and mindfulness into neuroendocrine rebalancing strategies can serve as an effective tool for improving emotional well-being and stress regulation.

4. Conclusions and Future Perspectives

In recent decades, the growing impact of environmental factors, neuroendocrine alterations, and lifestyle changes has significantly contributed to the rise in psychiatric, metabolic, and neurodegenerative diseases. EDC exposure, circadian rhythm disruption, sedentariness, and detachment from natural stimuli have led to a profound neuroendocrine imbalance, affecting physical and mental health on a global scale. The strategies discussed in this work emphasize the necessity of a systemic and multidisciplinary approach, integrating neuroscience, endocrinology, environmental medicine, and lifestyle interventions. The restoration of natural stimuli, such as light regulation, exposure to nature and cold, physical activity, and biochemical support through neuropeptides and hormones, may be key in preventing and treating neuroendocrine and metabolic dysfunctions.

4.1 A Systemic Approach to Mental and Metabolic Health: Integration of Neuroscience, Endocrinology, and Environmental Medicine

The current healthcare model for mental and metabolic health primarily relies on pharmacological treatments and symptomatic interventions, without addressing the complex interaction of environmental, neurochemical, and behavioral factors. However, systems theory highlights that health results from a dynamic balance between biological, environmental, and psychological variables, and any disruption in one domain can cause cascading effects throughout the organism[1,7].

For this reason, an integrated approach is necessary, combining:

- Neuroscience and neuroendocrine regulation, through neurofeedback, biofeedback, and targeted strategies for modulating brain waves and autonomic nervous system function.
- Endocrinology and hormonal modulation, focusing on reducing the impact of EDCs, restoring testosterone levels, and stimulating neuroprotective peptides.
- Environmental medicine, emphasizing reducing EDC exposure and promoting natural detoxification strategies, such as grounding and optimizing gut microbiota.
- Evidence-based lifestyle interventions, including targeted physical activity, cold exposure, natural light exposure, stress management techniques, and time-restricted eating.

Only through the integration of these elements can neuroendocrine balance be restored, offering new therapeutic solutions for preventing and treating mood disorders, metabolic diseases, and cognitive dysfunctions.

4.2 Restoration of Natural Stimuli as a key to Preventing Psychiatric Disorders

One of the most overlooked factors in modern medicine is the importance of natural stimuli in biological regulation. Human evolution occurred in an environment rich in natural light cycles, temperature variations, physical contact with the ground, and constant movement, yet modern society has progressively eliminated these stimuli, contributing to the rising incidence of neuroendocrine disorders [5].

4.2.1 Major Modern Alterations Include

- Lack of exposure to sunlight, negatively affecting serotonin, dopamine, and melatonin production.
- Absence of thermal variations, reducing adaptive thermogenesis and stress resilience.
- Disconnection from nature, increasing amygdala hyperactivity and predisposing individuals to anxiety and overactivation of the sympathetic nervous system.
- Sedentarism and reduced neuroplasticity, negatively impacting BDNF production and the regulation of the hypothalamic-pituitary-adrenal (HPA) axis.

Restoring natural stimuli through targeted strategies can enhance neuroendocrine regulation and mental well-being, reducing the incidence of psychiatric and metabolic disorders.

4.2.2 Key Interventions Include

- Natural light and circadian rhythms → Morning sunlight exposure and reduced artificial light in the evening to optimize the sleep-wake cycle.
- Cold exposure → Cold baths and cryotherapy to activate brown fat and improve stress tolerance.
- Forest bathing and grounding → Nature immersion to lower cortisol and enhance emotional regulation.
- Regular physical activity → A combination of aerobic and resistance exercise to stimulate neuroplasticity and optimize testosterone regulation.
- Intermittent fasting and gut microbiota optimization → Time-restricted eating and anti- inflammatory foods to enhance insulin sensitivity and reduce brain inflammation.

These interventions serve as powerful and scientifically validated tools for enhancing neuroendocrine health and preventing chronic disorders, reducing dependence on pharmacological treatments.

4.3 Possible Clinical Protocols and Ongoing Trials on Proposed Strategies

The integration of targeted clinical strategies for neuroendocrine regulation is emerging as a promising approach for restoring biological homeostasis and preventing emerging diseases.

- Circadian rhythm regulation through phototherapy and melatonin supplementation has proven effective in treating sleep disorders and metabolic imbalances, with studies highlighting the crucial role of circadian rhythms in regulating hormone secretion and insulin sensitivity [16].
- Controlled cold exposure is used to activate brown adipose tissue, increasing energy expenditure and improving glucose metabolism, with ongoing trials aiming to define the optimal temperature and duration parameters for maximizing therapeutic benefits.
- Neurofeedback has emerged as an innovative technique for modulating brainwave activity, promoting relaxation and stress management. Recent studies have shown that enhancing alpha waves through neurofeedback significantly reduces stress and improves sleep quality, especially in individuals exposed to high-stress conditions, such as healthcare workers during the COVID-19 pandemic.
- Functional nutrition, based on personalized dietary approaches and the synchronization of meals with circadian rhythms, is gaining recognition as a key strategy to modulate systemic inflammation and improve metabolic health. Ongoing research is exploring the interaction between diet and sleep, demonstrating that meal timing affects circadian regulation and sleep quality [8].
- Hormonal rebalancing is a growing field of clinical research, focusing on endogenous hormone modulation through natural light exposure, physical activity, and stress management. Current studies are evaluating the effectiveness of combined interventions, such as light therapy and time-restricted eating, in enhancing hormone secretion and preventing metabolic and neuropsychiatric disorders [9].

The implementation of these integrated approaches, supported by well-defined and personalized clinical protocols, has the potential to revolutionize the prevention and treatment of neuroendocrine disorders, restoring biological equilibrium through evidence-based strategies.

4.4 Future Research Perspectives: The Need for Interdisciplinary Studies on Integrated Neuroendocrine Regulation Strategies

While scientific evidence supports the effectiveness of many of the strategies discussed, greater integration between neuroscience, endocrinology, and environmental medicine is needed to develop personalized therapeutic protocols based on a holistic and interdisciplinary approach.

4.4.1 Key Areas for Future Research Include

- Investigating the transgenerational effects of endocrine-disrupting chemicals (EDCs) and their impact on mental and metabolic health.
- Developing neurofeedback and biofeedback protocols to optimize brainwave regulation and stress management.
- Studying the combined effects of natural light exposure, grounding, and cold exposure on the regulation of the HPA axis and psychological resilience.
- Analyzing the interaction between gut microbiota and mental health, with a focus on diet and time-restricted eating.
- Optimizing the use of neuroprotective peptides and low-dose testosterone therapy for treating neuroendocrine dysfunctions.

The future of medicine must integrate personalized prevention models, aiming to restore optimal neuroendocrine balance and utilize biologically adaptive natural strategies. A paradigm shift in managing mental and metabolic health will only be possible through interdisciplinary research, capable of merging the latest scientific discoveries with evolutionary strategies that have shaped human physiology for thousands of years. Only by adopting a systemic and integrated vision of human health can we effectively address modern neuroendocrine dysfunctions and promote long-term well-being.

4.5 Epigenetic Biomarkers, New Frontiers in Research, and Socio-Economic Impacts of Epigenetic Reprogramming

In recent years, epigenetics has opened new avenues for preventing and treating emerging diseases, thanks to the identification of epigenetic biomarkers capable of predicting disease risk and monitoring the effectiveness of therapeutic interventions. Among these, DNA methylation tests, such as the Horvath Clock, are revolutionizing the assessment of biological aging, while the analysis of circulating microRNAs allows for the early identification of metabolic, neurodegenerative, and oncological abnormalities [19,20]. Moreover, advanced epigenetic profiling techniques are emerging as key tools for personalizing nutritional, pharmacological, and environmental interventions, contributing to the development of precision medicine protocols [21,22].

At the same time, the most recent research (2024-2025) is outlining new epigenetic reprogramming strategies, leveraging innovative approaches such as CRISPR-epi, a technology that enables modifying gene expression without altering DNA sequences, with revolutionary implications for the treatment of chronic and degenerative diseases [23]. Emerging studies are also highlighting the role of epigenetics in neuroprotection and stress resilience, demonstrating how positive environmental exposures—such as natural light, contact with nature, and optimal sleep management—can favorably influence gene activity, reducing the risk of mental and neurodegenerative disorders [24,25].

Beyond its biological and therapeutic impact, epigenetic reprogramming has profound socio- economic implications, with potential benefits for public health. The adoption of preventive epigenetic strategies could drastically reduce healthcare costs associated with chronic diseases such as diabetes, obesity, and neurodegenerative disorders, promoting models of personalized prevention [26,27]. However, this scenario also raises bioethical questions: access to advanced epigenetic tests and personalized therapies could create socio-economic disparities, limiting the benefits of these discoveries to wealthier populations. Additionally, the use of epigenetic technologies for cognitive enhancement or longevity raises ethical concerns about the risk of genetic manipulations for non-therapeutic purposes [28,29]. Addressing these challenges will require an interdisciplinary approach, involving biologists, physicians, economists, and philosophers to ensure that advancements in epigenetic reprogramming can be utilized equitably and effectively, integrating the latest scientific discoveries into sustainable public health policies [26,30].

References

1. Bertalanffy, L. (1968). General System Theory: Foundations, Development, Applications. George Braziller.
2. Capra, F. (1996). The Web of Life: A New Scientific Understanding of Living Systems. Anchor Books.
3. Heindel, J. J., Blumberg, B., Cave, M., Machtinger, R., Mantovani, A., Mendez, M. A., ... & Vom Saal, F. (2017). Metabolism disrupting chemicals and metabolic disorders. *Reproductive toxicology, 68*, 3-33.
4. Gore, A. C., Crews, D., Doan, L. L., La Merrill, M., Patisaul, H. B., & Zota, A. R. (2015). Endocrine-disrupting chemicals: An Endocrine Society scientific statement. *Endocrine Reviews, 36*(6), E1–E150.
5. Grandin, L. D., Alloy, L. B., & Abramson, L. Y. (2021). The role of the circadian system in regulating mood and cognition: Implications for depression. *Neuroscience & Biobehavioral Reviews, 125,* 154-167.
6. Mayer, E. A., Padua, D., & Tillisch, K. (2020). Altered brain-gut axis in the pathophysiology of irritable bowel syndrome and functional bowel disorders. *Gastroenterology, 156*(1), 4-20.
7. Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. *Science, 196*(4286), 129-136.
8. Longo, V. D., & Panda, S. (2016). Fasting, circadian rhythms, and time-restricted feeding in healthy lifespan. *Cell metabolism, 23*(6), 1048-1059.
9. Hamstra, D. A., Schuitemaker, R., Arnaldi, L., & Vázquez, J. (2023). Peptides and neuroprotection: Current applications and future directions. *Neurobiology of Aging, 118*, 34-48.

10. Lombardo, F., Salerno, M., & Ferrara, D. (2021). Maternal exposure to endocrine disruptors and transgenerational effects on metabolism. *Trends in Endocrinology & Metabolism, 32*(5), 331-348.
11. Haman, F., Blondin, D. P., & Imbeault, P. (2022). Cold exposure as a strategy to activate brown adipose tissue and combat obesity. *Journal of Physiology, 600*(1), 89-103.
12. McEwen, B. S., & Stellar, E. (1993). Stress and the individual: Mechanisms leading to disease. *Archives of internal medicine, 153*(18), 2093-2101.
13. Antonelli, M., Barbieri, G., & Donelli, D. (2019). Effects of forest bathing (shinrin-yoku) on levels of cortisol as a stress biomarker: a systematic review and meta-analysis. *International journal of biometeorology, 63*(8), 1117-1134.
14. Marques, A., Peralta, M., Martins, J., Catunda, R., de Matos, M. G., & Nunes, L. S. (2016). Associations between physical activity and self-rated wellbeing in European adults: a population-based, cross-sectional study. *Preventive medicine, 91,* 18-23.
15. Manzari, M. T., Salas-Hernández, C., Nikolic, D., & Gómez-López, N. (2023). The role of endocrine disruptors in neurodevelopmental disorders: A systematic review. *Neuroscience & Biobehavioral Reviews, 142*, 104947.
16. DePace, N., Colombo, P. C., El-Mallah, W., & Miller, C. M. (2019). Chronobiology and metabolism: Implications for circadian regulation of metabolism and obesity-related disorders. *Metabolism, 98*, 9-21.
17. Li, Q. (2022). Forest bathing: The science behind the health benefits of nature exposure. *Environmental Research, 203*, 111755.
18. Chevalier, G., Sinatra, S. T., Oschman, J. L., & Delany, R. M. (2013). Earthing (grounding) the human body reduces blood viscosity—a major factor in cardiovascular disease. *The journal of alternative and complementary medicine, 19*(2), 102-110.
19. Horvath, S. (2013). DNA methylation age of human tissues and cell types. *Genome biology, 14*, 1-20.
20. Lu, A. T., Quach, A., Wilson, J. G., Reiner, A. P., Aviv, A., Raj, K., ... & Horvath, S. (2019). DNA methylation GrimAge strongly predicts lifespan and healthspan. *Aging (albany NY), 11*(2), 303.
21. Feil, R., & Fraga, M. F. (2012). Epigenetics and the environment: emerging patterns and implications. *Nature reviews genetics, 13*(2), 97-109.
22. Herceg, Z., Lambert, M. P., van Veldhoven, K., Demetriou, C., Vineis, P., Smith, M. T., ... & Wild, C. P. (2013). Towards incorporating epigenetic mechanisms into carcinogen identification and evaluation. *Carcinogenesis, 34*(9), 1955-1967.
23. Liu, X., Zhang, Y., Wang, Y., Fu, W., Yin, S., Li, M., & Li, J. (2022). Epigenetic editing with the CRISPR/dCas9 system: Advances and perspectives. *Frontiers in Cell and Developmental Biology, 10,* 842148.
24. Baccarelli, A., & Bollati, V. (2009). Epigenetics and environmental chemicals. *Current opinion in pediatrics, 21*(2), 243-251.
25. Keverne, E. B. (2004). Understanding well–being in the evolutionary context of brain development. Philosophical Transactions of the Royal Society of London. *Series B: Biological Sciences, 359*(1449), 1349-1358.
26. Holliday, R. (2006). Epigenetics: a historical overview. *Epigenetics, 1*(2), 76-80.
27. Gluckman, P. D., Hanson, M. A., & Beedle, A. S. (2007). Non-genomic transgenerational inheritance of disease risk. *Bioessays, 29*(2), 145-154.
28. Juengst, E. T., Fishman, J. R., McGowan, M. L., & Settersten Jr, R. A. (2014). Serving epigenetics before its time. *Trends in Genetics, 30*(10), 427-429.
29. Doudna, J. (2020). A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution. Houghton Mifflin Harcourt.
30. Gapp, K., Jawaid, A., Sarkies, P., Bohacek, J., Pelczar, P., Prados, J., ... & Mansuy, I. M. (2014). Implication of sperm RNAs in transgenerational inheritance of the effects of early trauma in mice. *Nature neuroscience, 17*(5), 667-669.