Biomedical & Translational Science

Review Article

Sources of Human's Aggression, Violence, Antisocial and Addictive Behaviors

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- Received Date: 27 May 2022
- Accepted Date: 03 Jun 2022
- Publication Date: 07 Jun 2022

Keywords: Malnutrition, poverty, violence, antisocial behavior, addiction, epigenetics

Abstract

In the 21st century hunger, starvation and malnutrition is still a scourge of mankind. According to World Bank reports a rise of millions of people lacked year-round access to adequate food in 2020 compared to 2019. Malnutrition, poverty, lack of quality education and insufficient health care are causes and consequences of each other. Preconceptual, prenatal and early postnatal malnutrition have life-long negative consequences on human's health and behavior via epigenetic processes that regulate gene expression providing short-term survival benefits but predispose to various pathological conditions in adulthood. Based on scientific research there is not any doubt that early epigenetic changes play a major role in the development of excessive aggression, violence, antisocial and addictive behaviors. A body of evidence shows that clinical pictures like oppositional defiant disorders (ODD), conduct disorders (CD) and antisocial personality disorders (APD) have a neurodevelopmental origin based on epigenetic changes of gene expression. It is suggested that only early intensive therapeutic interventions focusing on autonomy, sense of competence and social connectedness in an individualistic, systemic and tightly structured positive and safe environment including healthy lifestyle and nutrition could prevent the progression of ODD into CD and eventually into APD.

Quality nutrition, quality education and adequate health care for every human, starting at the very first days of life, are claimed to be unconditional premises to transform humanity into a peaceful species able to deal with the future challenges and dangers of life on planet earth.

Introduction

According to the WHO's definition malnutrition comprises deficiencies, excesses or imbalances of nutrients intake. The WHO definition covers undernutrition, micronutrient deficiencies, overweight, and diet-related noncommunicable diseases [1]. The WHO reported that almost two billion adults are overweight, while almost half of a billion are underweight. Millions of children under the age of 5 years were found to be overweight or obese, while other millions were found underweight, stunted and wasted. Another reported disturbing number indicates that almost one third of women of reproductive age on the planet are affected by anemia through iron deficiency. The WHO concluded that undernutrition results in people's reduced ability to recover after a crisis, impairs cognitive functions, increases susceptibility to chronic illnesses, results in reduced social skills and as an overall consequence causes dependence on ongoing support [1,2]. Agendas to eradicate malnutrition are made by the African Union as far as reaching till 2063 [3]. The effects of these plans are at least questionable within the next decades. New catastrophes, like the recently launched Ukrainian war, threaten the world with unforeseen fatal consequences.

In a recent report of the World Bank, Januray 31, 2022 we can read: "Many countries are facing growing levels of food insecurity, reversing years of development gains, and threatening the achievement of Sustainable Development Goals by 2030 (…)" [4]. This report tells us also that more than hundred million more people were suffering from chronic hunger in 2020 compared to 2019. Thus, despite of enormous efforts to eradicate hunger in the world the number of hungry people increases rapidly.

Wars, natural catastrophes and their consequences on human's health later in life

Wars and armed conflicts are one of the main causes of hunger and undernutrition of population groups. Because of its sharply

Citation: Franzek EJ, de Jager B, Heffels L, Poot JW, Ofehe S. Sources of Human's Aggression, Violence, Antisocial and Addictive Behaviors. Biomed Transl Sci. 2022; 2(2):1-8

defined period the "Dutch hunger winter 1944/45" during World War II became one of the most studied hunger periods in scientific history. During the last period of the Second World War the German authority commanded a total embargo on the western part of Netherland in retaliation for assisting the Allied troops in the well-known military operation Market-Garden in September 1944. The following period a whole population was confronted from one day to the other with severe famine and starvation. More than 22.000 inhabitants of the Western Netherlands died from direct consequences of starvation. The normalization of food supply took place just as suddenly after the day of liberation from Nazi-Germany on 12th May 1945. A great variety of somatic and mental disorders later in life were found to be a consequence of prenatal hunger exposure [5-7]. Interestingly, a strong association of male offspring with antisocial personality disorder and nutritional deficiency in the early stage of gestation have also been reported [8]. In addition, recent studies show that prenatal exposure to famine put the offspring at high risk for addictive behaviors later in life. The crucial periods of exposure were found to be the first trimester of gestation in men and the third trimester in women [9,10]. This remarkable gender effect has not an easy explanation. In addition, till today, there are other not yet sufficiently explained gender differences and correlations, such as that substance use disorders occur 2 – 3 times more often among men than women [11], antisocial personality traits are found to be highly comorbid among men with substance use disorders and the prevalence of antisocial personality disorder in general is estimated to be three times higher in male individuals with addictive behaviors compared to non-addicted populations [12]. Franzek et al. [10] replicated another puzzling finding: 1.7 up to 4.9 more boys than girls were born in the groups with addictive behaviors, whereas the ratios boys to girls range between 0.95 to 1.05 in those without addictive behaviors. It is important to know that the gender ratio males/females at time of birth without manipulation is normally found to be very stable since centuries at about 105 boys to 100 girls (1.05) with only little differences among different populations, countries and continents [13-17].

It is hypothesized that pre-conceptional exposure to malnutrition of both mothers and fathers would have a critical impact on sex determination in favor of male offspring. A continued prenatal and early postnatal exposure to malnutrition should then impact the brains development with persisting antisocial personality traits and liability to addictive behaviors in adolescence and adulthood [10].

Several other studies corroborate the findings of the "Dutch hunger winter". People who had been exposed prenatally to the Biafran famine during the Nigerian civil war in 1967 – 1970 were found to have increased rates of hypertension and type 2 diabetes at the age of 40 years compared to those not had been exposed in utero to the famine [18]. People prenatally exposed to famine during the Great Leap Forward in China 1959 – 1961 have shown an increased risk of developing diabetes, hypertension and schizophrenia compared to non-exposed individuals [19, 20]. In Austria people born around the three periods of famine that struck the country in 1918-1919, 1938 and 1946 – 1947 showed an excess risk of diabetes compared to non-exposed individuals [21]. Comparable effects were obvious as long-term effects of the Greek famine 1941 - 1942 [22]. People exposed prenatally to famine through the severe monsoon in Bangladesh in 1974-1975 that destroyed the majority of the annual rice crop had significantly higher rates of type 2 diabetes than non-exposed individuals [23]. In Gambia variations in periconceptional nutrient availability have been shown to affect health and longevity in adulthood [24].

Malnutrition and poverty

Malnutrition is linked to poverty as high rates of malnutrition are found in areas with chronic poverty [25,26]. The impact of poverty on populations includes poor nutritional status, food insecurity, vulnerability to disease, reduced productivity levels, and compromised physical and intellectual development. People living in poverty are unable to access necessities including healthy nutritious food, good living standards, hygienic environment, appropriate shelter and sanitation, and adequate education and health care [26,27]. Poverty is multifaceted and not limited to average income and wealth. The Multidimensional Poverty Index [28] described poverty to be a deprivation of basic amenities that restricts people from leading a good and healthy life taking into account the systemic disparities within a country and communities [29]. Especially countries afflicted by conflicts and war, poor governance, and natural disasters are prone to experience an enormous burden of poverty. Poverty leads to consumption of cheap, high-energy staple foods rather than nutritionally quality food. The consequences are nutrient deficiencies. The deficiency of micronutrients is a dangerous component of malnutrition, including deficiencies of iron, folate, vitamin A, iodine and zinc. Macro- and micro-malnutrition, in particular early in life and adolescence disrupts mental and physical development, cause impaired health and educational and economic performance later in life. Malnutrition and nutritional imbalances reduce human capital and work capacities, making countries and communities susceptible to poverty. Children who are not adequately nourished are at risk for failing to reach their developmental potential in cognitive, motor, and socioemotional abilities and these abilities are strongly linked to academic achievement and economic productivity [30]. A vicious cycle exists between poverty and malnutrition [26]. It has to be concluded that malnutrition, poverty, poor education levels and insufficient health care supply are causes and consequences of each other.

Epigenetic effects of (prenatal) malnutrition

Epigenetic processes are intensively studied during the last years and have influenced substantially our knowledge about the human genome and gene expression [31].

Epigenetic mechanisms are the link between genes and environmentally induced behavior and seem to allow an organism to respond to the environment through changes in gene expression. Recent research has demonstrated that complex 'epigenetic' mechanisms, which regulate gene activity without altering the DNA code, can have long-lasting effects within mature neurons [32]. Through epigenetic mechanisms gene expression can be turned on (gene activation) and turned off (gene silencing or deactivation). Epigenetics can change the way how and if at all a DNA sequence is read and translated into a gene product (protein). Epigenetic marks can be passed on from cell to cell as cells divide, and from one generation to the next. Epigenetic changes include DNA methylation, histone modification and non-coding RNA. Disruption of one or other of these interacting systems can lead to inappropriate expression or silencing of genes, resulting in 'epigenetic diseases':

- DNA methylation means adding a chemical group to specific places of DNA where it blocks reading the gene (= turn the gene off). DNA demethylation can turn a gene expression on.
- Histone modification is when DNA wraps around proteins called histones. DNA then cannot be accessed by proteins to read the gene, the gene is turned off. Genes not wrapped around histones are turned on. Chemical groups can be added or removed from histones and change whether a gene is unwrapped (= turned on) or wrapped (= turned off).
- Non-coding RNA regulates coding-RNA. Coding-RNA is used to make gene products (proteins). Non-coding RNA helps to control gene expression by attaching to coding RNA and can, along with certain proteins, breaks down the coding-RNA so that it cannot be used to make gene products (proteins). Non-coding RNA can also use certain proteins to modify histones to turn genes on (activation) or turn genes off (deactivation) [33, 34].

Epigenetic changes begin already prenatally [35], they can change throughout life span [36], and some can be added or removed in response to changes in behavior or environment [37]. A body of research indicates that epigenetic regulation of gene expression plays a critical role in linking prenatal malnutrition to the risk of later life (metabolic) disorders [38,39]. It has been postulated that both structure and physiology of the developing organism can be adapted to unfavorable growth conditions providing short-term survival benefits but predispose to various pathological conditions in adulthood [40]. Poor nutritional status during prenatal and early postnatal development may lead to compensatory epigenetic and functional alterations in key organs (liver, muscle, pancreas, heart, long, brain), which then persist throughout life, being no longer beneficial but a source of pathology later in life [35,41-47]. A comprehensive assessment of genome-wide DNA methylation differences in people exposed to the great Chinese famine in utero with an in vitro study (nutrition deprived fibroblasts) highlighted that the nervous system and neurogenesis pathways were the most affected by nutritional deprivation. The study revealed consistently hypomethylation in relation to nutrition deprivation in both Chinese famine and fibroblast in vitro samples. No occurrences of hypermethylation were identified. A reduced methylation efficacy, for instance, due to the limited production of the methyl donor S-adenosyl methionine (SAMe) which is dependent on nutrients such as betaine, folate, vitamin B1, B6, and B12, was suggested [48, 49]. This could mean that normal epigenetic regulations cannot be processed if nutrition does not contain essential basic components. Based on current science there is not any doubt that pre- and early postnatal malnutrition can have long-lasting negative effects via epigenetic modulations on health and behaviors of affected individuals later in life.

Epigenetics of aggression and violence

During evolution of all mammalian species, including humans, aggression provided (provides) the best chances for survival and reproduction [50,51]. Aggressive behavior is mostly determined by testosterone levels acting on the brain already in the embryonic stage. Testosterone activates the subcortical areas of the brain to produce aggression, while cortisol and serotonin act antagonistically with testosterone to reduce its effects through facilitating prefrontal area cognitive control on impulsive tendencies aroused in the subcortical structures [52]. In recent years modern science about epigenetics not only have transformed our knowledge and understanding of the fine interaction between genes and environment [34] but also have provided a novel tool to understand the molecular events that underlie aggression and violence. Periods of high sensitivity to the environment, such as prenatal life, infancy and early adolescence are vulnerable for lasting epigenetic changes in genes, involved in exaggerate aggression [53].

Research data show that repeated aversive life events and chronic stress during pregnancy, especially during the first trimester of gestation, and during childhood, here especially during the first 2 years of life, including emotional abuse or witnessing violence, can cause increased risk of aggressive tendencies, delinquency and conduct disorder in early childhood and adolescence and physical aggressive behavior in adulthood [54-57]. It has been found that low basal levels of blood cortisol have been associated with externalizing behavior in childhood and adolescents. A negative correlation of low cortisol levels was reported to low self-control and a positive correlation was found to delinquent behavior and proactive and reactive aggression [58-60]. Blood cortisol levels are controlled by the HPA axis (stress axis). It has been shown that hypomethylation of genes which translates into augmented inhibitory control of the HPA axis are induced by early adverse family environment and represent a risk factor for aggressive externalizing behavior in adolescence [61].

Based on recent research there is little doubt that early epigenetic changes through abnormal DNA methylation, both hypomethylation and hypermethylation, play a major role in the development of dysfunctional behaviors like conduct disorder, excessive aggression, violence and antisocial behavior in adolescence and adulthood [53, 62- 65].

Research also clearly indicates that nutrition has a direct role in the epigenetic regulation of DNA methylation pathways by altering the substrates, cofactors and enzymes that are necessary for proper DNA methylation [66]. Thus, unbalanced diet and malnutrition during crucial developmental periods in life, starting prenatally, are suggested to be important factors predisposing to aggression, violence and antisocial behaviors later in life.

Antisocial personality disorder: a neurodevelopmental disease

According to Raine [67] antisocial personality disorder (APD) and early onset conduct disorder (CD) should be defined as neurodevelopmental disorders. A neurodevelopmental disorder per definition has its origins in childhood, is characterized by abnormalities in brain structure and function, accompanied by neurocognitive impairments and has a genetic/epigenetic basis and a stable course throughout development continuing into adult life [68]. In order to diagnose an APD three of the following symptoms have to be present since age 15 years: criminal behavior, deceitfulness and conning, impulsivity and lack of planning, aggression and violence, reckless disregard for safety, irresponsibility, and lack of remorse. Furthermore,

evidence of CD with symptoms of oppositional defiant behavior before the age of 15 years are required for a proper diagnosis. A pervasive and callous violation of the rights of others is a special feature of psychopathy which should, proposed by Raine [67], and included in future DSM revisions as a specifier of APD.

Individuals with early (fetal) maldevelopment of the Limbic System (Cavum Septum Pellucidum) showed higher scores on APD, psychopathy and criminal behavior suggesting that this maldevelopment could predispose individuals to the spectrum of antisocial disorders [69]. A body of evidence showed impairments of prefrontal subregions of the brain, the amygdala and the striatum in APD which can be linked to features like impulsivity, poor behavior control, aggression and lack of planning, disinhibited reward driven behavior, and insensitivity to the threat of punishment [67]. Malnutrition during early prenatal brain development can surely be one important factor leading to brain maldevelopment possibly based on dysfunctional epigenetic changes. The prefrontal-amygdala-striatal brain system is also very susceptible to early stress and social adversity, very common in the social histories of individuals with APD [70] and a possible target area of epigenetic changes in individuals primarily vulnerable caused by prenatal and early postnatal adversities, for example malnutrition. Hypermethylation of the MAO-A (Mono-amino-oxidase) promoter has been found in offenders with APD [65], which can be linked to the finding of lower brain levels of MAO-A in the orbitofrontal cortex and ventral striatum in APD individuals [71] causing symptoms of high impulsivity, reward seeking behavior and liability to violent behavior. Greater methylation of the oxytocin gene (OXTR) in children with CDs has been associated with lower circulating levels of oxytocin [72], a finding that can explain lack of empathy and poor emotion recognition in callous-unemotional children with CDs. Methylation findings on aggression have also implicated the serotonin system in both boys and girls [73, 74]. There is little doubt that epigenetic processes, such as methylation processes, play an important role in the predisposition to develop CDs and APDs assigning them to the spectrum of neurodevelopmental disorders.

Early health risk factors with early teratogenic influences also can be linked to CDs and antisocial behavior [75]: Birth complications [76,77], prenatal smoking exposure [78], prenatal alcohol exposure [79-81], heavy metal exposure [82], air pollutants [83,84], traumatic brain injury [85, 86] and, as already outlined, prenatal nutritional deficiency.

Interestingly, neurodevelopmental disorders at all, tend to be more common in males than females, estimated at three males for every female.

Can antisocial and violent behavior be reversed with bio-psycho-social treatment strategies in childhood and adolescence?

Although APD is one of the most researched personality disorder, it is still surprisingly resistant to treatment and there is no specific medication recommended [67]. Studies suggest that symptoms of APD are worst around 24 to 44 years of age, then tend to improve slightly after age 45. Before age 18, the condition gets diagnosed as CD and the precursor of CD is oppositional defiant disorder (ODD), one of the most commonly diagnosed mental health conditions in childhood [87]. It is suggested that all three conditions, ODD, CD and APD should be viewed as neurodevelopmental disorders with a common pathway. Coexisting and complicating conditions are Attention Deficit Disorder (ADHD) and drug/alcohol addiction. As neurodevelopmental disorders particularly early therapeutic interventions should be considered. There is evidence that early intervention and school based programs along with individual therapy can help prevent ODD [88]. Studies have also shown that intervening with parents is one of the most effective ways to reduce the behavioral symptoms of ODD in all age groups [89, 90]. For those who do not have treatment, ODD can develop into CD, and those with CD almost 40% are found to develop APD in adulthood [91]. A progression from ODD to CD and APD, however, should be absolutely prevented in order to improve human coexistence in societies and communities. A recently developed treatment approach in a Youth Clinic and Health Care Group in the Netherlands might be able to stop this progression [92, 93]. The treatment aims to provide a solution for many young people aged 13 to 25 with behavioral disorders, such as ODD and CD, mood disorders, impulse control disorders and addictions. Both the youths and parents are satisfied with the treatment results and a great deal of them does not need any specialist mental health care anymore [94- 96]. The youngsters recover, go to school or work and give their quality of life a high score again [97,98]. The treatment approach seems to have halted the destructive negative spiral resulting in developing APD by intensively teaching alternative and socially positive behaviors breaking through dysfunctional survival behavior. Because of age and comorbidity mainly a transdiagnostic treatment is offered. Evidence based Methods as Motivational Interviewing, Cognitive Behavioral Therapy and Community Reinforcement Approach, Attachment Based Family Therapy are used. Treatment refers to the motivation to change. Based on the Self-determination theory of Deci and Ryan [99,100] treatment focuses on the three basis psychological needs: Autonomy, sense of competence and social connectedness with positive group dynamics to build a safe environment to learn. The treatment also promotes a healthy lifestyle with great awareness on healthy nutrition and unconditional acceptance of all people and is individualistic, systemic and tightly structured. The treatment is done in collaboration with remedial educationalists, psychologists, nurses and psychiatrists, coaches and experience experts in a 7 days/24 hours clinical setting, a day clinical setting and aftercare including self-help groups [93].

Summary

Hunger, starvation, macro- and micro-malnutrition are still major challenges of humanity, despite enormous progresses in economic and agricultural developments as well as nutrition and food sciences. Almost one third of the world's population has suffered at least once from food insecurity and lack of adequate food in 2020. Wars, armed conflicts, natural disasters, climate change, environmental degradations and other adversities are the main causes of severe malnutrition of population groups. A scientific established and often confirmed finding is that prenatal and early postnatal malnutrition predispose affected individuals to a variety of somatic and mental diseases, including antisocial and addictive behaviors later in life. Recently, it is hypothesized that pre-conceptional exposure to malnutrition of both mothers

and fathers would have a significant impact on sex determination in favor of male offspring. A continued prenatal and early postnatal exposure to malnutrition should then impact the brains development with persisting antisocial personality traits and liability to addictive behaviors in adolescence and adulthood. It is known that low socio-economic status is associated with poor health and unhealthy food consumption. Poverty leads to consumption of cheap, high-energy staple food rather than nutritionally quality food which can cause severe deficiencies of essential basic components like vitamins and minerals. It is known that low socio-economic status and malnutrition are risk factors for substance use disorders and antisocial personality disorders. Malnutrition is labeled as one of the most common causes for an individual's suboptimal physical and mental development, malnutrition reduces the developmental potential in cognitive, motor, and socio-emotional abilities of humans. It is known that a vicious cycle exists between malnutrition, poverty, lack of quality education and insufficient somatic and mental health care. All these factors are important issues contributing to a restricted development of nations.

Research clearly indicates that malnutrition has a direct role in the epigenetic regulation of gene products by altering the substrates, cofactors and enzymes that would be necessary for proper epigenetic processes. A body of evidence shows that unbalanced diet and malnutrition during crucial developmental periods in life, starting prenatally, are, via epigenetic changes, important factors predisposing to aggression, violence and antisocial behaviors later in life. There is also not any doubt that early epigenetic changes play a major role in the development of dysfunctional behaviors like oppositional defiant disorder, conduct disorder, excessive aggression, violence and antisocial behaviors in adolescence and adulthood. According to the literature it is suggested that oppositional defiant disorder, conduct disorder and antisocial personality disorder should be viewed as neurodevelopmental disorders with a common pathway and eventually based on early epigenetic changes. Coexisting and complicating conditions are Attention Deficit Disorder (ADHD) and drug/alcohol addiction. Interestingly, neurodevelopmental disorders at all, tend to be more common in males than females, estimated at three males for every female. This fits the recent finding that significantly more boys than girls were born in groups with addictive behaviors later in life compared to groups without addictive behaviors.

Although antisocial personality disorder is one of the most researched personality disorders, it is still surprisingly resistant to treatment and there is no specific medication available. In order to improve human's peaceful coexistence, however, a progression from oppositional defiant disorder to conduct disorder and eventually to antisocial personality disorder should be absolutely prevented. The main therapeutic focus could be laid on epigenetic deactivation of old genetically based behaviors, like excessive aggression and violence as they have been advantageous behaviors in ancient times for survival and reproduction. A promising approach in this direction has been recently developed in the Netherlands. Creating new and functional behaviors via an intensive therapeutically guided treatment approach in childhood and adolescence, individualistic, systemic and tightly structured, promoting autonomy, sense of competence and social connectedness, including healthy lifestyle with great awareness for healthy nutrition is proposed to help extinguishing and avoiding the settling of permanent antisocial behaviors.

Final conclusions

The eradication of malnutrition and poverty would mean to eradicate and ban wars and armed conflicts between population groups and countries first. As long as people were born, have to grow up and live in life threatening conditions and adverse environments with lack of proper food, lack of education and insufficient health care, high liabilities to aggression, violence, antisocial and addictive behaviors will persist as important character traits of humans. Future mankind, however, needs to be dominated by equality, justice, compassion, empathy and altruism based on strong self-confidence and mind. Access to and affordability of quality nutrition and education, access to adequate healthcare for every human from the very first days of life are claimed to be unconditional premises to transform humanity into a peaceful species that can successfully deal with the future challenges and dangers of life on planet earth.

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