



## In the Cloud of Stress- Revisiting the Complex Cycle of Junk Food Consumption, Micronutrient Imbalance and Cognitive Perturbation

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### Abstract

**Background:** The escalating prevalence of chronic stress in modern lifestyle dismantles the body's adaptive capacity leading to a spectrum of significant cognitive anomalies. This compromised cognitive state diminishes individuals' ability to make rational and health-promoting dietary choices, creating a predisposition for the consumption of junk food, which, in turn, exacerbates cognitive deficits and perpetuates a self-reinforcing loop of maladaptive dietary patterns and cognitive deterioration.

**Objective:** The present study, based on existing literature, explores the complex interplay encompassing stress-induced cognitive disruption, suboptimal dietary patterns, and micronutrient deficiencies.

**Methods:** The present work undertook extensive literature review to synthesize the findings of literature retrieved from searches of computerized databases, hand searches and authoritative texts.

**Results:** The study revealed confounding yet simultaneously occurring dual feedback loops which brings on surface the issues how appeal of unhealthy food is reinforced and taste-driven stress alleviation strengthens inclination toward such dietary choices. The neural circuitries in the whole affair unquestionably involve the mostly studied CNS areas, which collectively mediate their responses through dopamine in shaping reward-based motivation, emotional associations, and decision-making.

**Conclusion:** Although information in the current context is available in pieces, a comprehensive and consolidated presentation is lacking. The present review is engrossed to cater the deeper psycho-physiological crosstalk intelligibly satisfying an overall objective of reaching the common readers and to generate public awareness.

**Highlights:** Cognitive Perturbation Stemming Differentially from Stress in One Hand and Micronutrient Imbalance Due to Junk Food Consumption on the Other Hand Have Common Mediator Though Follow Different Neural Loops. Cognition is representative of brain functions which psychology refers to as mental processes involving tasks like- thinking, attention and language, learning, memory, perception and motor skill. None of the processes, in isolation, claims to be discrete ability rather they are all intimately interactive elements in a web. Collective, systematic and sequential interactions of the mental functions allow individuals to perform as healthy adults as evident from the Abilities of solving problems, retrieval of memory and decision making. Lifestyle denotes the mode of living either of an individual or a group with all the inherent sensations and characters namely- habits, attitudes, emotion, morality, economic status, likings and disliking etc. All these attributes assemble under an umbrella called cognition. Thus, it is somewhat obvious that lifestyle factors will influence cognition. The present review aims to discuss cognitive effects under situations of life stressors and stress-driven unhealthy eating habit(s). Overlapping reports are available from extensive literature search that emphasize the involvement of brain regions starting from the prefrontal cortex, hippocampus, amygdala to areas of the mesolimbic system and explore the magic role of dopamine neurotransmitter in either mechanism. However, the present work describes comprehensively the novel stimulus-effect circuitry through which the ultimate result of cognitive perturbation ensues.

**Keywords:** Junk Food; Cognitive Perturbation; Micronutrient Imbalance; Stress; Brain Reward System

Introduction

A stressful cognitive state frequently manifests cognitive perturbation which is nothing but a visible cognitive deficit representing a stressful personal or social lifestyle [1]. Lifestyle is a modifiable factor with immense impact (positive or negative) on cognitive attributes [2]. Addiction to food is a frequently experienced element of lifestyle showing an irresistible inclination to some specific food choices. Mood, behavior, emotion, stress, thoughts, and health awareness are all known lifestyle modifiers that directly or indirectly govern food intake patterns including food choices. Food choice is indeed a serious issue in terms of determining physical and mental health because food elements, both macro and micro, dictate health and well-being for which their quantity and quality both are important [3]. The requirements of micronutrients vary during periods of the life cycle. Such variation is based on functional challenges during different phases of the cycle [4]. Tissue constructions or re-constructions, different phases of growth and differentiation during the initial 1000 days of life starting from conception, altered/elevated metabolism, compromised digestive functions and above all various diseased states are indicative of increased demand for micronutrients [5]. The silent increased demand for micronutrients is referred to as ‘hidden hunger’ which, if not addressed properly, will display deficiency symptoms.

The present review emphasizes micronutrient issues - their deficiencies, link with wrong food choices and overall impact on cognitive activity. The work further envisages the possible interplay of integrated circuit(s) in the whole affair involving one or more signaling molecule(s). Authors in the current work target to present the piecemeal information in a wholesome comprehensive package for better understanding of a serious lifestyle phenomenon.

Methodology

This review article was developed to explain comprehensively the mechanism how stress creates an irresistible inclination toward junk food and junk food subsequently handle efficiently two simultaneously occurring vicious cycles, itself occupying the centre, and getting help from a single mediator dopamine (Figure 3). The diagram (Figure 3) is self explanatory which clearly depicts the co-occurrence of the positive and negative loops highlighting the central theme of the study.

The search was carried out in the months of October and November 2019, using the electronic database PubMed, through the medical subject headings (MeSH) combinations: (“caloric restriction” OR “calorie restriction”) AND (cognition OR “cognitive function” OR “clinical evaluation of dementia” OR “cognitive psychotherapies” OR “Mental Status and Dementia Tests” OR “cognitive therapies”). We identified 175 studies initially. Then, we decided to select only studies published between 2009 and 2019, in order to analyze a reasonable sample of works and more recent ones. Thus, we exclude studies not published in the last ten years and performed in vitro and with humans (n = 106), remaining only studies performed with experimental animals in vivo (n = 69). Publications such as reviews, comments, media, protocols, as well as duplicate articles, were excluded, resulting in the selection of 46 publications manuscripts. Then, we excluded studies addressing CR effects on humans, which still remained selected due to some error in the algorithm. Thus, 39 studies were analyzed in this review (Figure 1).

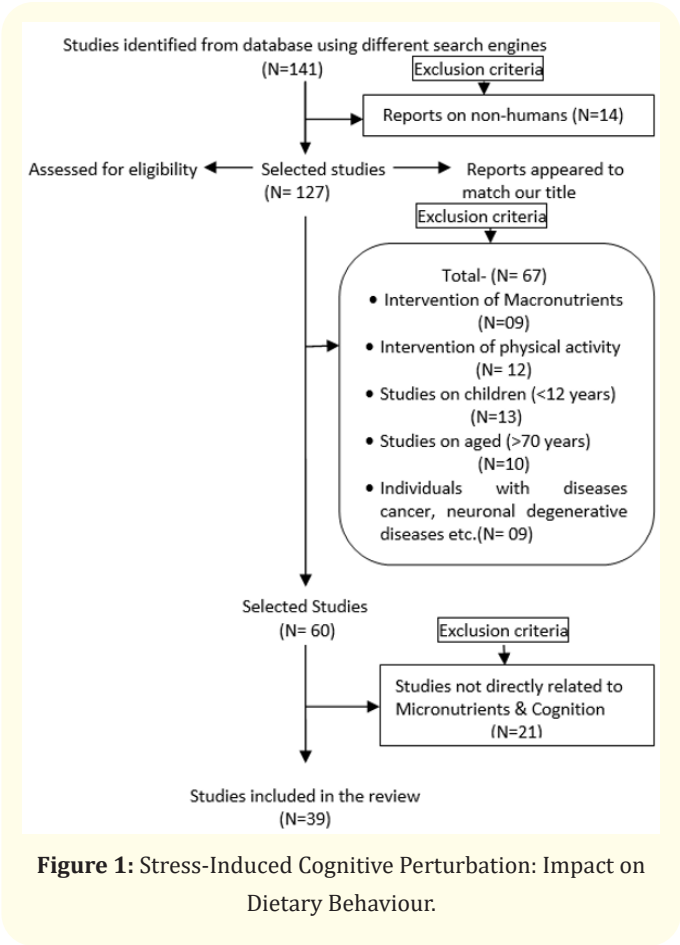


Figure 1: Stress-Induced Cognitive Perturbation: Impact on Dietary Behaviour.

**Stress-induced cognitive perturbation: impact on dietary behaviour**

The term ‘cognition’ encompasses different processes essentially connected with survival which make living organisms understand their environment [6]. Interaction between an organism and its environment starts with the input. As signals from the environment impinge upon the organism, sensations are detected by sense organs which end up with perception. Perception finally drives appropriate organismal response based on previous learning/current context. As we fit our everyday living into this general framework of stimulus-perception-response, we observe a subset of processes that make social living meaningful through appropriate motor movement, facial expressions, social decision making etc. [7]. The intricate interplay between these cognitive processes not only facilitates individual adaptation but also underpins the foundation of complex social interactions, allowing organisms to navigate and thrive within their ecological niches [8,9].

Modern lifestyles are often characterized by chronic stress stemming from various sources such as work pressure, financial burdens, interpersonal conflicts, and societal demands [10]. Chronic stress triggers a cascade of physiological responses, including the release of stress hormones (cortisol and adrenaline), oxidative stress, and inflammatory processes [11]. These responses, when prolonged, can lead to a state of “allostatic load,” wherein the body’s adaptive capacity is overwhelmed, leading to negative health outcomes, including cognitive impairment (Figure 2) [10]. For example, depression and anxiety are the leading causes of mental disability in all societies worldwide, [12] no matter if it is visible or beyond diagnosis. Subclinical symptoms of depression and anxiety affect the mental well-being of a far greater population than those suffering from similar conditions appropriately diagnosed [13]. Depression, anxiety and lifestyle (particularly eating habits) are seemingly correlated in a neural network as causal and consequences [14].

**Amygdala and emotional reactivity**

Central to the stress response is the amygdala, a vital brain region implicated in the processing of emotional and fear-related stimuli [15]. In response to stress, the amygdala undergoes heightened activation, leading to increased emotional reactivity and vigilance [16]. This heightened emotional state can enhance the motivational value of food, making unhealthy options more appealing (Figure 2) [17].

**Involvement of prefrontal cortex in decision-making**

The dorsolateral area within the prefrontal cortex has a participatory role in an array of cognition related functions namely mobilization of working memory, decision-making and similar controlling functions related to cognition [18]. During stress, however, the delicate balance between the amygdala and the prefrontal cortex is disrupted (Figure 2). The prefrontal cortex’s inhibitory control

over the amygdala is attenuated, leading to heightened amygdala-driven reactivity and emotional responses [19]. Consequently, the DLPFC’s (Dorsolateral Prefrontal Cortex) capacity for effective top-down control over cognitive processes is compromised, contributing to impaired decision-making, impulsivity, and the inability to consider long-term consequences [20]. This can lead individuals to seek immediate gratification through the consumption of rewarding foods, notably junk food (Figure 2,3) [21].

**Hippocampus and memory impairment**

The hippocampus, a critical hub for memory formation and consolidation is also intricately affected by stress [22]. The chronic release of stress hormones, particularly glucocorticoids like cortisol, can lead to structural alterations in the hippocampus, including dendritic retraction and reduced neurogenesis. These changes culminate in impairments in spatial memory, episodic memory, and context-dependent learning, thereby exacerbating cognitive perturbations (Figure 2) [23]. The HPA (hypothalamic-pituitary-adrenal) axis, is a functionally well-known system that regulates stress with which the hippocampus has an intimate association and the circuitry is the element that mediates stress-induced altered cognitive functions by feedback mechanisms [24]. Impaired regulation of this axis can lead to changes in appetite-regulating hormones like leptin and ghrelin, potentially contributing to over-eating (Figure 2) [25].

**Neuroplasticity and long-term effects**

Chronic stress can cause enduring modifications to cognitive functions by altering synaptic plasticity within the corresponding neural circuits. Repeated activation of the stress response systems can lead to maladaptive plasticity, contributing to the persistence of cognitive perturbations even after the stressor has subsided [26]. This can create a predisposition for heightened emotional reactivity, cognitive biases, and difficulties in regulating emotions [26].

*Illustration Fig-2:* The schematic diagram delineates the neural dynamics that propels the consumption of junk food in the face of stress in contemporary lifestyles. Stress activates the amygdala to its heightened state of activity and influences food motivation. The prefrontal cortex loses inhibitory control, impairing executive functions and fostering impulsive decision-making. Chronic stress also impacts the hippocampus, compromising memory functions. The depicted negative reinforcement loop illustrates how the brain associates junk food consumption with stress relief, reinforcing a pattern of seeking comfort through unhealthy eating behaviors.

**The negative reinforcement loop**

Negative reinforcement represents a behavioral phenomenon in which certain behaviour is strengthened by the removal/avoidance of an aversive or unpleasant stimulus. In the context of stress-induced consumption of junk food, negative reinforcement operates

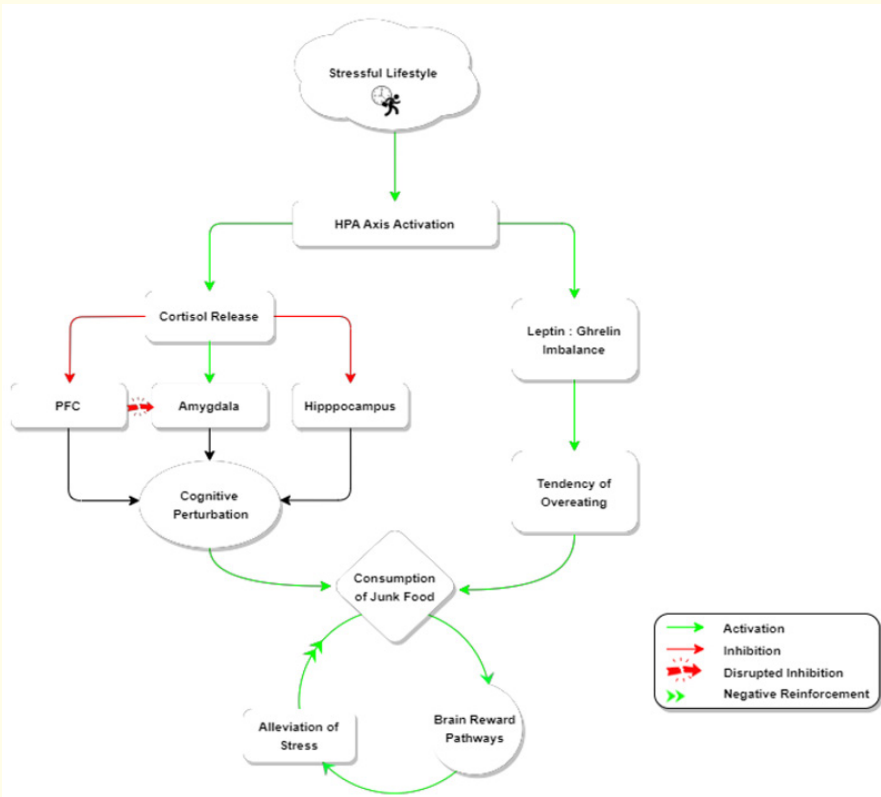


Figure 2: The Neural Symphony of Emotional Eating.

through a learned association between the consumption of such foods and the alleviation of stress [27]. Chronic stress triggers the release of stress hormones like cortisol by activating the brain's stress response systems (Figure 2) [28]. The consumption of high-calorie, palatable foods, often referred to as “comfort foods,” can activate brain reward pathways, including the release of dopamine in the striatum (Figure 2) [29-31]. This activation provides a temporary relief from the physiological and psychological effects of stress, establishing a negative reinforcement loop where the act of consuming junk food is reinforced by the reduction in stress-related discomfort (Figure 2,3) Over time, this association can become ingrained, leading to a pattern of seeking out and consuming unhealthy foods as a way to cope with stress [32-34].

Dopamine and desire: Understanding the pull of junk food

Junk food, scientifically referred to as “energy-dense, nutrient-poor” food, is a category of consumable products that are characterized by their high caloric content relative to their minimal nutritional value [35]. These mainly include convenience food, for example, high sugar-containing cereals, foods with saturated fats, junk items like chicken nuggets even soft drinks- which are all basically packaged foods. The phenomenon of positive reinforcement from junk food is intricately rooted in the neurobiology of reward processing (Figure 3) [35].

Neurotransmitters and reward pathways

Food is a versatile reward element to the animal world including humans [36]. Reward is a desired target of all living creatures. Reward feeling is a signal-dependent perception processed by a

specific neural network in the CNS. Dopamine is the key player in the arousal of reward sensation and its release reinforces the causal stimulus to maintain the great subjective feeling (Figure 2,3) [37].

Mesolimbic system

The mesolimbic system, responsible for reward processing, plays a key role in generating the final perception of reward [38]. The system includes several diverse structures involved in cooperative activity for a single output in the form of ‘reward feeling’. ‘Reward’ is a natural process that drives an individual’s behavior in search of a known positive stimulus [37]. Neurotransmitters being ultimate scorers of neural functions often play in combination to generate the desired output. In reward perception, the various structures and neurotransmitters of the mesolimbic system play under the captaincy of dopamine which recognizes food, drink, sex, social interaction, substance abuse etc. as positive stimuli [39]. The ventral striatum, specially the NAcc (Nucleus Accumbens) have a major contribution in the event of reward processing (Figure 3) [40]. However certain other brain substrates such as the striatal GABAergic neurons cannot be overlooked as they carry out the overall striatal output [41-43]. It is enough relevant to explain the fact of addiction owing to substance abuse where the mesolimbic reward producing system is hijacked without any obvious biological significance resulting in the development of a villainous cycle of irresistible inclination toward the substance of abuse [44-46].

Motivation: Rationale of doing things we do

The ‘brain reward system’ is constituted of a complex neural network displaying sophisticated circuit functions [47]. These cir-



cuitries amazingly make us capable of differentiating between necessities and rewards [48].

When junk food is consumed, sensory cues associated with taste and smell activate the VTA (Ventral Tegmental Area) (Figure 3), prompting the release of dopamine. This dopamine surge is

then transmitted to the NAcc, where it binds to dopamine receptors [49]. The activation of these receptors gives rise to an intense feeling of pleasure, effectively reinforcing the behavior that led to the release of dopamine – in this case, consuming junk food. This process forms the basis of positive reinforcement, where the pleasurable effects of consuming junk food serve to increase the likelihood of repeating the behavior (Figure 2,3).

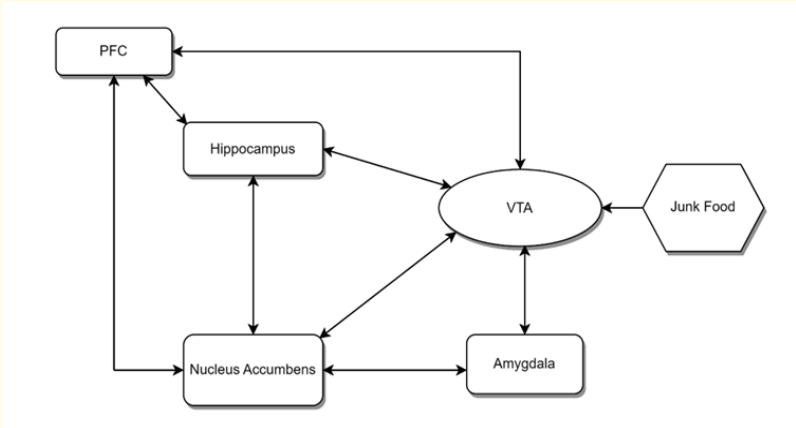


Figure 3: Dopamine Dynamics: The Neuroscience of Pleasure.

*Illustration Fig-3:* A simplified schematic illustrates the intricate network of reciprocal connections among several key brain regions, namely the hippocampus, amygdala, Prefrontal Cortex (PFC), Ventral Tegmental Area (VTA), and Nucleus Accumbens (NAc) in the context of dopamine signaling. In standard physiological conditions, this circuit regulates an individual’s motivation and incentive drive, prompting to repeat actions that lead to reward, thus forming the basis of positive reinforcement. The primary reward circuit involves dopaminergic projections from the VTA to the NAc, where dopamine release is triggered by reward-related cues, notably the consumption of “junk food”. Dopamine’s influence also extends beyond the reward pathway as it enhances the reward-associated memories, intensifies the emotional association between reward and pleasure, and influences decision-making through the multifaceted interplay among the hippocampus, amygdala and PFC, thus contributing to the development of strong emotional cravings for such indulgent food choices over time.

**Dopamine, memory enhancement, and emotion processing**

Dopamine signaling extends beyond the confines of the reward pathway; it is also characteristically involved in the enhancement of memories associated with reward and this is accomplished through the strengthening of synapses within the hippocampus (Figure 2,3) [50]. Consequently, experiences associated with pleasure, such as the consumption of highly palatable junk food, are more likely to be sculpted into memory, further reinforcing the preference for such foods [51]. Dopamine also significantly influences the amygdala and prefrontal cortex (Figure 2,3) [52]. The amygdala, a key structure for processing emotions, is deeply involved in the emotional aspect of reward perception. The influx of dopamine in the amygdala during junk food consumption strengthens the emotional association between the act of eating junk food

and the pleasure derived from it [15]. As a result, the brain begins to link the consumption of junk food with positive emotional states, reinforcing the desire to repeat this behavior to recreate those feelings of pleasure (Figure 3) [53]. Concurrently, reasoning, planning, executive functions and the regulation of emotions are remarkable higher order cognitive functions which essentially involve the prefrontal cortex. The heightened dopamine levels within this region during the consumption of junk food can not only lead to the creation of emotional associations with the rewards derived from junk food, but it can also affect decision-making processes by biasing individuals toward seeking out rewarding experiences, such as consuming junk food (Figure 2,4) [54]. Over time, this neural interplay contributes to the development of strong emotional cravings for and associations with these unhealthy foods, making it challenging for individuals to resist their allure [55].

Remarkably, this intricate interplay between the brain’s reward system and junk food consumption aligns with the concept of reward learning in neuroscience, where it is well-established that the anticipation of a reward often exerts a more substantial influence on emotional reactions and memories than the reward itself [37]. In this context, the unexpected or greater-than-expected pleasure derived from junk food consumption serves to increase dopamine signaling, further reinforcing the development of unhealthy food habits and cravings [56]. However, it is worth mentioning that the dopamine response varies from person to person [57]. Some individuals exhibit heightened reward sensitivity, with their brains releasing more dopamine in response to pleasurable stimuli, including the sensory experience of junk food. For them, this heightened dopamine release creates a potent positive reinforcement loop, making junk food consumption exceptionally rewarding. Consequently, they may develop a stronger preference and craving

for such foods, potentially leading to habit formation. Conversely, individuals more sensitive to punishment might experience guilt or discomfort after consuming junk food, acting as a hindrance against such dietary choices [50].

**Hedonic Overdrive and Craving**

Junk food’s composition triggers a release of dopamine that surpasses the levels elicited by natural, nutrient-dense foods. This intense dopamine release creates what is often termed a “hedonic overdrive,” wherein the brain perceives the experience as exceptionally pleasurable. The result is a potent reinforcement loop – individuals come to associate the consumption of junk food with a heightened sense of reward, motivating them to seek out and consume these foods repeatedly (Figure 2,4) [56].

**Classical conditioning and neural associations**

Beyond the immediate biochemical effects, junk food consumption becomes intertwined with environmental cues and contextual factors through classical conditioning [58]. The brain forms strong associations between the act of consuming junk food and the circumstances in which it occurs. These associations are established through neural connections that link the sensory experiences of consuming junk food with the release of dopamine and the ensuing pleasure (Figure 2) 59].

Over time, these connections lead to the formation of neural pathways, creating an intricate web of associations between cues like sight, smell, or even emotional states and the pleasurable experience of consuming junk food. Consequently, encountering these cues triggers cravings and anticipatory responses, even when the individual is not hungry. This further solidifies the preference for junk food and perpetuates the cycle of positive reinforcement (Figure 2,3) [60].

**Neuroplasticity prepares the ground of habit formation**

With repeated consumption, the brain’s neuroplasticity – its capacity to reorganize and adapt – plays a crucial role in habit formation. The positive reinforcement loop (Figure 2,3) reinforces the neural pathways that underlie the behavior of seeking out and consuming junk food. These pathways become increasingly entrenched, making the act of consuming junk food an automatic, habit-driven behavior [61].

**Micronutrient issues: Long-term impact of junk food consumption - mechanisms and consequences**

Energy Generation and cellular functioning are the two aspects that are met by macro and micronutrients for the sustenance of the life cycle [62]. For humans, the principal source of nutrients (both macro and micro) is our diet [63]. The requirements of the macro and micronutrients are keenly associated with the lifestyle [62]. In a broader perspective the various micronutrients are irreplaceable owing to their individual discrete properties and

functions. Contrary to this macronutrients can transiently substitute one another until the internal milieu gets deranged [63]. But surprisingly modern dietary landscape is characterized by an unprecedented abundance of ultra-processed products that, while often fulfilling macronutrient requirements, tend to fall short in delivering adequate levels of essential micronutrients, namely vitamins and minerals [64]. These micronutrients play pivotal roles in numerous physiological processes, supporting immune function, cellular metabolism, and overall well-being. However, the prevalence of ultra-processed foods, characterized by their convenience, extended shelf life, and palatability, has led to a concerning trend of inadequate micronutrient intake among individuals [65]. While the immediate pleasures of indulging in such foods are undeniable, their long-term consequences on human health justify closer examination. This comprehensive exploration searches for the intricate mechanisms through which the persistent habit of consuming junk food can lead to a chronic micronutrient imbalance.

**Diminished nutrient density**

Junk foods are often high in calories but low in vital nutrients. These foods are typically laden with unhealthy fats, refined sugars, and sodium while being deficient in essential vitamins, minerals, and dietary fiber. Consequently, individuals who predominantly consume junk food may inadvertently ingest an excess of calories without meeting their micronutrient requisites [66].

**Inadequacy of essential vitamins and minerals**

Junk food is deficient in several essential vitamins and minerals that are indispensable for the sustenance of diverse bodily functions. For instance:

- **Vitamins:** Junk food tends to be deficient in vitamins such as A, C, D, E,K, and various B vitamins (B1, B2, B3, B6, B12), all of which play integral roles in supporting the immune system, energy metabolism, bone health, and overall cellular functionality.
- **Minerals:** These foods often lack minerals including calcium, magnesium, potassium, iron, zinc, and selenium, all of which are pivotal for bone integrity, nerve and muscular function, and antioxidant defense mechanisms [67].

**Impact on digestion and absorption**

The extensively processed nature of junk food can negatively impact the digestive system, impeding the absorption of vital nutrients. Prolonged consumption of unhealthy fats and refined sugars can lead to gut inflammation and compromise the integrity of the gut lining, ultimately reducing nutrient absorption [68].

**Enhanced nutrient excretion**

The excessive sodium content commonly found in junk food can lead to increased excretion of critical minerals such as calcium, magnesium, and potassium. This exacerbates the propensity for micronutrient imbalances within the body [69].

**Displacement of nutrient-rich foods**

Regular consumption of junk food may supersede the inclusion of nutrient-rich whole foods in the diet. Opting for junk food over fruits, vegetables, whole grains, and other nutrient-dense options can lead to a dearth of essential micronutrients that are abundant in whole foods [70].

**Detrimental effects on gut microbiota**

The lack of dietary fiber in junk food can perturb gut health, diminishing the diversity and population of beneficial gut bacteria. A thriving gut microbiome is essential for optimal nutrient absorption and overall well-being [71].

**Development of poor eating habits**

Habitual consumption of junk food can lead to a preference for unhealthy, nutrient-poor foods. This can create a cycle of poor dietary choices, perpetuating micronutrient deficiencies over time [72]. Over time, the combination of these factors can culminate in various micronutrient deficiencies or imbalances, which may manifest in symptoms such as fatigue, weakened immune system, poor skin health, decreased cognitive function, bone-related issues, and an increased risk of chronic diseases.

**Micronutrient imbalance and cognitive perturbation**

Micronutrients are essential for brain development, neurotransmitter synthesis, and maintenance of neuronal integrity [73]. Functions such as the synthesis of diverse neurotransmitters, the metabolic breakdown of macromolecules, and the subsequent elimination of resulting by-products underscore the indispensable need for micronutrients in brain tissue [74]. Symptoms like amnesia, ataxia, confusion, psychosis etc. associated with thiamin deficiency as seen in Wernicke-Korsakoff syndrome, dementia in pellagra which is characterized by niacin and tryptophan deficiency are examples of cognitive impairment associated with specific micronutrient deficiency [75].

Vitamin B complex, along with vitamin C and several key minerals like zinc, magnesium, and calcium, plays a vital role in ensuring optimal cognitive functions through their metabolic interdependence [76]. Each member participates actively to maintain a chain of biochemical reactions. Members of the B complex family are known to function as cofactors of a good number of enzymes involved in intermediary metabolism. Apart from the role of vitamin C in collagen synthesis of the skin,[77] its prevalence in the brain tissue [78] justifies the role in the maintenance of cognitive behavior [79]. The minerals, in addition to their role as cofactors in metabolic reactions are also crucial in the elicitation and maintenance of membrane excitability and neurotransmission [67]. Unlike calcium, other minerals characteristically associated with cognitive performance cannot be stored in the tissues, hence dietary supplementation of those minerals appears to be essential. Mechanisms by which micronutrients influence cognitive functions can be categorized into four groups: (a) by influencing brain energy require-

ments; (b) by neuronal membrane and receptor modification; (c) via their role in homocysteine metabolism; and (d) through their role in neurotransmitter synthesis [76].

- **Influencing Brain Energy Requirements:** Micronutrients participate in energy metabolism within the brain, which is highly energy-demanding. Vitamin B complex, particularly thiamine (B1), riboflavin (B2), niacin (B3), and pantothenic acid (B5), are important co-factors in energy-producing pathways such as the Krebs's cycle and glycolysis [80].
- **Neuronal Membrane and Receptor Modification:** Micronutrients like omega-3 fatty acids, vitamin E, and zinc are instrumental in maintaining the integrity of neuronal membranes and modulating neurotransmitter receptor function. In view of signal transmission and receptor sensitivity, the importance of Omega-3 fatty acids in the cell membrane is well known [81]. Vitamin E's antioxidant properties protect neuronal membranes from oxidative stress. Zinc is implicated in synaptic plasticity and receptor signaling. Deficiencies in these micronutrients can disrupt neuronal communication and increase vulnerability to neurodegenerative diseases [81].
- **Homocysteine Metabolism:** Homocysteine is an amino acid derived from methionine metabolism, and its accumulation in the blood is associated with cognitive decline and neurodegenerative disorders. Micronutrients such as folate, vitamin B12, and vitamin B6 are crucial for homocysteine metabolism. These vitamins participate in converting homocysteine to other beneficial molecules, thereby reducing its neurotoxic effects. Deficiencies in these vitamins contribute to elevated homocysteine levels and increase the risk of cognitive impairment and neurodegenerative diseases [82].
- **Neurotransmitter Synthesis:** Micronutrients, such as vitamins and minerals, are crucial for the synthesis of neurotransmitters. For instance, vitamin B6 (pyridoxine) is essential for the synthesis of dopamine, serotonin and norepinephrine, which are involved in mood regulation, reward mechanisms, and focus. Deficiencies in vitamin B6 can lead to mood disorders and cognitive impairment [67].

The influence of micronutrient imbalances on cognitive perturbation thus extends deeply into the intricate neural circuitry of the brain, notably in regions focal for cognitive and emotional processes. The prefrontal cortex, responsible for executive functions and decision-making, is susceptible to compromised function due to inadequate micronutrient intake, potentially leading to impulsivity and decision-making impairments [76]. The hippocampus, crucial for memory and spatial navigation, is highly sensitive to oxidative stress and inflammation which get worse due to micronutrient inadequacy, ultimately leading to potential memory deficits. Furthermore, the amygdala, critical for emotional processing, can experience dysregulation of neurotransmitter systems due to micronutrient deficiencies, potentially intensifying stress-induced cognitive perturbation (Figure 2-4) [15].

Therefore, the accrued information strongly suggests that optimum nourishment is the key factor to fight stress. The “hidden brain hunger,” which encompasses the cognitive and emotional deficits resulting from nutrient (both micro and macro) imbalances, is fundamental to cause aggression and emotional outbursts sometimes well beyond courteousness in public speaking.

Conclusion

Chronic stress, stemming from the relentless demands and pace of modern lifestyle, has become an increasingly prevalent concern. The constant exposure to environmental stressors, work-related pressures, societal expectations and a lack of time for relaxation and self-care pushes individuals into prolonged unphysiological stress leading to manifestations of multiple adverse consequences on physical health and mental well-being. Cognitive perturbation or cognitive dysfunction as a result of such persistent activation of the body’s stress response system has emerged as one of the most serious concerns. In the present review authors have made an attempt to highlight the complex relationships encompassing stress-induced cognitive perturbation, dopamine-driven unhealthy dietary habits and micronutrient imbalance.

Chronic stress-induced cognitive perturbation imposes pronounced down-modulation of various cognitive performances including executive dysfunction, reduced working memory capacity, and impaired cognitive flexibility, rendering individuals less capable of making rational and health-conscious dietary choices. Such cognitive deficits, marked by compromised information processing, impulse control and prospective planning, set the stage for the allure of junk food consumption (Figure 2 and 4). Consequently, the allure of immediate gratification conferred by the consumption

of junk food becomes even more potent within the context of cognitive perturbation. Junk food provides a readily accessible means to mitigate cognitive discomfort (Figure 4).

As individuals persist in their consumption of nutritionally deficient, yet palatable foods, micronutrient deficiencies continue to compound. Essential vitamins and minerals, integral for synaptic plasticity, neurotransmission, and neuroprotection, remain suboptimal, further compromising cognitive performance and emotional regulation. The synergy involving cognitive perturbation, maladaptive dietary patterns, and micronutrient deficiencies begets a self-reinforcing loop, wherein cognitive deficits not only perpetuate but intensify the proclivity towards unhealthy dietary habits, and the continuation of such dietary habits further solidifies cognitive deterioration (Figure 3). Such interdependence results in a pernicious cycle that poses formidable challenges to interruption without the implementation of targeted, multidimensional interventions.

*Illustration Fig-4:* The schematic depiction captures the complex relationship between stress-induced cognitive perturbation, unhealthy dietary habits, and micronutrient deficiencies. The cognitive disruption sets the stage for an increased attraction to junk food. Consequently, the sustained consumption of nutritionally deficient yet palatable foods perpetuates micronutrient deficiencies, further compromising cognitive functions. The diagram also elucidates the reinforcement dynamics between cognitive states and dietary choices through dual feedback loops: a positive loop wherein the allure of junk food (R) is strengthened by the pleasurable effects (S) it induces, and a negative loop where the inclination towards junk food (R) is reinforced by the ameliorative impact (S) stemming from stress alleviation.

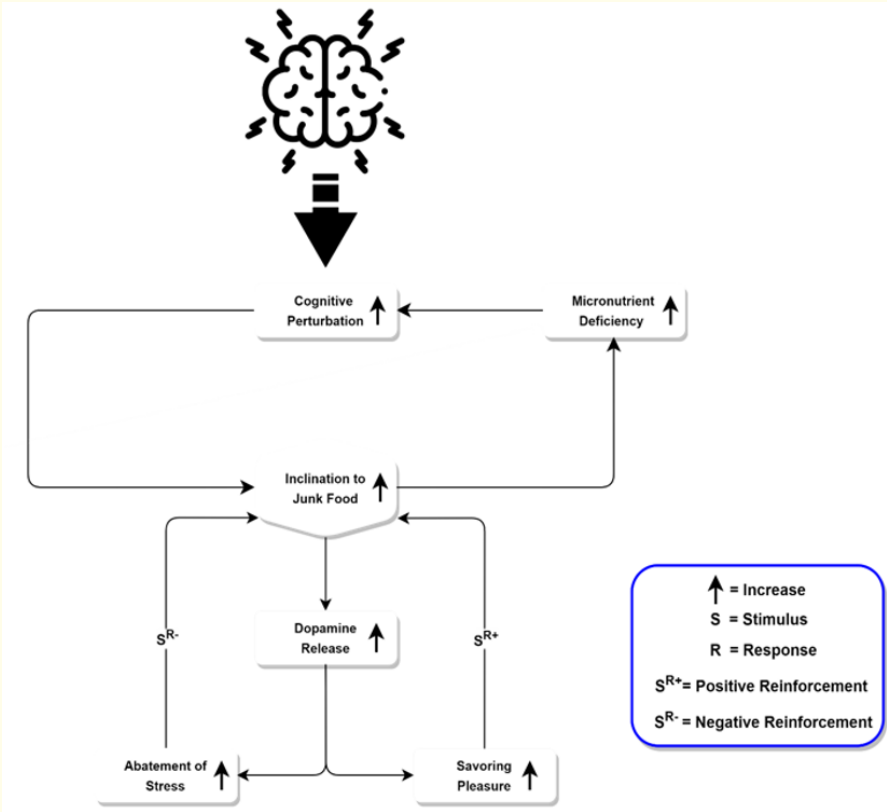


Figure 4: Dietary Dystopia: A Ballet of Stress, Dietary Choice and Cognitive Health.



In this context, it is highly relevant to mention that doctors even confronted with stressed patients complaining of non-specific, especially cognitive symptoms, should consider the possibility of marginal micronutrient deficiency and the potential benefits of micronutrient supplementation. Recognizing the role of micronutrients in cognitive health underscores the importance of a balanced and nutrient-rich diet in maintaining cognitive function and overall well-being, offering a potential avenue for intervention to break this detrimental cycle. This not only promotes cognitive resilience but also contributes to fostering a more harmonious and emotionally balanced society, where individuals are better prepared to navigate the challenges of modern life while upholding civil and rational discourse.

Authorship

The first and the second authors have equal contribution in the present review work. Aindrila Das participated in initial planning of the review, did the literature survey, referencing and initial drawing. Swarnabha Chowdhury helped to navigate the direction of the study and assisted providing some critical references. Swarnabha also did the final modification of the figures to make those more meaningful and presentable. Swarnabha also checked the similarity of the manuscript. Both Aindrila and Swarnabha constantly motivated the corresponding author through their positive inputs relating to the analysis. The entire study is the brain child of Samir Kumar Ghosh who also composed the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest (Financial or any other) with respect to the research, authorship, and/or publication of this article.

Bibliography

1. Pechtel P and Pizzagalli DA. "Effects of early life stress on cognitive and affective function: An Integrated Review of Human Literature". *Psychopharmacology (Berl)* 214.1 (2011): 55-70.

2. Hughes TF and Ganguli M. "Modifiable Midlife Risk Factors for Late-Life Cognitive Impairment and Dementia". *Current Psychiatry Reviews* 5.2 (2009): 73-92.

3. Chen Y., et al. "Importance of Nutrients and Nutrient Metabolism on Human Health". *Yale Journal of Biology and Medicine* 91.2 (2018): 95-103.

4. K Biesalski Hans and Tinz Jana. "Micronutrients in the life cycle: Requirements and sufficient supply". *NFS Journal* 11 (2018): 1-11.

5. Beluska-Turkan K., et al. "Nutritional Gaps and Supplementation in the First 1000 Days". *Nutrients* 11.12 (2019): 2891.

6. Kaplan S and Berman MG. "Directed attention as a common resource for executive functioning and self-regulation". *Perspectives on Psychological Science* 5 (2010): 43-57.

7. Frith CD. "Social cognition". *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 363.1499 (2008): 2033-2039.

8. Shatil E. "Does combined cognitive training and physical activity training enhance cognitive abilities more than either alone? A four-condition randomized controlled trial among healthy older adults". *Frontiers in Aging Neuroscience* 5 (2013): 8.

9. Atkinson RC and Shiffrin RM. "Human memory: A proposed system and its control processes. In K. Spence (Ed.)". *The Psychology of Learning and Motivation* 2 (1968).

10. Schneiderman N., et al. "Stress and health: psychological, behavioral, and biological determinants". *Annual Review of Clinical Psychology* 1 (2005): 607-628.

11. Mifsud KR and Reul JMHM. "Mineralocorticoid and glucocorticoid receptor-mediated control of genomic responses to stress in the brain". *Stress* 21.5 (2018): 389-402.

12. Friedrich MJ. "Depression is the leading cause of disability around the world". *JAMA* 317 (2017): 1517.

13. Johnson J., et al. "Service utilization and social morbidity associated with depressive symptoms in the community". *JAMA* 267 (1992): 1478-1483.

14. Firth J., et al. "Food and mood: how do diet and nutrition affect mental wellbeing?" *BMJ* 369 (2020): m2382.

15. Šimić G., et al. "Understanding Emotions: Origins and Roles of the Amygdala". *Biomolecules* 11.6 (2021): 823.

16. Yamamoto T., et al. "Increased amygdala reactivity following early life stress: a potential resilience enhancer role". *BMC Psychiatry* 17.1 (2017): 27.

17. Yau YH and Potenza MN. "Stress and eating behaviors". *Minerva Endocrinology* 38.3 (2013):255-267.

18. Friedman NP and Robbins TW. "The role of prefrontal cortex in cognitive control and executive function". *Neuropsychopharmacology* 47 (2022): 72-89.

19. Tottenham N and Galván A. "Stress and the adolescent brain: Amygdala-prefrontal cortex circuitry and ventral striatum as developmental targets". *Neuroscience and Biobehavioral Reviews* 70 (2016): 217-227.

20. Zhai T., et al. "Functional connectivity of dorsolateral prefrontal cortex predicts cocaine relapse: implications for neuromodulation treatment". *Brain Communications* 3.2 (2021): fcab120.

21. Veit R., et al. "Diminished prefrontal cortex activation in patients with binge eating disorder associates with trait impulsivity and improves after impulsivity-focused treatment based on a randomized controlled IMPULS trial". *NeuroImage. Clinical* 30 (2021): 102679.

22. Kim EJ., *et al.* "Stress effects on the hippocampus: a critical review". *Learning and Memory (Cold Spring Harbor, N.Y.)* 22.9 (2015): 411-416.

23. McEwen BS. "Physiology and neurobiology of stress and adaptation: central role of the brain". *Physiol Rev* 87.3 (2007): 873-904.

24. Smith SM and Vale WW. "The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress". *Dialogues in Clinical Neuroscience* 8.4 (2006): 383-395.

25. Yeung AY and Tadi P. "Physiology, Obesity Neurohormonal Appetite and Satiety Control. [Updated 2023 Jan 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing (2023).

26. Radley J., *et al.* "Chronic stress and brain plasticity: Mechanisms underlying adaptive and maladaptive changes and implications for stress-related CNS disorders". *Neuroscience and Biobehavioral Reviews* 58 (2015): 79-91.

27. Schaumberg K., *et al.* "The role of negative reinforcement eating expectancies in the relation between experiential avoidance and disinhibition". *Eating Behaviors* 21 (2016): 129-134.

28. Hargreaves KM. "Neuroendocrine markers of stress". *Anesthesia Progress* 37.2-3 (1990): 99 -105.

29. Rangel A. "Regulation of dietary choice by the decision-making circuitry". *Nature Neuroscience* 16.12 (2013): 1717-1724.

30. Jauch-Chara K and Oltmanns KM. "Obesity--a neuropsychological disease? Systematic review and neuropsychological model". *Progress in Neurobiology* 114 (2014): 84-101.

31. Weltens N., *et al.* "Where is the comfort in comfort foods? Mechanisms linking fat signaling, reward, and emotion". *Neurogastroenterology and Motility* 26.3 (2014): 303-315.

32. Volkow ND., *et al.* "Food and drug reward: overlapping circuits in human obesity and addiction". *Current Topics in Behavioral Neurosciences* 11 (2012): 1-24.

33. Davis C., *et al.* "Evidence that 'food addiction' is a valid phenotype of obesity". *Appetite* 57.3 (2011): 711-717.

34. Potenza MN. "Obesity, food, and addiction: emerging neuroscience and clinical and public health implications". *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology* 39.1 (2014): 249-250.

35. Vanderkooy A., *et al.* "High unhealthy food and beverage consumption is associated with poor diet quality among 12-35-month-olds in Guédiawaye Department, Senegal". *Frontiers in Nutrition* 10 (2023): 1125827.

36. Alonso-Alonso M., *et al.* "Food reward system: current perspectives and future research needs". *Nutrition Reviews* 73.5 (2015): 296-307.

37. Lewis RG., *et al.* "The Brain's Reward System in Health and Disease". *Advances in Experimental Medicine and Biology* 1344 (2021): 57-69.

38. Small DM., *et al.* "Feeding-induced dopamine release in dorsal striatum correlates with meal pleasantness ratings in healthy human volunteers". *Neuroimage* 19 (2003): 1709-1715.

39. Hernandez L and Hoebel BG. "Food reward and cocaine increase extracellular dopamine in the nucleus accumbens as measured by microdialysis". *Life Sciences* 42.18 (1988): 1705-1712.

40. Marche K., *et al.* "Differences between Dorsal and Ventral Striatum in the Sensitivity of Tonically Active Neurons to Rewarding Events". *Frontiers in Systems Neuroscience* 11 (2017): 52.

41. Balleine BW., *et al.* "The role of the dorsal striatum in reward and decision-making". *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 27.31 (2007): 8161-8165.

42. Schultz W., *et al.* "Neuronal activity in monkey ventral striatum related to the expectation of reward". *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 12.12 (1992): 4595-4610.

43. Daniel R and Pollmann S. "A universal role of the ventral striatum in reward-based learning: evidence from human studies". *Neurobiology of Learning and Memory* 114 (2014): 90-100.

44. Kemp JM and Powell TP. "The structure of the caudate nucleus of the cat: light and electron microscopy". *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 262.845 (1971): 383-401.

45. Graveland GA and DiFiglia M. "The frequency and distribution of medium-sized neurons with indented nuclei in the primate and rodent neostriatum". *Brain Research* 327.1-2 (1985): 307-311.

46. Dorothy O. "The percentage of interneurons in the dorsal striatum of the rat, cat, monkey and human: A critique of the evidence". *Basal Facts* 3 (2013): 19-24.

47. Michaelsen MM and Esch T. "Understanding health behavior change by motivation and reward mechanisms: a review of the literature". *Frontiers in Behavioral Neuroscience* 17 (2023): 1151918.

48. Smith AD., *et al.* "Quantitative microdialysis of dopamine in the striatum: effect of circadian variation". *Journal of Neuroscience Methods* 44 (1992): 33-41.

49. Sorokowska A., *et al.* "Food-Related Odors Activate Dopaminergic Brain Areas". *Frontiers in Human Neuroscience* 11 (2017): 625.

50. Bromberg-Martin ES., *et al.* "Dopamine in motivational control: rewarding, aversive, and alerting". *Neuron* 68.5 (2010): 815-834.

51. Samson L and Buijzen M. "Craving healthy foods?! How sensory appeals increase appetitive motivational processing of healthy foods in adolescents". *Media Psychology* 23.2 (2020): 159-183.

52. Jackson ME and Moghaddam B. "Amygdala regulation of nucleus accumbens dopamine output is governed by the prefrontal cortex". *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 21.2 (2001): 676-681.

53. Adams RC., *et al.* "Food Addiction: Implications for the Diagnosis and Treatment of Overeating". *Nutrients* 11.9 (2019): 2086.

54. Tyng CM., *et al.* "The Influences of Emotion on Learning and Memory". *Frontiers in Psychology* 8 (2017): 1454.

55. Giuliani NR., *et al.* "Neural systems underlying the reappraisal of personally craved foods". *Journal of Cognitive Neuroscience* 26.7 (2014): 1390-1402.

56. Volkow ND., *et al.* "Dopamine and the control of food intake: implications for obesity". *Trends in Cognitive Sciences* 15.1 (2011): 37-46.

57. Sonne J., *et al.* "Dopamine. In: StatPearls [Internet]". Treasure Island (FL): StatPearls Publishing (2023).

58. Johnson AW. "Eating beyond metabolic need: how environmental cues influence feeding behavior". *Trends in Neurosciences* m36.2 (2013): 101-109.

59. Singh M. "Mood, food, and obesity". *Frontiers in Psychology* 5 (2014): 925.

60. Morales I and Berridge KC. "Liking' and 'wanting' in eating and food reward: Brain mechanisms and clinical implications". *Physiology and Behavior* 227 (2020): 113152.

61. Mendelsohn AI. "Creatures of Habit: The Neuroscience of Habit and Purposeful Behavior". *Biological Psychiatry* 85.11 (2019): e49-e51.

62. Carreiro AL., *et al.* "The Macronutrients, Appetite, and Energy Intake". *Annu Rev Nutr* 36 (2016): 73-103.

63. Biesalski Hans K and Tinz Jana. "Micronutrients in the life cycle: Requirements and sufficient supply". *NFS Journal* 11 (2018): 1-11.

64. Brouwer I., *et al.* "Reverse thinking: taking a healthy diet perspective towards food systems transformations". *Food Security* (2021): 13.

65. Capozzi F., *et al.* "A Multidisciplinary Perspective of Ultra-Processed Foods and Associated Food Processing Technologies: A View of the Sustainable Road Ahead". *Nutrients* 13.11 (2021): 3948.

66. Singh SA., *et al.* "Junk food-induced obesity- a growing threat to youngsters during the pandemic". *Obesity Medicine* 26 (2021): 100364.

67. Tardy AL., *et al.* "Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence". *Nutrients* 12.1 (2020): 228.

68. Fuhrman J. "The Hidden Dangers of Fast and Processed Food". *American Journal of Lifestyle Medicine* 12.5 (2018): 375-381.

69. Schiefermeier-Mach N., *et al.* "Electrolyte Intake and Major Food Sources of Sodium, Potassium, Calcium and Magnesium among a Population in Western Austria". *Nutrients* 12.7 (2020): 1956.

70. Taillie LS., *et al.* "Governmental policies to reduce unhealthy food marketing to children". *Nutrition Reviews* 77.11 (2019): 787-816.

71. Fu J., *et al.* "Dietary Fiber Intake and Gut Microbiota in Human Health". *Microorganisms* 10.12 (2022): 2507.

72. Poti JM., *et al.* "The association of fast food consumption with poor dietary outcomes and obesity among children: is it the fast food or the remainder of the diet?" *The American Journal of Clinical Nutrition* 99.1 (2014): 162-171.

73. Gómez-Pinilla F. "Brain foods: the effects of nutrients on brain function". *Nature Reviews. Neuroscience* 9.7 (2008): 568-578.

74. Briguglio M., *et al.* "Dietary Neurotransmitters: A Narrative Review on Current Knowledge. *Nutrients* 10.5 (2018): 591.

75. Cusick SE and Georgieff MK. "The Role of Nutrition in Brain Development: The Golden Opportunity of the "First 1000 Days". *The Journal of Pediatrics* 175 (2016): 16-21.

76. Huskisson E., *et al.* "The Influence of Micronutrients on Cognitive Function and Performance". *The Journal of International Medical Research* 35 (2007): 1-19.

77. DePhillipo NN., *et al.* "Efficacy of Vitamin C Supplementation on Collagen Synthesis and Oxidative Stress After Musculoskeletal Injuries: A Systematic Review". *Orthopaedic Journal of Sports Medicine* 6.10 (2018): 2325967118804544.

78. Chambial S., *et al.* "Vitamin C in disease prevention and cure: an overview". *Indian Journal of Clinical Biochemistry* 28.4 (2013): 314-328.

79. Travica N., *et al.* "Vitamin C Status and Cognitive Function: A Systematic Review". *Nutrients* 9.9 (2017): 960.

80. Kennedy DO. "B Vitamins and the Brain: Mechanisms, Dose and Efficacy-A Review". *Nutrients* 8.2 (2016): 68.

81. Cardoso BR., *et al.* "Importance and management of micronutrient deficiencies in patients with Alzheimer's disease". *Clinical Interventions in Aging* 8 (2013): 531-542.

82. Fratoni V and Brandi ML. "B vitamins, homocysteine and bone health". *Nutrients* 7.4 (2015): 2176-2192.