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Mini Review

Correlation Between Coffee, Neurotransmitters and Obesity - A State-Of-The-Art Review Around the Past Decade

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Abstract

Coffee, a habitual drinking nowadays, starts to be explored more in medical research. Moreover, in the last decade, it represented a main preoccupation for some groups of the researchers, the medical literature being improved with many science articles about its positive and negative effects, starting with the organs benefits and damage, the knowledge about its involvement progressing till molecular mechanism and establish influences in metabolic processes. The current state-of-the-art review related the last eleven years (2014-2024) medical concepts about this topic, focusing on the triad of coffee, neurotransmitters and obesity interplay, an incomplete discovered axis and few debated one, in spite of the coffee effects and its actions on human body.

Keywords: Coffee, Obesity, Neurotransmitters, Serotonin, Dopamine, Acetylcholine, GABA, Hormones.

Introduction

Coffee consumption is a habitual practice nowadays, the presence of frequent consumption and the chemical consideration about its effects starting to create medical curiosity in the research field, through beneficially properties and negative effects in human health caused by excessive drinking. The intricate relationship between coffee consumption, obesity, and neurotransmitter activity has been an interesting topic for the researchers, around the last decade, 2014-2024. This paper synthesizes recent findings, emphasizing the biochemical mechanisms and epidemiological evidence that link coffee and their bioactive compounds to obesity and neurotransmitters in modulation of the metabolic processes.

Discussion

Coffee and Obesity Correlations

Coffee is a beverage that is obtained from a multitude of dried and roasted types of grains with a large worldwide variety – *Arabica* and *Canephora* (*Robusta),* those being the most frequent consumed types, but there are much more types like *Racemosa, Liberica, Dewevrei* [1,2]. The interplay between coffee consumption and obesity is complex and multifactorial. Based on the fact that caffeine increases energy expenditure, suppresses appetite, and influences gut microbiota, all of that being key elements in weight loss, it

could be hypothesized that caffeine may represent a therapeutic target for patients with obesity and cardiovascular diseases. Coffee consumption could lead to a lower incidence of obesity, type 2 diabetes or cardiovascular disease [3]. The effect of caffeine on food intake are mediated through multiple pathways, being known the interaction of caffeine with the sympathetic nervous system, corticotropin-releasing factor, ghrelin, neurotransmitters or leptin. All these mechanisms lead to a decreased appetite and weight loss [4]. Even if higher concentrations of caffeine are needed in obese patients compared to lean patients in order to determine changes in metabolism response, there are a lack of evidence between caffeine concentrations that are necessarily for obese vs. lean patients in order to increase energy expenditure and glycemic postprandial response [5].

Furthermore, it was found that regular coffee consumption can influence satiety regulation and energy intake, suggesting that coffee may contribute to body weight loss by increasing body fat catabolism [1]. It was proved the potential of main bioactive components from coffee regarding obesity, type 2 diabetes, insulin resistance or lipid disorders. Coffee silver skin, a by-product of coffee processing, through his compounds like chlorogenic acid, may improve glucose metabolism, by reducing intestinal sugar absorption, inhibiting glucose-6-phosphate translocase enzyme, or lipid metabolism by pancreatic lipase inhibition, regulation of hepatic enzymes involved in lipid metabolism or reduction in hepatic fat. All these conclusions are made based on animal studies, being necessarily more ones to be conducted on patients in order to validate this information [6]. Also, in a recent article published in 2024, it was summarized that in elderly population, a moderate coffee consumption preserves the health span upon aging, caffeine lowering the plasma triglycerides and low-density-lipoproteins, it being associated with a lower risk of metabolic syndrome [7-14].

Coffee and Neurotransmitters Interplay

Coffee contains plenty of bioactive compounds, including caffeine, chlorogenic acids, trigonelline, and diterpenes, which act on the central nervous system through multiple and intricate biochemical pathways. Recent research indicates that coffee may influence neurotransmitters levels, including cyclic adenosine monophosphate, which plays an important role in energy metabolism and appetite regulation [15]. It was established that a regular consumption of coffee antagonizes adenosine receptors and it ensures neuroprotection effects [16]. Contrastingly, a long-term caffeine beverages consumption alters brain functional connectivity, associated with synaptic dysfunction [16-19]. Caffeine acts primarily as an antagonist of adenosine receptors, specifically A1 and A2A subtypes, and by blocking these receptors, caffeine inhibits the effects of adenosine, a neurotransmitter that promotes sleep and relaxation [20] it generating an increased release of excitatory neurotransmitters, notably dopamine and norepinephrine [21]. In medical studies, it was revealed that caffeine enhances dopamine release by disinhibiting dopaminergic pathways, which can improve cognitive functions and mood [21]. Moreover, norepinephrine release is also stimulated by caffeine, contributing to its well-known effects on alertness and arousal [22]. Also, caffeine increases serotonin release, by counteracting the breakdown of tryptophan, a precursor to serotonin, and thereby increasing serotonin synthesis and potentially improving mood and quality of life and reducing anxiety [23,24]. The role of brain-derived neurotrophic factor in this context is also significant, modulating the activity of serotonin and dopamine and linking caffeine consumption to neuroplasticity and cognitive functions [16,25]. In addition, caffeine's effects on neurotransmitters release are not uniform; they can depend on the duration and amount of caffeine exposure. Acute caffeine administration has been shown to promote neurotransmitters release effectively, while chronic exposure may lead to receptors upregulation, diminishing the stimulatory effects over time [16,26]. This phenomenon evidences the importance of understanding individual differences in caffeine metabolism and sensitivity, which can influence the overall impact of coffee consumption on neurotransmitter dynamics and cognitive function [27]. Caffeine also interacts with gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain. By modulating GABA-A receptors, caffeine can reduce the inhibitory input in neuronal networks, which may contribute to its stimulatory effects [20,28]. This interaction is particularly relevant in the context of anxiety, as GABA's role in regulating anxiety levels is well-established, some studies suggesting that caffeine may have anxiolytic effects under certain conditions, although excessive consumption can lead to increased anxiety and restlessness [29,30].

Last, but not least, another neurotransmitter that is influenced by caffeine exposure is acetylcholine, coffee beverages increasing its level, that can improve cognitive performance [28, 31]. The relationship between coffee consumption and brain health is benefic in moderate consumption, thanks to the potential neuroprotective effects of caffeine. Epidemiological studies suggest that regular coffee drinkers may have a lower risk of neurodegenerative diseases. For example, in Alzheimer and Parkinson diseases, it is appreciated to contribute in enhancing neuroplasticity and reducing neuroinflammation [32,33]. So, the modulation of neurotransmitter systems by caffeine, may contribute to these protective effects, because the neurotransmitters balance is crucial for maintaining cognitive health and preventing neurodegeneration.

Obesity and Neurotransmitters Reciprocation

Obesity is often associated with dysregulation of neurotransmitter systems, particularly dopamine and serotonin, that are involved in appetite control and reward pathways. The relationship between obesity and neurotransmitter's function is bidirectional, brain structure's changes being responsible for the modifications of signaling pathways [25]. This creates a vicious cycle where obesity exacerbates neurotransmitters dysregulation, leading to further weight gain and health risks associations. Patients with obesity often have reduced dopamine receptor availability, especially in the striatum, which is associated with decreased release of dopamine in response to food stimuli [34]. This reduced release of dopamine is seen in patients which consume high-calories food to compensate this "reward deficiency syndrome" [35]. Also,

alternations in dopamine signaling may lead to an unhealthy eating behavior [36]. Serotonin influences various physiological processes, including thermogenesis and glucose homeostasis and regulate energy balance, which are critical in the context of obesity [37,38]. The serotonergic system's involvement in obesity could be explained by certain serotonin receptors, such as the 5-HT2C (5-hydroxytryptamine subtype 2C) receptor, which are associated with weight gain, particularly in the context of antipsychotic medication use [39]. Obesity leads to modifications in brain structures and functions, particularly in regions involved in reward processing and interoception [40]. Additionally, brain responses to food stimuli have been observed being different in men and women [41,42], suggesting that may be necessary different approaches in treating obesity based on gender. Leptin, primarily produced by adipose tissue, have an important role in energy balance. In obesity, the brain does not respond to high levels of leptin, leading to continued food intake and weight gain [43]. Insulin is another hormone that modulate appetite and energy expenditure. In obese persons, insulin resistance complicates the hormonal interplay and lead to increased appetite and reduced energy expenditure [44]. Ghrelin, or the hunger hormone, secreted by the stomach, usually stimulate appetite. In obese persons, ghrelin levels may be altered, leading to hunger and food intake, and the balance between ghrelin and leptin is essential for energy homeostasis [45].

Other hormones such as peptide YY and glucagon-like peptide-1 are involved in satiety pathways and are often found to be dysregulated in obesity [46]. The hormonal landscape in obesity is characterized by a complex interplay between various hormones and neurotransmitters effects that regulate appetite and energy balance. these interactions being crucial for developing effective strategies for obesity prevention and treatment, coffee could be considered a part of the diet strategy in metabolic management of the overweight patients.

Neurotransmitters, Obesity, and Coffee - possible interconnections debated

The interplay between coffee, obesity and neurotransmitters can be interpreted as a complex biochemical network of cause-effect reactions [Figure 1] It is well known that coffee influences both metabolic and neurochemical processes, playing an important role in the neurotransmitters pathways that mediate translation into appetite and energy. Important to mention, that it was debated how coffee modulates clock gene expression and satiety signals, potentially disrupting feeding rhythms, the dopaminergic stimulation from caffeine enhancing the reward value of high-calorie foods, complicating its role in weight gain. Even if caffeine is the most recognized compound in coffee, there are also other components that contribute to its effects:

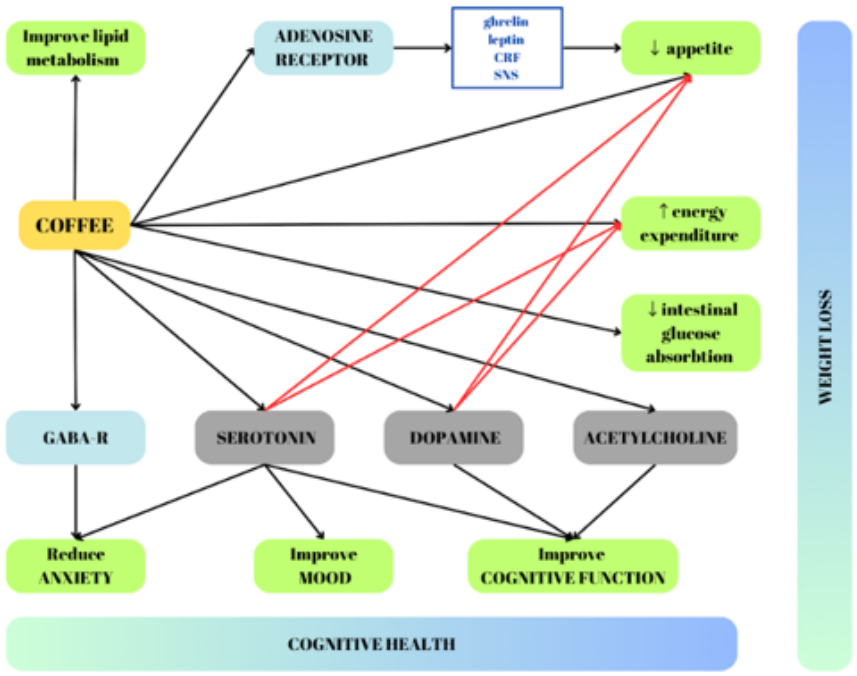

Figure 1: The effect of coffee in metabolic and cognitive functions. Coffee (*yellow box*) consumption improves lipid metabolism (*green left upper box*), reduce anxiety through GABA-R (*blue box*) interventions, it improving mood and cognitive function through neurotransmitters (*gray boxes*) involvement, like serotonin, dopamine and acetylcholine. Also, coffee beverages prepared in a correct brew way, decrease intestinal glucose (right lower vertical green box). Moreover, the interplay between coffee, neurotransmitters and hormones like ghrelin and leptin, sympathetic nervous system (SNS) and corticotropin-releasing factor (CRF) (*dark-blue middle outlined box*), through adenosine receptor involvement (middle upper blue box), conducts to a lower appetite (*right middle vertical green box*) and increases energy expenditure (*right middle vertical green box*).

1) Chlorogenic acids are the second most abundant components in coffee, exhibiting antioxidant properties, reducing oxidative stress and inflammation, and also contributing as a antimutagenic, antiviral and anticarcinogenic factor [47].

2) Trigonelline promotes neuronal regeneration and may play an important role in weight regulation by enhancing insulin sensitivity, it being also known for the hepatoprotective effects [48-51].

3) Diterpenes (*Cafestol* and *Kahweol*) promote anti-inflammatory effects and metabolic benefits, hypercholesterolemia considered to be associated with an incorrect brew preparation procedure [49,52].

Challenges and Individual Variability – future directions and perspective for research

The effects of coffee on neurotransmitters and obesity are not uniform across populations, it being demonstrated that genetic polymorphisms in caffeine metabolism (e.g., CYP1A2 variants) influence individual responses to coffee [53]. Fast metabolizers may have more metabolic benefits in coffee consumption, while slow metabolizers risk adverse effects like anxiety or palpitations [15]. Moreover, habitual coffee consumption can lead to tolerance, reducing its thermogenic and appetite-suppressing effects over time, that underscores the importance of personalized recommendation [48,54,55].

Conclusions

The current literature revealed a high correlation between coffee consumption, obesity, and neurotransmitters activities. Coffee, through its effects on neurotransmitters like dopamine, serotonin, and norepinephrine could be considered an efficient dietary tool for the weight regulation and it also could have protective effects against obesity. These effects could be explained by different mechanisms, including the modulation of insulin sensitivity and inflammation, individual variability, lifestyle factors, and consumption patterns. Personalized approaches that account for genetic, metabolic, and behavioral factors will likely yield the most significant insights into its potential in weight management and efficient diet choices for health and maintaining wellness. Future research should focus on individual variability, optimizing coffee's role as a functional food for brain and metabolic regulation, balancing its benefits and potential drawbacks.

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None

Conflict of Interest

No conflict of interest to declare.

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