**KNYCHALSKA, Karolina, SIKORA, Jakub, ŁABUDA, Mikołaj, KRÓLIKOWSKA, Klaudia, SŁOJEWSKA, Aleksandra, KOTKOWIAK, Agata, SOWIŃSKA, Teresa, MENTEL, Oliwia, BOGUCKA , Adrianna and SZEMA, Agnieszka. The Impact of Caffeine on Anxiety Levels and Stress Responses - a literature review. Journal of Education, Health and Sport. 2025;81:59947. eISSN 2391-8306.**
**https://doi.org/10.12775/JEHS.2025.81.59947**
**https://apcz.umk.pl/JEHS/article/view/59947**

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). 
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 31.03.2025. Revised: 25.04.2025. Accepted: 30.04.2025. Published: 03.05.2025.

# The Impact of Caffeine on Anxiety Levels and Stress Responses - a literature review

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## Abstract

**Introduction and Purpose:**
Caffeine is one of the most widely consumed stimulants worldwide, primarily due to its stimulating properties. However, its effects on mental health, particularly in relation to anxiety and stress responses, remain a subject of debate. This study aims to analyze the mechanisms through which caffeine affects the nervous system and assess its impact on anxiety levels and physiological responses to stress. Additionally, it discusses individual differences in caffeine metabolism and their implications for tolerance to this compound.

**State of Knowledge:**
Previous research indicates that caffeine modulates nervous system function by affecting neurotransmission, particularly by increasing the release of dopamine, noradrenaline, and serotonin. Evidence suggests that caffeine's effects can be both beneficial and detrimental, depending on the dose consumed, individual genetic predispositions (such as polymorphisms in the *ADORA2A* and *CYP1A2* genes), and the presence of anxiety disorders.

**Conclusion:**
The findings of this review suggest that caffeine can exert both positive and negative effects on mental health. Dosage, individual metabolic differences, and genetic predispositions strongly influence these effects. Further research is necessary to precisely determine the conditions under which caffeine consumption is safe and when it may contribute to heightened anxiety and stress.

**Keywords:** caffeine; anxiety; physiological stress; stress response; mental health

## 1. Introduction

Caffeine (1,3,7-trimethylxanthine) is a purine alkaloid and a methylxanthine derivative with the molecular formula $C_8H_{10}N_4O_2$ [1]. It naturally occurs in plants such as coffee, tea, cocoa, and guarana.

| **Product** | **Average Caffeine Content** | **Range (mg)** |
|---|---|---|
| Filtered Coffee (125 mL) | 85 mg | 60–135 |
| Instant Coffee (125 mL) | 65 mg | 35–105 |
| Decaffeinated Coffee (125 mL) | 3 mg | 1–5 |
| Espresso (30 mL) | 60 mg | 35–100 |
| Loose Leaf or Bagged Tea (150 mL) | 32 mg | 20–45 |
| Iced Tea (330 mL) | 20 mg | 10–50 |
| Hot Chocolate (150 mL) | 4 mg | 2–7 |
| Caffeinated Soft Drinks (330 mL) | 39 mg | 30–48 |
| Sugar-Free Soft Drinks (330 mL) | 41 mg | 26–57 |
| Energy Drinks (330 mL) | 80 mg | 70–120 |
| Chocolate Bar (30 g) | 20 mg | 5–36 |
| Dark Chocolate (30 g) | 60 mg | 20–120 |
| Milk Chocolate (30 g) | 6 mg | 1–15 |

Table 1. Caffeine Content in Various Food Products
Data from http://www.coffeeandhealth.org.

Caffeine exerts its effects through several mechanisms, including adenosine receptor antagonism, phosphodiesterase inhibition, intracellular calcium release, and *GABAA* receptor antagonism [2,3,4]. Its primary effect is mediated by the blockade of adenosine $A_1$ and $A_2$ receptors, which are found in the brain, blood vessels, kidneys, heart, and gastrointestinal tract [5]. Inhibiting adenosine activity leads to increased neurotransmitter release—particularly dopamine, noradrenaline, and serotonin—resulting in heightened alertness, improved concentration, and reduced fatigue.

Caffeine is absorbed from the gastrointestinal tract within 30 to 120 minutes (*T*max) and freely crosses both the blood-brain barrier and the placenta. Its average plasma half-life ranges from 2.5 to 4.5 hours [6]. The majority of caffeine metabolism occurs in the liver via the microsomal cytochrome P450 enzyme system [7,8]. The *CYP1A2* isoenzyme is responsible for approximately 90% of caffeine metabolism, breaking down 95% of the compound [9]. Around 80% of caffeine is converted into paraxanthine [7], while the remaining portion is metabolized into theobromine (~11%) and theophylline (~4%) [10]. Caffeine is primarily eliminated via the kidneys, with approximately 3% excreted unchanged [11].

Caffeine consumption affects multiple physiological systems. It stimulates the autonomic nervous system, alters heart rhythm, and induces vasoconstriction or vasodilation in peripheral blood vessels [12,13,14]. Additionally, it influences skeletal muscles, kidney function, and lung tissue [15,16]. Some beneficial effects of caffeine consumption have been reported that are absent when consuming decaffeinated beverages [17]. However, caffeine may also impact emotional and psychological functioning, particularly in the context of anxiety and stress responses. Notably, caffeine-induced stimulation, palpitations, and dizziness can resemble panic attacks [18]. Furthermore, excessive caffeine intake has been associated with increased stress perception due to elevated cortisol levels, the primary stress hormone [19].

The aim of this study is to analyze the current state of knowledge regarding the impact of caffeine on anxiety and stress responses. This review discusses the mechanisms of caffeine action, factors that modulate the body's response to caffeine, and the potential consequences of excessive intake.

## 2. Description of State of Knowledge

Scientific literature provides evidence that the effect of caffeine on anxiety depends on the amount of caffeine consumed and the frequency of intake. Low to moderate doses (50–200 mg, equivalent to 1–2 cups of coffee) may improve mood and concentration without causing significant anxiety symptoms. In healthy individuals, caffeine in these amounts can lead to increased alertness and energy, mood enhancement, and cognitive function improvement, which is beneficial in situations requiring focus and rapid information processing [13,20,21,22].

High doses (>400 mg per day, equivalent to 4–5 cups of coffee) are often associated with increased nervous tension, restlessness, and heightened anxiety. Studies have shown that individuals consuming large amounts of caffeine may experience symptoms resembling anxiety disorders, including rapid heartbeat, excessive excitability, and hand tremors [13,20,22]. Caffeine-induced panic attacks were perceived similarly to spontaneous panic attacks, exhibiting symptoms such as fear of death, shortness of breath, palpitations, and dizziness. Approximately half of the patients and fewer than 2% of healthy control individuals experienced a panic attack after caffeine administration, whereas none did so after placebo administration [18].

A healthy adult should limit daily caffeine intake to 400 mg to avoid adverse health effects [23]. No safe dose has been established for children; however, they should not consume more than 2.5 mg per kilogram of body weight [13].

Not everyone responds to caffeine in the same way. Differences in the body's response may result from genetic factors, lifestyle, consumption habits, and overall mental health status.

### Genetics and Caffeine Metabolism

Genetics, tolerance, and individual sensitivity play a key role in the response to caffeine. Polymorphisms in genes encoding the caffeine-metabolizing enzyme *CYP1A2* can influence the rate of caffeine metabolism, which in turn determines the body's reaction to its intake[24,25,26]. Individuals with the "slow metabolizer" variant (*CYP1A2* C/C and A/C)

break down caffeine more slowly, meaning its effects last longer and may induce stronger anxiety symptoms. Conversely, individuals with the "fast metabolizer" variant (*CYP1A2* A/A) eliminate caffeine more rapidly and are less likely to experience its negative effects [27].

A similar relationship is observed in the *ADORA2A* gene, which encodes the adenosine A2A receptor, an antagonist of caffeine. Studies indicate that individuals with specific polymorphisms in the *ADORA2A* gene may experience stronger anxiety reactions after caffeine intake. For example, the rs5751876 (T1083C) polymorphism in the *ADORA2A* gene has been associated with heightened anxiety symptoms even after consuming smaller amounts of caffeine (<150 mg). Individuals with the TT variant of this polymorphism exhibited greater susceptibility to anxiety compared to carriers of other genotypes [28,29].

Although studies have examined the separate effects of *ADORA2A* and *CYP1A2* polymorphisms, there is a lack of research analyzing their combined impact on anxiety responses following caffeine consumption.

**Differences in Caffeine Sensitivity**

Some individuals may experience anxiety or irritability even after consuming small amounts of caffeine, while others can tolerate larger doses without consequences. These differences arise due to various factors.

**Tolerance Levels**

One of the factors is tolerance levels. Regular caffeine consumption leads to physiological adaptation, meaning that higher doses are required to achieve the same stimulating effect [30]. Studies have also demonstrated that even individuals with the *ADORA2A* genotype rs5751876 TT (a genotype that has been associated with heightened anxiety symptoms after consuming caffeine) develop central nervous system tolerance with frequent caffeine intake, reducing its anxiety-inducing effects [29]. It has been shown that a group that abstained from caffeine experienced heightened anxiety upon reintroduction, whereas individuals who maintained a daily intake of 900 mg did not react similarly [31].

**Mental Health Status**

Mental health status is an important factor. The presence of certain anxiety disorders affects the perception of caffeine’s effects. Studies have shown increased sensitivity to caffeine-

induced anxiety at high doses (typically above 400 mg) in patients with panic disorder, individuals with generalized anxiety disorder, and patients with social anxiety disorder related to public speaking [32,33,34,35]. In a caffeine challenge test (480 mg caffeine administered acutely), patients with panic disorder and their healthy first-degree relatives were more sensitive to panic attack symptoms than healthy volunteers [36]. Furthermore, panic disorder patients who experience panic attacks after caffeine consumption exhibit more frequent nonspecific psychopathological behaviors[37].

Regarding depression, some studies suggest an inverse relationship between caffeine intake and depressive symptoms. Higher caffeine consumption has been associated with a lower risk of developing depressive symptoms [38]. Additionally, a meta-analysis of observational studies indicated a significant reduction in depression risk with caffeine consumption above 68 mg/day and below 509 mg/day [39]. However, in individuals with depression, greater sensitivity to caffeine's anxiety-inducing effects at high doses has been observed [40].

**Interactions with Medications and Diet**

It is also important to note that caffeine interacts with medications and diet. Certain substances can influence its metabolism, either enhancing or reducing its stimulating effects. Smoking decreases caffeine's stimulant effects [30,41,42]. Oral contraceptives and female sex increase caffeine's stimulating effects [30]. During pregnancy, caffeine's effects are intensified as its half-life extends: by the end of pregnancy, it is 3–4 times longer[43,44]. Some medications, including fluvoxamine (a serotonin reuptake inhibitor), mexiletine (an antiarrhythmic drug), clozapine (an antipsychotic), furafylline and theophylline (bronchodilators), and enoxacin (a quinolone), may slow caffeine metabolism [45].

**Amount of Caffeine Consumed**

Another important factor is the amount of caffeine consumed. Caffeine’s half-life is directly related to the administered dose. Doses lower than 10 mg resulted in a half-life of 2.5 to 10 hours, whereas higher doses resulted in a longer half-life[46,47].

**Cortisol Levels**

Caffeine, as an adenosine receptor antagonist, stimulates the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased secretion of cortisol—the stress hormone [19,48]. Excessive

activation of the HPA axis induced by caffeine may heighten negative emotions, arousal, stress susceptibility, and exacerbate anxiety symptoms. This effect is particularly pronounced when caffeine is consumed in the morning when natural cortisol levels are at their peak [48].

## Methods

To assess the impact of caffeine on anxiety levels and stress responses, a systematic literature review was conducted using databases such as PubMed and Google Scholar. Articles were searched using keywords: "caffeine," "anxiety," "stress," "stress response," "mental health." Experimental and observational studies, as well as systematic reviews on the effects of caffeine on these aspects, were included. Then, we analyzed the selected materials.

## 3. Summary

The effect of caffeine on anxiety is dose-dependent—low doses may improve mood and alertness, whereas higher doses (>400 mg per day) increase the risk of anxiety symptoms, particularly in individuals sensitive to caffeine.

Individuals with anxiety disorders should limit caffeine consumption due to its potential to exacerbate symptoms such as restlessness, heart palpitations, and hand tremors.

Genetics and individual tolerance play a key role—polymorphisms in the ADORA2A gene, slower caffeine metabolism (CYP1A2 gene), and psychological predispositions may increase susceptibility to its negative effects.

Caffeine may elevate stress levels by increasing cortisol production and stimulating the nervous system. This can lead to long-term issues, especially in individuals consuming high amounts of caffeine.

Regular caffeine consumption may reduce sensitivity to its negative effects—the body adapts to caffeine exposure, meaning that individuals who consume it daily may experience fewer anxiety-related effects than those who consume it sporadically.

**Disclosure**

Author's contribution

- Conceptualization: Karolina Knychalska, Agnieszka Szema
- Methodology: Adrianna Bogucka, Oliwia Mentel
- Software: Agnieszka Szema, Jakub Sikora
- Check: Jakub Sikora, Agata Kotkowiak, Teresa Sowińska
- Formal analysis: Karolina Knychalska, Adrianna Bogucka
- Investigation: Karolina Knychalska, Agata Kotkowiak, Aleksandra Słojewska
- Data curation: Aleksandra Słojewska, Teresa Sowińska
- Writing - rough preparation: Karolina Knychalska, Agnieszka Szema
- Writing - review and editing: Mikołaj Łabuda, Klaudia Królikowska
- Visualization: Oliwia Mentel, Teresa Sowińska
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- Project administration: Mikołaj Łabuda, Jakub Sikora, Adrianna Bogucka
- Receiving funding: Not applicable.

All authors have read and agreed with the published version of the manuscript.

**Funding:**

This research received no external funding.

**Institutional Review Board Statement:**

Not applicable.

**Informed Consent Statement:**

Not applicable.

**Data Availability Statement:**

Not applicable.

**Acknowledgements:**

Not applicable.

**Conflicts of Interest:**

The authors declare no conflict of interest.

**Declaration of the use of generative AI and AI-assisted technologies in the writing process.**

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability. After using this tool, the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

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