International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	THE ROLE OF CAFFEINE IN HEADACHE INDUCTION, TREATMENT AND PREVENTION - A LITERATURE REVIEW
DOI	https://doi.org/10.31435/ijitss.4(48).2025.4177
RECEIVED	10 October 2025
ACCEPTED	19 December 2025
PUBLISHED	24 December 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

THE ROLE OF CAFFEINE IN HEADACHE INDUCTION, TREATMENT AND PREVENTION - A LITERATURE REVIEW

Adrianna Świerzyńska *[AŚ] (Corresponding Author, Email: ada199805@gmail.com)*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0007-1451-3009

Natalia Jankowska *[NJ]*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0000-3618-6247

Natalia Pawelec *[NP]*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0004-3478-9350

Weronika Mazur *[WM]*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0008-4347-4077

Artur Hawajski *[AH]*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0003-7592-2114

Katarzyna Naja *[KN]*
Medical University of Warsaw, Warsaw, Poland
ORCID ID: 0009-0008-6513-6984

Tomasz Puszkiel *[TP]*
University of Technology and Humanities in Radom, Radom, Poland
ORCID ID: 0009-0006-5413-7530

ABSTRACT

Introduction: Migraine is a chronic disorder with which caffeine has been associated for many years. It acts as both a trigger and an alleviating factor. Caffeine consumption has a significant effect on the nervous system. Through its mechanism of action, it can trigger headaches, especially migraines. Both overuse and sudden withdrawal of caffeine can trigger migraine attacks, but can also be the cause of chronic migraine. People who suffer from migraines are advised to control their daily caffeine intake in order to avoid the symptoms associated with caffeine consumption. Caffeine has positive effects, boosting cognitive function, alertness, physical performance and endurance. Through its neuroprotective effects, it reduces the risk of Alzheimer's disease and Parkinson's disease.
Aim of the study: The aim of this review is to summarise the existing knowledge on the effects of caffeine as an inducer of migraine headache, non-migraine headache, its role in withdrawal syndrome and its potential use in the treatment of various forms of headache.
Material and methods: Our research method involved searching publicly accessible online databases of academic articles, such as PubMed, Google Scholar, and others. The research team used the keyword “migraine” in combination with various terms, including “caffeine consumption”, “treatment”, “prevention”, “caffeine intake” and “caffeine withdrawal”. The collected data were then manually analyzed.
Results and Conclusions: Caffeine has a dual role in migraine, acting both as a potential trigger and as an effective adjunct in treatment. Its impact on adenosine receptors explains both analgesic and pain-inducing effects. Controlled use can support acute migraine therapy, especially with analgesics, while awareness of withdrawal risks and individual tolerance is crucial to precluding headaches.

KEYWORDS
Headache, Caffeine, Migraine, Caffeine Withdrawal

CITATION

Adrianna Świerzyńska, Natalia Jankowska, Natalia Pawelec, Weronika Mazur, Artur Hawajski, Katarzyna Naja, Tomasz Puszkiel. (2025) The Role of Caffeine in Headache Induction, Treatment and Prevention – A Literature Review. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4177

Introduction

Migraine is the third most common neurological disorder in the world, affecting more than one billion people. It manifests as recurrent attacks of severe headache associated with somatosensory and motor disturbances. It is often accompanied by nausea and vomiting, photophobia, and hypersensitivity to sound [1,2]. Migraines may occur with or without an aura. The former is characterized by headache attacks lasting from 4 to 72 hours. During a migraine attack, neuropathic pain (allodynia) and cranial autonomic symptoms may occur [3]. Migraine without aura accounts for 75% of migraine cases [4]. In migraine with aura, symptoms such as sensory, visual and speech disturbances appear before the headache. The attack often lasts several minutes [3,4]. The postdromal phase, which occurs after the headache has subsided, is mainly characterized by poor concentration and general fatigue [5]. Migraine pain in adults is usually unilateral in the frontotemporal region, whereas in children and adolescents it tends to be bilateral [3]. Chronic migraine is a condition in which headache occurs on at least 15 days per month for more than 3 months. At least 8 of these days have migraine-specific symptoms [4]. The mechanisms responsible for the development of migraine are complex. Both genetic and environmental factors influence the onset of the disease. The activation of the trigeminovascular system is believed to play a major role in the development of migraine pain via circulating pro-inflammatory substances and oxidative stress [1].

Pathophysiology and treatment of migraine

Adenosine is a vasoactive amine that is produced by adenosine monophosphate (AMP) or S-adenosylhomocysteine (SAH). It has a role in physiological processes such as respiration, metabolism, inflammation and pain. It binds to A1, A2A, A2B and A3 receptors, exerting specific functions in the body. A1 and A3 receptors are present in the trigeminal system. The combination of adenosine with A1 and A3 receptors reduces nerve activity and inhibits this system, exerting an analgesic effect. A2A and A2B receptors are present in blood vessel cells and nerves. Stimulation of them causes vasodilation in the meninges, resulting in activation of the trigeminal vascular system, which contributes to causing pain [6].

Emergency treatment of episodic migraine includes drug groups such as triptans, nonsteroidal anti-inflammatory drugs, calcitonin gene-related peptide receptor antagonists, lasmiditan (5-HT receptor agonist), dihydroergotamine, ergotamine with caffeine, acetaminophen, antiemetics, butorphanol and tramadol in combination with acetaminophen [7]. The choice of the appropriate drug is based on its availability and side effect profile. For mild to moderate migraine, the first-line drugs used are non-steroidal anti-inflammatory drugs. If the course of migraine is moderate or severe, triptans are chosen as the first choice, and the decision of which specific type to choose is determined individually depending on the needs of the patient. Attention is paid to the route of administration, pharmacokinetics and cost of treatment. Parenteral dihydroergotamine, opioids, magnesium sulfate, valproate are given for refractory migraine. They should be administered with caution, as they can cause more side effects, as well as lead to addiction due to their abuse [8]. The above treatments used have been associated with improvements in pain and function [7]. The patient must understand the treatment strategy and start therapy early in the onset of a migraine attack [8].. In addition to drug therapy, migraine treatment includes lifestyle modifications, environmental factors, and dietary changes. The appearance of a headache after the onset of a particular factor depends on the amount of the factor and the time of exposure [1]. Short-term exposure to a headache-triggering stimulus is thought to increase the sensitivity of the nervous system, leading to a faster and stronger pain response. In contrast, chronic exposure decreases sensitivity due to the activation of adaptive mechanisms. Triggers for migraine attacks include stress, lack of sleep, fatigue, auditory, olfactory, visual, bright light, alcohol and weather factors [1, 5]. During a night's sleep,

the likelihood of a sudden migraine attack is relatively low, while it increases after a sleepless night. A correlation of mutations in the casein kinase Iδ gene has been discovered to cause both sleep problems and also be a cause of migraine onset [9]. Foods are considered triggers when the headache occurred more than 50% of the time within one day of exposure to the ingredient. Such triggers include citrus fruits, chocolate, caffeine, ice cream, nuts, onions, tomatoes, alcoholic beverages, coffee, monosodium glutamate, phenylethylamines, nitrites, aspartame, sucralose and gluten [1].

Caffeine is one substance that is associated with migraine. It is considered both a trigger and a therapeutic agent [2].

Mechanism of Action and Physiological Effects of Caffeine

Caffeine is a purine alkaloid, one of the most widely consumed psychostimulants in the world, extracted from coffee beans, tea and some cocoa beans. It has gained its popularity due to its positive effects on cognitive function, alertness, physical capacity and endurance [10,11]. More and more is known about its beneficial effects on chronic diseases such as type II diabetes, cardiovascular disease, cancer risk reduction and neurodegenerative diseases [1]. Caffeine is a non-selective and competitive antagonist of adenosine A1, A2A, A2B and A3 receptors. Since adenosine receptors are found throughout the body, caffeine has a systemic effect and can penetrate the blood-brain barrier [10]. This action on the latter receptor is responsible for influencing wakefulness and causing vasodilation by stimulating the vascular endothelium to release nitric oxide [10,12]. On the other hand, the vasodilatory effect is counteracted by increased sympathetic tone, since at the same time caffeine, through antagonism of the A1 receptor, produces an inotropic and positive chronotropic effect and increases the release of catecholamines. As a final result of the complexity of the mechanisms by which caffeine affects the vasculature, the response to it is individual [10]. By inhibiting adenosine activity, there is an increased concentration of dopamine in mesocorticolimbic structures, which are responsible for cognitive and executive functions, among other things. As a result of modulation of dopaminergic pathways, caffeine exhibits neuroprotective effects, thereby reducing the risk of Alzheimer's disease and Parkinson's disease [1,11]. Coffee is ranked among the most preferred products that contain caffeine. It has been shown that young people's coffee consumption has increased significantly over the past decades, with the main reason for drinking coffee being increased efficiency. Consumers were mostly young, unmarried men, with poor sleep hygiene (sleep lasted about 3-5 hours) and smokers [13]. It should be borne in mind that hypersensitivity to caffeine can lead to neurotoxicity. Its stimulant effects can cause deterioration of sleep quality, prolonging sleep latency, eventually leading to nocturnal insomnia. In addition to the fatigue and cognitive impairment that occurs, one can see increased susceptibility to stress and preparation of the body for a state of escape. Consumption of large doses of caffeine can trigger seizures and panic attacks [11].

Effects of caffeine on cerebral blood flow

Some purine alkaloids, especially methylxanthines, cause vasodilation of blood vessels, the exception being the effect of caffeine in the central nervous system, where it increases cerebrovascular resistance and reduces cerebral blood flow [12]. Other studies have found that caffeine consumption of 2 to 4 cups of coffee reduces cerebral blood flow by 22 to 30%, but has no effect on cerebral vascular velocity [14]. There are studies that conclude that caffeine both improves and impairs vascular endothelial function striking a balance between vasodilation and vasoconstriction. Higashi found the so-called “coffee paradox,” according to which caffeine causes endothelium-dependent vasodilation but does not cause endothelium-independent dilation, imposing the conclusion that it does not affect vascular smooth muscle function [15]. A study by Gaspar et al. using transcranial Doppler ultrasound of the middle cerebral artery (VMCA) found that after caffeine administration, there was a decrease in flow velocity in all VMCAs and consequently cerebral vasodilation [14].

Caffeine withdrawal headache

Caffeine withdrawal headache has been classified as a separate diagnostic entity by the International Classification of Head Disorders (ICHD-3) [5]. The prevalence is estimated to be between 10% and 55% in the general population of caffeine consumers [16]. The symptoms of the prodromal or warning phase of migraine are similar to those of caffeine withdrawal. These include drowsiness, mood swings, nausea, difficulty concentrating, and muscle stiffness. However, the main symptom of migraine like sensory hypersensitivity is not present in caffeine withdrawal syndrome. The overlap of symptoms may be due to the fact that caffeine withdrawal is a trigger for a migraine attack [9]. Sudden caffeine withdrawal causes withdrawal symptoms to appear in a minority of patients. They are usually moderate and transient. With regular

use of caffeine, some subjective effects become less noticeable and tolerance is produced. In contrast, some withdrawal symptoms, especially those related to the central nervous system, are not subject to full tolerance [17]. It is also worth considering the differences in the perception of side effects between the sexes, with women having more than three times the incidence of side effects than men, and the most commonly reported symptoms being increased nervousness and anxiety. One potential factor contributing to these differences may be the different fat-free mass content between the sexes, which tends to be lower in women [18].

Diagnostic criteria for caffeine withdrawal syndrome include prolonged daily consumption of caffeine, sudden cessation or reduction of caffeine, the appearance of characteristic symptoms, impairment in social and occupational functioning, and the inability to explain such a condition with other psychiatric disorders [5]. Caffeine withdrawal studies provide evidence of a number of symptoms, i.e. headache, fatigue, reduced energy, lowered mood, reluctance to socialize, difficulty concentrating, irritability and flu-like somatic symptoms [19]. The 4th edition of the DSM-IV Diagnostic and Statistical Manual of Mental Disorders does not include a category related to dependence and abuse of caffeinated substances. For a diagnosis of psychoactive substance dependence, three out of seven criteria must be met, i.e. tolerance; withdrawal symptoms; taking the substance in large quantities, over an extended period of time; ineffective attempts to reduce consumption of the substance; spending a large amount of time acquiring, using or recovering from the effects of the substance; reduced social and occupational functioning; and continued consumption of the substance despite knowledge of its negative mental and physical effects. Broderick and Benjamin present a model by which caffeine-induced mental disorders could be prevented. They propose that a patient with caffeine-induced symptoms should be recognized at the outset. They stress that educating the patient about the sources of caffeine and its effects is also a very important step. They suggest that manufacturers of products containing large amounts of caffeine should mark accurate information about the content of this substance in the product, the safe dose to consume, warn children to avoid such products and also mark that large amounts of caffeine and long-term use are dangerous to health [20]. The semilateral nucleus accumbens is a key component of the reward system, responsible for the release of dopamine in reaction to classic addictive substances. In the case of caffeine, its daily intake does not result in increased dopamine release in the hemifrontal nucleus. Instead, an increase in dopamine levels in the prefrontal cortex is observed, suggesting that caffeine exhibits reinforcing properties, albeit by a different mechanism than typical substances of abuse. Additionally, in large doses, caffeine increases glucose consumption in the shell of the nucleus accumbens. Such large amounts of caffeine affect most brain structures and reflect adverse symptoms, but these do not occur with daily caffeine consumption. Although caffeine shares some characteristics with addictive substances, i.e. amphetamine or cocaine it does not act on those areas of the brain that are responsible for feeling reward, motivation and the development of addiction [17]. Long-term use of caffeine leads to up-regulation of adenosine receptors and an increase in plasma adenosine concentrations, causing vasodilation and accelerating the onset of migraine headaches. Caffeine withdrawal pain occurs within 24 hours with regular caffeine consumption in excess of 200 mg/day and subsides within 2 weeks after caffeine cessation [5, 9]. Other sources indicate that it lasts from 2 to 3 days after discontinuation [21]. Withdrawal symptoms subside for up to 9 days and peak on the first and second days. Non-daily coffee drinkers experienced fewer withdrawal effects compared to those who drink coffee daily. Cessation of coffee drinking and the discomforts that come with it can lead to impaired daily functioning. Excessive fatigue is felt and performance is significantly impaired, affecting activities such as driving, concentrating and studying [19]. The mechanism of headache after caffeine withdrawal is probably a rebound effect. Caffeine has a vasoconstrictive effect. Regular consumption of it causes the body to become accustomed to its effects. When this substance is discontinued, blood vessels dilate, resulting in increased blood flow and the onset of headaches [5]. People with a history of frequent headaches, especially migraine headaches, are more likely to develop a headache when they stop consuming caffeine. It is pulsatile in nature, moderate to severe, worsens with exertion and can last for 2-3 days. The coexistence of depression and anxiety has also been proven in people who have experienced such pain. Although the headache after caffeine withdrawal is described as non-migraine, its characteristics are similar to migraine [5]. It has been argued in the literature that, in patients who regularly consume caffeine, caffeine withdrawal before surgery may contribute to headaches in the postoperative period, prompting some researchers to consider preventive actions in this regard. According to the Enhanced Recovery After Surgery (ERAS) fasting guidelines, in the preoperative period it is recommended to consume up to 800 ml of a carbohydrate-rich beverage and it is acceptable to take up to 400 ml of clear liquid - including black coffee (without added milk or cream) no later than two hours before surgery. While the introduction of the above recommendations may help to prevent caffeine withdrawal symptoms,

further research is needed on the validity of preventive use and caffeine supplementation in the postoperative period [22].

Caffeine restriction can be a challenge for people who experience unpleasant discomfort. Often repeated attempts to reduce or stop caffeine intake prove unsuccessful. The recommendation was to reduce the substance in a gradual manner over a period of 4 to 6 weeks. The goal was to avoid and reduce withdrawal symptoms [16]. Current guidelines recommend swapping coffee or tea for water and sticking to a set specific amount that can be consumed. Behavior change techniques were introduced, which consist of creating a comprehensive classification system of behavior change strategies and methods for dealing with the harms and symptoms of caffeine withdrawal. The classification used involved an extensive dataset that would reflect people's actual experiences. The results obtained can help create effective interventions by indicating why and how to support caffeine-restrictors, increasing their proficiency and self-efficacy [16].

The role of caffeine as a trigger for migraines and its importance in treatment

Caffeine has an ambivalent role in the context of migraine headache - on the one hand, it can be used therapeutically, while on the other hand, it can be a trigger for an attack. According to some studies, it is responsible for the induction of migraine in 6.3% to 14.5% of incidents [12]. A cohort study published by Maggie R. Mittleman et al. involved 101 adults with confirmed episodic migraine who were asked to record headache diaries for six weeks. The researchers analysed the link between the occurrence of migraine attacks, their duration, intensity, and habitual consumption of caffeinated beverages and found no association between the two [23]. Another prospective cohort study found that the consumption of one to two servings of caffeinated beverages does not significantly affect the risk of migraine on any given day, while consumption of three or more servings may increase the likelihood of a headache [24]. Similar conclusions are drawn in other studies, with no significant differences found between headaches in patients with migraine or non-migraine headaches who consumed caffeine. However, it was noted that stress and depression levels decreased in migraine patients as caffeine consumption increased [25]. Adjusting caffeine consumption may play an important role in both seizure prevention and migraine treatment, as well as increasing the effectiveness of migraine therapy. Consumption of high amounts of caffeine, >500 mg per day, has been shown to reduce the incidence of headaches in patients with chronic headaches (>14 days per month) to less than seven days, classifying them as intermittent headaches, which may be related to the analgesic properties of caffeine. At the same time, among the remaining participants, high caffeine consumption increased the frequency of sporadic headaches [26]. Importantly, giving up caffeine consumption is characterised by a better response to treatment of acute migraine attacks with triptans [27]. Some studies indicate that caffeine may have an important role as an adjunct in the analgesic treatment of migraine and tension-type headache, especially when combined with OTC drugs such as paracetamol, ibuprofen or acetylsalicylic acid. Doses of caffeine ≥100mg or 130mg increase the benefits and efficacy of treatment in migraine and paroxysmal headache, respectively, and are well tolerated, but caution should be taken to ensure that patients do not overuse this type of medication, as they risk developing medication overuse headache [28]. The mechanism by which caffeine potentiates the analgesic effect has not yet been elucidated. However, several hypotheses have been put forward in the scientific literature to explain this phenomenon. One hypothesis is that caffeine, by increasing blood flow through the gastric mucosa, may enhance the absorption of paracetamol from the gastrointestinal tract, resulting in a more rapid achievement of its effective concentration in the central nervous system compared to monotherapy [29]. In addition, caffeine increases the production of cyclic AMP, which accelerates and enhances the absorption process in the stomach [30]. Another hypothesis suggests that caffeine directly affects the pharmacokinetics of paracetamol, increasing the maximum drug concentration, clearance and AUC_{0}-t (total exposure of the body to the drug over time). This effect may be due to the competitive effect of caffeine on adenosine receptors, which indirectly affects the metabolism and distribution of paracetamol [29]. Caffeine may also have a role in interrupting migraine attacks - a pilot study in 2014 showed that intravenous caffeine citrate 60 mg was a well-tolerated and safe treatment for acute migraine attacks [31].

Conclusions

Caffeine has an ambivalent role in the context of migraine and other non-migraine headaches. It can be both a trigger for a headache attack and an effective adjunct to their treatment. Caffeine acts on the central nervous system through adenosine receptor antagonism, which affects the cerebral vasculature and increases dopamine release in mesocorticolimbic structures. This explains both its analgesic and potentially pain-triggering effects. At the same time, neurotransmitter modulation improves cognitive function and shows neuroprotective effects. Withdrawal symptoms after abrupt cessation of caffeine intake have clinical similarities to migraine symptoms, but are not the same. Caffeine withdrawal can be a potent trigger of migraine in predisposed individuals. Both excessive and sudden reduction in caffeine intake can lead to the onset or worsening of migraines. Individual tolerance and the establishment of a safe, moderate daily dose is important. In controlled amounts, caffeine can assist in the treatment of acute migraine attacks, especially when combined with analgesics. Awareness of the potential effects of caffeine, its presence in foods and the possible consequences of withdrawal is crucial in the prevention of headaches and in the rational use of caffeine in migraine therapy.

Disclosure

Author's contribution

Conceptualization: [AŚ], [NJ]
Methodology: [AŚ], [NJ], [NP], [WM]
Software: [AŚ], [AH], [WM]
Check: [AŚ], [NJ], [NP], [KN]
Formal analysis: [TP], [AH], [NP], [KN]
Investigation: [AŚ], [NJ], [TP],[AH]
Resources: [WM], [NP], [TP], [NJ]
Data curation: [AŚ], [NJ]
Writing -rough preparation: [AŚ], [NJ]
Writing -reviewand editing: [NP], [TP], [KN]
Visualization: [AŚ], [NJ]
Supervision: [AŚ], [WM], [AH], [KN]
Project administration: [AŚ], [NJ]
All authors have read and agreed with the published version of the manuscript.

Funding Statement: No funding was sought or obtained in relation to this review article.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors wish to emphasize that they do not express gratitude to any individuals or institutions.

Conflict of Interest Statement: The authors declare no conflicts of interest.

REFERENCES

1. Gazerani P. (2020). Migraine and Diet. *Nutrients*, *12*(6), 1658. https://doi.org/10.3390/nu12061658
2. Nowaczewska, M., Wiciński, M., & Kaźmierczak, W. (2020). The Ambiguous Role of Caffeine in Migraine Headache: From Trigger to Treatment. *Nutrients*, *12*(8), 2259. https://doi.org/10.3390/nu12082259
3. Barbanti, P., Allais, G., Cevoli, S., Guerzoni, S., Valeriani, M., & Vernieri, F. (2024). The Role of the Combination Paracetamol/Caffeine in Treatment of Acute Migraine Pain: A Narrative Review. *Pain and therapy*, *13*(3), 319–346. https://doi.org/10.1007/s40122-024-00581-x
4. Pescador Ruschel, M. A., & De Jesus, O. (2024). Migraine Headache. In *StatPearls*. StatPearls Publishing.
5. Alstadhaug, K. B., & Andreou, A. P. (2019). Caffeine and Primary (Migraine) Headaches-Friend or Foe?. *Frontiers in neurology*, *10*, 1275. https://doi.org/10.3389/fneur.2019.01275
6. Thuraiaiyah, J., Kokoti, L., Al-Karagholi, M. A., & Ashina, M. (2022). Involvement of adenosine signaling pathway in migraine pathophysiology: a systematic review of preclinical studies. *The journal of headache and pain*, *23*(1), 43. https://doi.org/10.1186/s10194-022-01412-0
7. VanderPluym, J. H., Halker Singh, R. B., Urtecho, M., Morrow, A. S., Nayfeh, T., Torres Roldan, V. D., Farah, M. H., Hasan, B., Saadi, S., Shah, S., Abd-Rabu, R., Daraz, L., Prokop, L. J., Murad, M. H., & Wang, Z. (2021). Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis. *JAMA*, *325*(23), 2357–2369. https://doi.org/10.1001/jama.2021.7939
8. Mayans, L., & Walling, A. (2018). Acute Migraine Headache: Treatment Strategies. *American family physician*, *97*(4), 243–251.
9. Zduńska, A., Cegielska, J., Zduński, S., & Domitrz, I. (2023). Caffeine for Headaches: Helpful or Harmful? A Brief Review of the Literature. *Nutrients*, *15*(14), 3170. https://doi.org/10.3390/nu15143170
10. Evans, J., Richards, J. R., & Battisti, A. S. (2024). Caffeine. In *StatPearls*. StatPearls Publishing.
11. Low, J. J., Tan, B. J., Yi, L. X., Zhou, Z. D., & Tan, E. K. (2024). Genetic susceptibility to caffeine intake and metabolism: a systematic review. *Journal of translational medicine*, *22*(1), 961. https://doi.org/10.1186/s12967-024-05737-z
12. Nowaczewska, M., Wiciński, M., & Kaźmierczak, W. (2020). The Ambiguous Role of Caffeine in Migraine Headache: From Trigger to Treatment. *Nutrients*, *12*(8), 2259. https://doi.org/10.3390/nu12082259
13. Lone, A., Alnawah, A. K., Hadadi, A. S., Alturkie, F. M., Aldreweesh, Y. A., & Alhedhod, A. T. (2023). Coffee Consumption Behavior in Young Adults: Exploring Motivations, Frequencies, and Reporting Adverse Effects and Withdrawal Symptoms. *Psychology research and behavior management*, *16*, 3925–3937. https://doi.org/10.2147/PRBM.S427867
14. Gaspar, C., Rocha, C., Balteiro, J., & Santos, H. (2024). Effects of caffeine on cerebral blood flow. *Nutrition (Burbank, Los Angeles County, Calif.)*, *117*, 112217. https://doi.org/10.1016/j.nut.2023.112217
15. Higashi Y. (2019). Coffee and Endothelial Function: A Coffee Paradox?. *Nutrients*, *11*(9), 2104. https://doi.org/10.3390/nu11092104
16. Rodda, S., Booth, N., McKean, J., Chung, A., Park, J. J., & Ware, P. (2020). Mechanisms for the reduction of caffeine consumption: What, how and why. *Drug and alcohol dependence*, *212*, 108024. https://doi.org/10.1016/j.drugalcdep.2020.108024
17. Ogawa, N., & Ueki, H. (2007). Clinical importance of caffeine dependence and abuse. *Psychiatry and clinical neurosciences*, *61*(3), 263–268. https://doi.org/10.1111/j.1440-1819.2007.01652.x
18. Domaszewski P. (2023). Gender Differences in the Frequency of Positive and Negative Effects after Acute Caffeine Consumption. *Nutrients*, *15*(6), 1318. https://doi.org/10.3390/nu15061318
19. Juliano, L. M., Huntley, E. D., Harrell, P. T., & Westerman, A. T. (2012). Development of the caffeine withdrawal symptom questionnaire: caffeine withdrawal symptoms cluster into 7 factors. *Drug and alcohol dependence*, *124*(3), 229–234. https://doi.org/10.1016/j.drugalcdep.2012.01.009
20. Nehlig A. (1999). Are we dependent upon coffee and caffeine? A review on human and animal data. *Neuroscience and biobehavioral reviews*, *23*(4), 563–576. https://doi.org/10.1016/s0149-7634(98)00050-5
21. van Dusseldorp, M., & Katan, M. B. (1990). Headache caused by caffeine withdrawal among moderate coffee drinkers switched from ordinary to decaffeinated coffee: a 12 week double blind trial. *BMJ (Clinical research ed.)*, *300*(6739), 1558–1559. https://doi.org/10.1136/bmj.300.6739.1558
22. Agritelley, M. S., & Goldberger, J. J. (2021). Caffeine supplementation in the hospital: Potential role for the treatment of caffeine withdrawal. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, *153*, 112228. https://doi.org/10.1016/j.fct.2021.112228
23. Mittleman, M. R., Mostofsky, E., Vgontzas, A., & Bertisch, S. M. (2024). Habitual caffeinated beverage consumption and headaches among adults with episodic migraine: A prospective cohort study. *Headache*, *64*(3), 299–305. https://doi.org/10.1111/head.14673
24. Mostofsky, E., Mittleman, M. A., Buettner, C., Li, W., & Bertisch, S. M. (2019). Prospective Cohort Study of Caffeinated Beverage Intake as a Potential Trigger of Headaches among Migraineurs. *The American journal of medicine*, *132*(8), 984–991. https://doi.org/10.1016/j.amjmed.2019.02.015

25. Cho, S., Kim, K. M., & Chu, M. K. (2024). Coffee consumption and migraine: a population-based study. *Scientific reports*, *14*(1), 6007. https://doi.org/10.1038/s41598-024-56728-5
26. Hagen, K., Thoresen, K., Stovner, L. J., & Zwart, J. A. (2009). High dietary caffeine consumption is associated with a modest increase in headache prevalence: results from the Head-HUNT Study. *The journal of headache and pain*, *10*(3), 153–159. https://doi.org/10.1007/s10194-009-0114-6
27. Nowaczewska, M., Wiciński, M., & Kaźmierczak, W. (2020). The Ambiguous Role of Caffeine in Migraine Headache: From Trigger to Treatment. *Nutrients*, *12*(8), 2259. https://doi.org/10.3390/nu12082259
28. Lipton, R. B., Diener, H. C., Robbins, M. S., Garas, S. Y., & Patel, K. (2017). Caffeine in the management of patients with headache. *The journal of headache and pain*, *18*(1), 107. https://doi.org/10.1186/s10194-017-0806-2
29. Barbanti, P., Allais, G., Cevoli, S., Guerzoni, S., Valeriani, M., & Vernieri, F. (2024). The Role of the Combination Paracetamol/Caffeine in Treatment of Acute Migraine Pain: A Narrative Review. *Pain and therapy*, *13*(3), 319–346. https://doi.org/10.1007/s40122-024-00581-x
30. Espinosa Jovel, C. A., & Sobrino Mejía, F. E. (2017). Caffeine and headache: specific remarks. Cafeína y cefalea: consideraciones especiales. *Neurologia (Barcelona, Spain)*, *32*(6), 394–398. https://doi.org/10.1016/j.nrl.2014.12.016
31. Boppana, S. H., Peterson, M., Du, A. L., Kutikuppala, L. V. S., & Gabriel, R. A. (2022). Caffeine: What Is Its Role in Pain Medicine?. *Cureus*, *14*(6), e25603. https://doi.org/10.7759/cureus.25603