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# BREAKING THE CYCLE: CAFFEINE USE AS A SELF-MEDICATION STRATEGY FOR FATIGUE AND ITS ROLE IN SLEEP DISTURBANCE AND ANXIETY: A NARRATIVE REVIEW

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## ABSTRACT

Caffeine is widely used to counteract fatigue and maintain alertness in demanding daily contexts. Although this strategy may be effective in the short term, repeated fatigue-driven caffeine use may have unintended consequences for subsequent sleep and emotional regulation. This narrative review aims to synthesize current evidence on caffeine use as a self-medication strategy for fatigue and to examine its potential role in sleep disturbance, hyperarousal, and anxiety-like symptoms. Targeted literature searches were conducted in PubMed, PubMed Central, and Google Scholar. Evidence from review articles, randomized controlled trials, observational studies, meta-analyses, and relevant position statements was synthesized narratively. The reviewed literature indicates that caffeine may temporarily reduce perceived fatigue and support alertness by antagonizing central adenosine receptors. However, this pharmacological effect masks fatigue rather than resolving the underlying biological need for rest. At higher doses or when consumed later in the day, caffeine may impair sleep initiation, sleep continuity, restorative sleep architecture, and perceived sleep quality. Furthermore, in susceptible individuals, escalating caffeine intake may contribute to central nervous system hyperarousal and anxiety-like symptoms, which can further disrupt sleep and reinforce next-day fatigue. Based on these findings, this review proposes a conceptual fatigue–caffeine–sleep disturbance–anxiety cycle, in which short-term fatigue management may unintentionally sustain longer-term impaired recovery. Public health and behavioral recommendations should therefore emphasize dose, timing of intake, sleep hygiene, and individual susceptibility rather than simple caffeine avoidance.

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**KEYWORDS**Caffeine, Fatigue, Self-medication, Sleep Disturbance, Hyperarousal, Anxiety

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## 1. Introduction

Caffeine remains one of the most widely consumed psychoactive substances worldwide and is commonly present in coffee, tea, energy drinks, and dietary supplements [1,2,15]. Its use is widely normalized and socially accepted, and moderate caffeine intake is generally considered safe for most healthy adults [1,2]. In many contexts, individuals routinely use caffeine to enhance alertness, vigilance, and cognitive performance, relying on its stimulant properties to meet the demands of modern life [1,15].

A central context for this widespread caffeine consumption is the experience of fatigue. Fatigue is a prevalent physical and cognitive state characterized by a reduced capacity to sustain physical or mental exertion, and it is frequently linked to chronic sleep restriction, high cognitive load, and demanding academic or occupational environments [3,13,14,17,19]. This state may diminish concentration, vigilance, motivation, and overall performance, creating a strong motivation to seek rapid methods of restoring perceived functioning [3,14]. Because contemporary lifestyles often limit opportunities for immediate rest or adequate recovery, individuals may turn to accessible countermeasures that allow them to maintain daily functioning despite fatigue [17,18,19].

In this context, caffeine use can be conceptualized as a form of self-medication: a behavioral strategy in which an individual uses a substance to alleviate an unpleasant or distressing internal state, which in this case is fatigue [16]. Caffeine is well positioned for this role because of its widespread availability, legal status, affordability, familiarity, and social acceptance [1,16,17]. Through competitive antagonism of central adenosine receptors, caffeine may temporarily reduce the subjective perception of fatigue and effort while improving perceived alertness and readiness to function [12,15]. This mechanism provides an accessible means of pharmacological coping when biological rest is not immediately feasible [12,15,17].

However, while this short-term relief may be useful, it can also carry a physiological cost. Caffeine may mask the sensation of fatigue, but it does not eliminate the underlying biological need for rest and recovery [12]. When consumed in higher doses, later in the day, or by susceptible individuals, caffeine may disrupt subsequent sleep [12,21]. This disruption may affect sleep onset, total sleep duration, sleep continuity, restorative sleep architecture, and subjective sleep quality [5,21,22,23]. Consequently, impaired nocturnal recovery may contribute to persistent next-day fatigue, which in turn may increase the likelihood of further fatigue-driven caffeine use [3,21,22].

Furthermore, this cycle of fatigue and sleep disruption may be complicated by secondary psychological and physiological effects. Caffeine-induced central nervous system arousal appears to operate on a continuum: while low-to-moderate doses may promote functional alertness, higher doses or intake by susceptible individuals may contribute to overstimulation [2,10,12]. This hyperarousal may manifest as anxiety-like symptoms, including jitteriness, restlessness, nervousness, psychological tension, and autonomic arousal [2,4,7]. Importantly, caffeine should not be described as a direct underlying cause of clinical anxiety disorders. Rather, its acute physiological effects may induce or exacerbate anxiety-like symptoms, particularly at higher intake levels or in vulnerable individuals [4,7,10]. These symptoms may interact with sleep disturbance, as heightened psychological tension and physiological arousal can further impair sleep initiation and perceived sleep quality, thereby increasing daytime distress and reinforcing the maladaptive behavioral loop [4,19,21,22].

Despite extensive literature on caffeine, previous research has often examined its effects in separate domains, focusing on cognitive performance, sleep, anxiety, dependence, or withdrawal [1,7,12,15,21]. There remains a need to integrate these perspectives into a cohesive framework that explains how caffeine use may become embedded in a broader fatigue-driven cycle. Therefore, this narrative review aims to synthesize current evidence on caffeine use as a self-medication strategy for fatigue and to examine how this pattern may contribute to a self-perpetuating cycle involving sleep disturbance, hyperarousal, anxiety-like symptoms, and repeated fatigue-driven caffeine consumption. By integrating these mechanisms, this review seeks to clarify how short-term fatigue management may unintentionally sustain longer-term patterns of impaired recovery and to highlight potential avenues for more sustainable fatigue management [12,16,21].

## 2. Methodology

This article was designed as a narrative review aimed at synthesizing current evidence on caffeine use as a self-medication strategy for fatigue and its potential role in sleep disturbance, hyperarousal, and anxiety-like symptoms. The primary objective was to integrate findings from diverse physiological, psychological, and behavioral domains into a cohesive conceptual framework illustrating how short-term fatigue countermeasures may inadvertently contribute to longer-term disruption.

To construct this narrative synthesis, targeted literature searches were conducted across multiple electronic databases and academic search engines, including PubMed, PubMed Central, and Google Scholar. The search focused on English-language publications representing various methodological designs, including review articles, systematic reviews, meta-analyses, randomized controlled trials, observational studies, and relevant position statements. Although priority was given to recent literature, selected earlier foundational publications were included when they provided important mechanistic, methodological, or conceptual context directly relevant to the review topic. Searches were conducted using combinations of terms including “caffeine,” “fatigue,” “self-medication,” “sleep disturbance,” “sleep quality,” “sleep architecture,” “adenosine,” “hyperarousal,” “anxiety,” “CYP1A2,” and “ADORA2A.” The final literature search was updated in July 2026. A total of 24 publications were included in the final narrative synthesis.

During the literature selection process, publications were prioritized if they directly addressed caffeine’s pharmacological mechanisms, fatigue-related use, subsequent sleep outcomes, anxiety-like symptoms, individual susceptibility, or broader behavioral and public health implications. Articles were excluded or considered only secondarily if they focused on topics unrelated to the fatigue–caffeine–sleep disturbance–anxiety cycle, described purely clinical cases of acute caffeine toxicity, lacked peer review, were unavailable in English, or primarily investigated psychoactive substances other than caffeine.

Rather than performing a quantitative statistical analysis, the collected findings were synthesized narratively. The evidence was organized into thematic domains to facilitate a logical progression of concepts. These domains included caffeine pharmacology, fatigue as a behavioral driver, caffeine-related sleep disruption, hyperarousal and anxiety-like symptoms, and the integrated fatigue–caffeine–sleep disturbance–anxiety cycle. This organizational structure was chosen to construct a conceptual model rather than to evaluate isolated clinical variables or estimate pooled effect sizes.

It is important to acknowledge the inherent methodological limitations of this approach. Because this article was designed as a narrative review, it does not claim to be fully systematic or exhaustive in its literature capture. No formal meta-analysis or systematic risk-of-bias assessment was conducted. The selection of literature was primarily guided by relevance to the proposed conceptual model. Consequently, the synthesis and conclusions presented herein should be interpreted as conceptual, integrative, and hypothesis-generating rather than as definitive quantitative estimates of effect size.

### 3. Results: Narrative Synthesis

The literature synthesized in this review was organized into four thematic domains: caffeine pharmacology, fatigue as a behavioral driver of caffeine use, caffeine-related sleep disruption, and caffeine-associated hyperarousal and anxiety-like symptoms. These domains provide the basis for the integrative model discussed in the following section.

#### 3.1. Caffeine Pharmacology, Tolerance, and Withdrawal

##### Mechanism of Action

Caffeine is the most widely consumed psychoactive substance worldwide, and its stimulant effects are primarily mediated by competitive antagonism of adenosine receptors, particularly the A1 and A2A receptor subtypes [1,5]. During prolonged wakefulness, extracellular adenosine concentrations gradually increase, contributing to homeostatic sleep pressure and reduced wakefulness [12]. By competitively occupying adenosine receptors without activating them, caffeine effectively blocks adenosine from exerting its inhibitory effects [1]. Consequently, caffeine may temporarily mask the physiological perception of fatigue and promote wakefulness, which may delay sleep onset when consumed later in the day [12,21].

Furthermore, the blockade of adenosine receptors initiates a cascade of downstream neurochemical changes [4]. The inhibition of adenosine's regulatory function indirectly promotes the release of excitatory neurotransmitters, enhancing dopaminergic and noradrenergic neurotransmission [4,12]. This secondary mechanism may contribute to the short-term cognitive benefits associated with caffeine intake, including enhanced alertness, improved concentration, attention, vigilance, and overall cognitive performance [15]. Although these neurochemical changes contribute to the beneficial cognitive effects of caffeine, they may also promote physiological hyperarousal. In susceptible individuals or following high caffeine intake, this heightened state of arousal has been associated with increased anxiety-like symptoms, restlessness, and physiological tension [6,7].

##### Metabolism and Pharmacokinetics

Following oral administration, caffeine is rapidly and almost completely absorbed from the gastrointestinal tract, reaching peak plasma concentrations within 30 to 120 minutes [8]. Caffeine is primarily metabolized in the liver by the cytochrome P450 enzyme CYP1A2, which converts it into three major metabolites: paraxanthine, theobromine, and theophylline [4,8]. In healthy adults, the average half-life of caffeine ranges from approximately 3–7 hours; however, this duration exhibits significant interindividual variability [8].

Crucially, the rate of caffeine clearance is substantially influenced by both genetic and environmental factors. Polymorphisms in the *CYP1A2* gene can classify individuals as "fast" or "slow" metabolizers, thereby influencing the circulating caffeine concentrations and potentially modifying individual susceptibility to sleep disturbances and anxiety [10]. Furthermore, exogenous factors such as tobacco smoking significantly accelerate CYP1A2 activity, shortening the half-life, whereas oral contraceptives and certain medications, particularly fluvoxamine, can inhibit the enzyme, substantially prolonging caffeine's presence in the systemic circulation [10]. These pharmacokinetic differences may partially explain why identical caffeine doses produce markedly different physiological and psychological responses across individuals.

##### Tolerance

Regular or chronic caffeine consumption is associated with the development of pharmacological tolerance, primarily driven by the neuroadaptation of adenosine receptors [1,12]. In response to the continuous receptor blockade by caffeine, the compensatory neuroadaptive mechanisms include the upregulation (increasing the density of) A1 and A2A adenosine receptors [1,12]. Consequently, an individual may require notably higher doses of caffeine to achieve the same stimulatory and anti-fatigue effects that were previously attained with lower doses [1,2]. This phenomenon of tolerance may contribute to the self-perpetuating cycle, as escalating intake may fail to resolve fatigue while increasing the likelihood of adverse effects, such as sleep disruption and hyperarousal [1,2].

## **Withdrawal Symptoms**

When chronic caffeine intake is abruptly reduced or completely discontinued, individuals experience caffeine withdrawal symptoms [1]. Because the brain has upregulated its adenosine receptors, the sudden absence of caffeine allows endogenous adenosine to interact with the upregulated receptor population, resulting in an exaggerated inhibitory response [1]. Common withdrawal symptoms may include daytime sleepiness, lethargy, headache, impaired concentration, and low mood [1,11]. In the context of self-medication, these symptoms may be misinterpreted as baseline fatigue or reduced mood, prompting renewed caffeine consumption to alleviate discomfort [1,11]. This pattern may reinforce habitual caffeine consumption and contribute to the broader self-perpetuating cycle of fatigue, caffeine use, and sleep disturbance [1,11].

### **3.2. Fatigue as a Driver of Caffeine Consumption**

Fatigue is a pervasive, multifaceted phenomenon that represents an important behavioral driver of caffeine consumption in modern society [13,14]. Beyond its traditional role as a widely consumed dietary component, caffeine is increasingly used as a functional strategy to counteract fatigue associated with chronic sleep restriction, demanding lifestyles, and psychological stress [12,15]. Whether resulting from insufficient sleep, prolonged cognitive demands, or work-related demands, fatigue significantly impairs both physiological and cognitive functioning, creating a strong motivation to consume caffeine in an attempt to restore alertness and maintain daily functioning [13,14]. Understanding fatigue not merely as a subjective sensation, but as an important behavioral catalyst, is essential for analyzing the self-perpetuating cycle of caffeine self-medication and its broader implications for public health [12]. Among the various strategies used to cope with fatigue, caffeine remains one of the most accessible and widely consumed psychoactive substances, making it a common self-medication strategy despite its potential unintended consequences [1,15,17].

### **Fatigue as a Physiological and Cognitive Signal**

Fatigue can be understood as a physiological and cognitive signal indicating a reduced capacity to sustain physical or mental activity [13,14]. Rather than being merely a subjective sense of discomfort, it functions as a critical regulatory mechanism that encourages rest, recovery, and the conservation of biological resources [13]. In this sense, fatigue serves an adaptive role: it alerts the individual that continued exertion may compromise performance, increase error risk, or delay recovery [13,14]. It may therefore manifest across both somatic and cognitive domains, including reduced physical endurance, diminished concentration, impaired vigilance, and decreased motivation to continue effortful activity [13,14].

Within the sleep-wake system, fatigue is closely related to the progressive accumulation of sleep pressure during prolonged wakefulness, a process in which extracellular adenosine plays a central role [12]. By competitively antagonizing adenosine receptors, caffeine temporarily interferes with this sleep-promoting signal and reduces the subjective perception of fatigue [12,15]. However, this effect should not be interpreted as true restoration. Although caffeine may acutely improve alertness and perceived readiness to function, it does not eliminate the underlying physiological need for rest or recovery [12,15]. This distinction between suppressing the perception of fatigue and resolving its biological causes is essential for understanding why caffeine may become a repeated self-medication strategy [12,15].

### **Physical and Mental Fatigue**

Physical and mental fatigue represent distinct but overlapping pathways through which individuals may become motivated to consume caffeine. Physical fatigue may involve both peripheral and central components. Peripheral fatigue refers to a decline in the capacity of skeletal muscle to generate force, whereas central fatigue reflects changes within the central nervous system that reduce the ability to initiate or sustain effortful activity [13]. In everyday life, these mechanisms may be experienced as bodily exhaustion, reduced stamina, or a decreased readiness to engage in routine physical tasks. Caffeine may be attractive in this context because it can reduce the subjective perception of effort and support perceived readiness to function, particularly through its central nervous system effects [15]. However, such effects should be understood as temporary improvements in perceived capacity rather than resolution of the underlying causes of fatigue [13,15].

Mental fatigue, in contrast, is more closely associated with prolonged cognitive effort, sustained attention, heavy information processing, and psychological demands [14]. It is commonly reflected in declining concentration, reduced vigilance, slower cognitive performance, and decreased motivation to continue effortful mental activity [14]. In occupational, academic, and everyday settings, these symptoms may create a strong motivation to seek rapid restoration of alertness. Caffeine is particularly attractive for this purpose because it is easily accessible, familiar, and capable of acutely enhancing alertness and perceived cognitive readiness [1,15]. As a result, caffeine may become a routine strategy for maintaining functioning during periods of mental fatigue, even when the fatigue itself reflects an unmet need for rest, recovery, or reduced cognitive load [12,14].

### **Caffeine as a Self-Medication Strategy for Fatigue**

The concept of self-medication involves the use of a substance to alleviate an unpleasant or distressing internal state, which in this context manifests as physical or mental fatigue [16]. Caffeine is particularly well positioned for this role because of its wide accessibility, low cost, legal status, and strong social normalization [1]. Unlike many other psychoactive substances, daily caffeine consumption is culturally accepted and frequently integrated into occupational, academic, and social routines [1,17]. Consequently, caffeine may become a readily adopted strategy for individuals who feel compelled to maintain daily functioning despite significant fatigue, particularly in high-demand educational or occupational contexts [17,18].

Repeated reliance on caffeine as a coping strategy is largely reinforced by its short-term efficacy. Following ingestion, caffeine can rapidly reduce perceived sleepiness and attenuate the subjective experience of fatigue [12,15]. By acutely enhancing alertness, vigilance, and perceived readiness to function, it provides tangible benefits that may facilitate performance across work, study, and routine obligations [15]. This rapid alleviation of symptoms may reinforce repeated use, as individuals learn to associate caffeine consumption with restored cognitive capacity and the ability to continue functioning despite fatigue [1,15,19].

However, using caffeine as a primary countermeasure against fatigue may become problematic when it replaces rest, recovery, or behavioral adjustment. Caffeine does not resolve the underlying physiological causes of exhaustion; rather, it temporarily masks fatigue by interfering with sleep-promoting adenosine signaling [12]. Although this pharmacological masking may allow individuals to continue functioning despite daily demands, it may also delay rest and reduce opportunities for adequate recovery [3,12]. Ultimately, this dynamic may contribute to a maladaptive behavioral loop: persistent fatigue promotes caffeine consumption, caffeine enables continued exertion despite the need for recovery, and insufficient recovery may further intensify fatigue. In this way, caffeine-based self-medication may be effective in the short term while simultaneously reinforcing a self-sustaining cycle of fatigue-driven caffeine use [1,12,19].

### **Short-Term Relief and the Beginning of the Cycle**

The short-term efficacy of caffeine makes it an attractive countermeasure against fatigue. Following consumption, caffeine can acutely improve alertness, vigilance, reaction time, and perceived readiness to function [15]. These benefits may be particularly relevant in states of marked fatigue or sleep deprivation, where caffeine has been shown to partially mitigate specific cognitive deficits [20]. However, these effects remain inherently incomplete. Although caffeine can temporarily restore certain aspects of performance, it does not constitute true physiological recovery, nor does it fully reverse the broader cognitive and somatic consequences of sleep loss [3,20].

Because caffeine provides rapid and noticeable relief, individuals may learn to rely on it as a primary coping mechanism. This behavioral reinforcement can enable them to continue occupational or academic tasks while temporarily overriding the biological drive to rest [12]. However, this strategy may carry physiological costs. Evidence from a randomized crossover trial suggests that high-dose caffeine may negatively affect subsequent sleep in a dose- and timing-dependent manner, particularly by delaying sleep initiation, increasing sleep fragmentation, altering sleep architecture, and reducing perceived sleep quality when consumed closer to bedtime [21]. Consequently, poorer sleep quality or reduced sleep duration may exacerbate fatigue the following day [3,21]. This diminished nocturnal recovery may set the stage for continued, and sometimes escalating, caffeine consumption, marking the beginning of a self-perpetuating cycle: fatigue promotes caffeine use, caffeine enables continued functioning despite the need for recovery, and impaired sleep may generate greater fatigue, reinforcing further self-medication [12,21].

### 3.3. Effects of Caffeine on Sleep

Caffeine use as a self-medication strategy for fatigue is closely linked to the regulation of sleep–wake processes. The same pharmacological mechanism that makes caffeine effective in the short term for restoring alertness—competitive antagonism of central adenosine receptors—also underlies its potential to interfere with subsequent sleep [12]. Because the progressive accumulation of extracellular adenosine contributes to homeostatic sleep pressure, blocking adenosine signaling may impair sleep initiation, sleep continuity, and restorative sleep processes, particularly when caffeine is consumed in higher doses or later in the day [12,21]. Understanding caffeine’s impact on sleep is therefore critical, as impaired nocturnal recovery may intensify next-day fatigue and further reinforce fatigue-driven caffeine use [3,12,21].

#### Sleep Onset and Sleep Duration

The transition from wakefulness to sleep is strongly influenced by homeostatic sleep pressure, which increases during prolonged wakefulness and is closely linked to the accumulation of extracellular adenosine [12]. By competitively binding to central adenosine receptors, caffeine can attenuate this sleep-promoting signal and promote continued wakefulness [12]. As a result, caffeine consumption, particularly at higher doses or when consumed closer to bedtime, may delay sleep initiation and increase sleep onset latency [21]. In a randomized crossover trial involving 23 young men, 400 mg of caffeine, but not 100 mg, significantly delayed sleep initiation and altered subsequent sleep when consumed within 12 hours of bedtime, with stronger effects observed when intake occurred closer to bedtime [21].

In addition to delaying sleep onset, caffeine may contribute to shorter total sleep duration, especially when its alerting effects persist into the intended sleep period [21]. This effect is particularly relevant for individuals who maintain a fixed wake time for occupational, academic, or social obligations, as delayed sleep initiation may reduce the available sleep window. Importantly, the magnitude of these effects depends on both dose and timing: lower doses may have minimal measurable impact, whereas higher doses consumed later in the day are more likely to impair sleep initiation and reduce subsequent sleep opportunity [21]. Thus, caffeine-related disruption of sleep onset and sleep duration represents an important pathway through which short-term fatigue relief may compromise nocturnal recovery [3,12,21].

#### Sleep Quality, Sleep Efficiency, and Fragmentation

Beyond delaying sleep onset, caffeine may also affect the continuity and perceived quality of the sleep period. Sleep efficiency, commonly defined as the proportion of time in bed that is actually spent asleep, may be reduced when caffeine-related arousal persists into the intended sleep episode [21]. Even when individuals successfully initiate sleep, residual caffeine activity may contribute to increased nocturnal arousal, more frequent awakenings, and greater wake after sleep onset (WASO), particularly after higher doses consumed closer to bedtime [12,21]. Such fragmentation may reduce the continuity of sleep and limit the degree to which the sleep episode is experienced as restorative [21].

In addition to objective disruptions, caffeine may be associated with poorer subjective sleep experience [21,22]. Over time, reduced sleep continuity or poorer perceived recovery may contribute to next-day fatigue, thereby strengthening the behavioral motivation to use caffeine again [3,9,21,22].

#### Sleep Architecture and Recovery Sleep

Beyond altering sleep duration and continuity, caffeine may also affect sleep architecture and sleep-related EEG markers. Under normal physiological conditions, restorative sleep is partially supported by sufficient time spent in deep, slow-wave sleep, corresponding to N3 sleep within non-rapid eye movement (NREM) sleep [5]. Experimental evidence suggests that higher-dose caffeine exposure may shift sleep toward a lighter profile, with reductions in N3 sleep and relative increases in lighter NREM stages, particularly when caffeine is consumed closer to the sleep period [5,21]. In addition to these macrostructural changes, quantitative electroencephalography (EEG) studies indicate that caffeine can attenuate slow-wave activity and low-frequency delta power during NREM sleep [5,23]. Because slow-wave activity is widely considered an electrophysiological marker of sleep intensity and homeostatic sleep pressure, its reduction suggests that caffeine may attenuate aspects of physiological sleep depth and restorative potential [5,23].

The effects of caffeine on sleep architecture may be particularly relevant in the context of recovery sleep following sleep deprivation. Under conditions of prior sleep loss, the central nervous system typically shows

increased homeostatic pressure, often reflected in greater slow-wave activity during subsequent recovery sleep [5]. However, caffeine exposure during periods of prolonged wakefulness may interfere with this compensatory response by continuing to antagonize adenosine signaling during the subsequent sleep opportunity [5,23]. As a result, caffeine may attenuate aspects of the expected recovery-sleep response, including slow-wave activity and other EEG markers of sleep homeostasis [5,23]. This is especially important for the present review because it suggests that caffeine may not only mask daytime fatigue but also reduce the quality of the recovery process needed to resolve it. In this way, caffeine-related alterations in sleep architecture and recovery sleep may contribute to persistent next-day fatigue and reinforce repeated fatigue-driven caffeine use [3,5,23].

### **Dose, Timing, and Individual Susceptibility**

The magnitude of caffeine-induced sleep disruption is not uniform; rather, it appears to be strongly influenced by the administered dose and the temporal proximity of consumption to bedtime. Evidence from a randomized crossover trial suggests a dose- and timing-dependent relationship: while a lower dose of caffeine, such as 100 mg, may have minimal measurable impact on subsequent nocturnal sleep, a higher dose, such as 400 mg, is more likely to disrupt sleep, particularly when consumed closer to bedtime [21]. Timing is therefore a critical factor. When caffeine is consumed later in the day, circulating caffeine levels may remain elevated during the intended sleep period, increasing the likelihood of interference with sleep initiation, sleep continuity, and sleep architecture [12,21]. Thus, behavioral patterns involving high-dose or late-day caffeine consumption appear especially relevant for understanding caffeine-related sleep disruption [21].

However, even when dose and timing are similar, there may be substantial inter-individual variability in sleep-related responses to caffeine due to differences in metabolism and receptor sensitivity [8,10]. As noted in earlier sections, polymorphisms in the CYP1A2 gene may influence the rate of hepatic caffeine clearance, meaning that some individuals metabolize caffeine more slowly and may experience prolonged exposure after a given dose [8,10]. In addition, variation in the ADORA2A gene has been associated with individual sensitivity to caffeine's central nervous system effects, including susceptibility to caffeine-related sleep disturbance [10]. Although recent experimental work has included CYP1A2 and ADORA2A genotyping, not all studies observe significant genotype effects on sleep outcomes, highlighting the need for further research [21]. Consequently, a caffeine dose that has little observable effect on sleep in one individual may produce more pronounced sleep disruption in another, particularly among those with slower caffeine metabolism or greater sensitivity to caffeine-induced arousal [10,21]. These individual differences highlight the limitations of universal caffeine recommendations and support the need for personalized guidance regarding dose, timing, and susceptibility.

### **Subjective vs Objective Sleep Perception**

A clinically relevant aspect of caffeine-related sleep disruption is the potential discrepancy between subjective sleep perception and objective sleep parameters. Some individuals may conclude that caffeine does not affect their sleep because they are still able to fall asleep or because they do not perceive major changes in sleep quality. However, experimental evidence suggests that subjective perception may not fully capture caffeine-related changes in subsequent sleep [21]. In a randomized crossover trial, high-dose caffeine altered objective sleep outcomes, including sleep initiation, fragmentation, and sleep architecture. The authors also noted that individuals may have difficulty accurately perceiving caffeine's influence on sleep quality [21].

This discrepancy is important because subjective sleep perception may shape future caffeine-related behavior. If individuals do not recognize that caffeine affects their sleep, they may be less likely to modify the dose or timing of intake. Evidence from wearable-based and self-reported sleep research further suggests that perceived sleep quality and device-derived sleep parameters do not always align, with self-assessed sleep quality sometimes worsening even when objective wearable metrics show limited or inconsistent changes [22]. Such misalignment may reinforce continued caffeine use, particularly when individuals attribute next-day fatigue to workload, stress, or insufficient time rather than to caffeine-related sleep disruption. Over time, reduced sleep continuity, poorer perceived recovery, or unrecognized sleep impairment may contribute to next-day fatigue and strengthen the motivation to use caffeine again [3,9,21,22].

### 3.4. Caffeine, Hyperarousal, and Anxiety

Beyond its role in counteracting fatigue and promoting wakefulness, caffeine may also influence emotional arousal and anxiety-like symptoms. This is particularly relevant in the context of fatigue-driven caffeine use, because individuals who consume caffeine to maintain functioning may unintentionally shift from adaptive alertness toward excessive physiological and psychological activation. The relationship between caffeine and anxiety is dose-dependent and moderated by individual susceptibility, sleep disruption, and baseline psychological vulnerability [4,6,7,10,12]. Therefore, caffeine-related hyperarousal may represent an important mechanism linking fatigue self-medication with sleep disturbance, emotional dysregulation, and repeated caffeine use.

#### Caffeine-Induced Arousal and Anxiety-Like Symptoms

The central nervous system arousal induced by caffeine operates on a continuum. At low-to-moderate doses, competitive antagonism of central adenosine receptors may reduce perceived fatigue and promote a desirable state of alertness [12]. However, the boundary between optimal alertness and excessive central nervous system stimulation, often described as hyperarousal, is not fixed. Depending on the administered dose and individual physiological susceptibility, the same pharmacological mechanism that facilitates wakefulness may also contribute to overstimulation [2,12].

When caffeine intake exceeds an individual's tolerance or sensitivity threshold, intended alertness may shift into a cluster of adverse anxiety-like symptoms. These commonly include nervousness, restlessness, irritability, palpitations, jitteriness, and increased physical tension [2,7]. It is important to note that caffeine should not be described as a direct underlying cause of clinical anxiety disorders. Rather, its acute physiological effects may induce somatic and psychological responses that resemble or exacerbate feelings of anxiety, particularly at higher doses or in susceptible individuals [4,7]. Meta-analytical evidence suggests that higher caffeine intake is associated with an increased risk of anxiety symptoms, especially at elevated consumption levels [7].

Consequently, individuals who consume high doses of caffeine to counteract pronounced fatigue may inadvertently induce a state of counterproductive hyperarousal. Instead of achieving calm, focused readiness, they may experience an uncomfortable state of agitation, bodily tension, and heightened psychological distress [2,4]. This paradoxical effect underscores that pharmacologically masking fatigue may carry a physiological cost: excessive activation of arousal systems can hinder, rather than support, optimal daily functioning [2,12].

#### Dose-Dependent Anxiety Effects

Psychological and somatic responses to caffeine appear to be dose-related and may follow an inverted-U pattern, in which beneficial effects at lower intake levels are progressively offset by adverse effects at higher doses. At low-to-moderate levels of intake, caffeine is generally well tolerated and may support alertness, vigilance, and wakefulness, making it attractive as a short-term countermeasure against fatigue [12,15]. Within this lower dose range, caffeine may therefore serve its intended function without necessarily producing marked psychological distress, although individual sensitivity remains an important modifying factor [2].

However, as consumption increases, the beneficial cognitive effects of caffeine may plateau, while signs of central nervous system overstimulation become more likely. Higher doses are more consistently associated with anxiety-like symptoms, including nervousness, heightened psychological tension, jitteriness, restlessness, and symptoms of autonomic arousal [2,4,7]. Meta-analytical evidence suggests that caffeine intake is associated with an increased risk of anxiety symptoms, particularly when daily intake exceeds approximately 400 mg [7]. This threshold should not be interpreted as universal, since caffeine sensitivity varies substantially across individuals; nevertheless, it provides a clinically useful reference point for identifying potentially problematic consumption patterns [2,7].

This dose-dependent shift from enhancement to hyperarousal is particularly relevant for individuals using caffeine to manage persistent or accumulating fatigue. In an effort to compensate for exhaustion, individuals may progressively increase their caffeine intake, thereby increasing the likelihood of crossing from functional alertness into overstimulation [1,6,7]. Consequently, rather than simply improving daily functioning, higher caffeine intake may generate a secondary burden of anxiety-like symptoms that further complicates concentration, emotional regulation, and overall well-being [4,7].

**Individual Vulnerability: Metabolism, Receptor Sensitivity, and Baseline Anxiety**

Physiological and psychological responses to caffeine are not uniform across the population; rather, they are characterized by substantial inter-individual variability. A dose that produces mild, focused alertness in one individual may produce more pronounced hyperarousal, sleep disruption, or anxiety-like symptoms in another [10]. This variability may be partly explained by genetic polymorphisms affecting both caffeine metabolism and pharmacodynamic sensitivity. Variations in the CYP1A2 gene may influence the rate of hepatic caffeine clearance, meaning that slower metabolizers can experience more prolonged systemic exposure after a given dose [8,10]. In addition, polymorphisms in the ADORA2A gene may contribute to individual differences in sensitivity to caffeine's central nervous system effects, including susceptibility to caffeine-induced arousal and anxiety-like responses [10].

Beyond genetic factors, an individual's psychological baseline may also shape how caffeine-induced arousal is experienced. Individuals with higher baseline anxiety or greater sensitivity to bodily sensations may be more vulnerable to interpreting caffeine-related somatic effects as distressing [4,7]. Symptoms such as palpitations, tremor, restlessness, or increased bodily tension may therefore amplify pre-existing psychological discomfort, particularly when caffeine is consumed in higher doses or under conditions of stress and fatigue [2,7]. In this context, caffeine-induced arousal may act as an additional burden, intensifying rather than relieving the subjective strain associated with fatigue.

Finally, the manifestation of these symptoms may be influenced by prior patterns of caffeine consumption and the development of tolerance. Habitual caffeine consumers may develop partial tolerance to some of caffeine's subjective and autonomic effects, although tolerance is variable and may not fully protect against sleep disruption or anxiety-like symptoms [1,10,21]. Conversely, individuals who consume caffeine infrequently, or who rapidly increase their intake during periods of acute fatigue, may be more likely to experience noticeable somatic and psychological side effects [1,8]. Thus, vulnerability to caffeine-induced hyperarousal reflects a complex interaction between genetic predisposition, baseline psychological state, habitual use, and situational factors such as stress, sleep loss, and fatigue.

**Caffeine, Sleep Disturbance, and Anxiety**

Sleep disturbance may represent an important pathway through which fatigue-driven caffeine use contributes to anxiety-like symptoms. As discussed in previous sections, caffeine consumption, particularly at higher doses or later in the day, may delay sleep initiation, increase sleep fragmentation, and reduce the restorative value of sleep [21,22]. Impaired nocturnal recovery may then contribute to next-day fatigue, irritability, and increased vulnerability to stress-related arousal [4,19,21,22,24]. In this way, the psychological consequences of caffeine use may not result solely from its acute stimulant effects, but also from its indirect impact on sleep continuity and recovery.

When nocturnal recovery is inadequate, individuals may wake with a lower threshold for psychological distress and poorer emotional regulation [4,24]. In demanding contexts, particularly high-pressure academic environments, this vulnerability may interact with maladaptive coping patterns such as problematic overstudying and excessive caffeine intake [19]. Consequently, anxiety-like symptoms attributed to caffeine's stimulant properties may be partly amplified by caffeine-related sleep disruption and insufficient recovery [4,9,19,24].

Ultimately, the interaction between caffeine, sleep disturbance, and emotional dysregulation may contribute to a maladaptive behavioral loop. Poor sleep may lead to daytime fatigue and heightened psychological tension. To compensate for exhaustion and maintain daily functioning, individuals may consume more caffeine, which can further increase physiological arousal and anxiety-like symptoms [4,19]. If this caffeine intake occurs at high doses or later in the day, it may further impair subsequent sleep, thereby reinforcing the cycle: caffeine use disrupts sleep, impaired sleep contributes to fatigue and emotional dysregulation, and this distressed state increases the motivation for further fatigue-driven caffeine consumption [4,19,21,22,24].

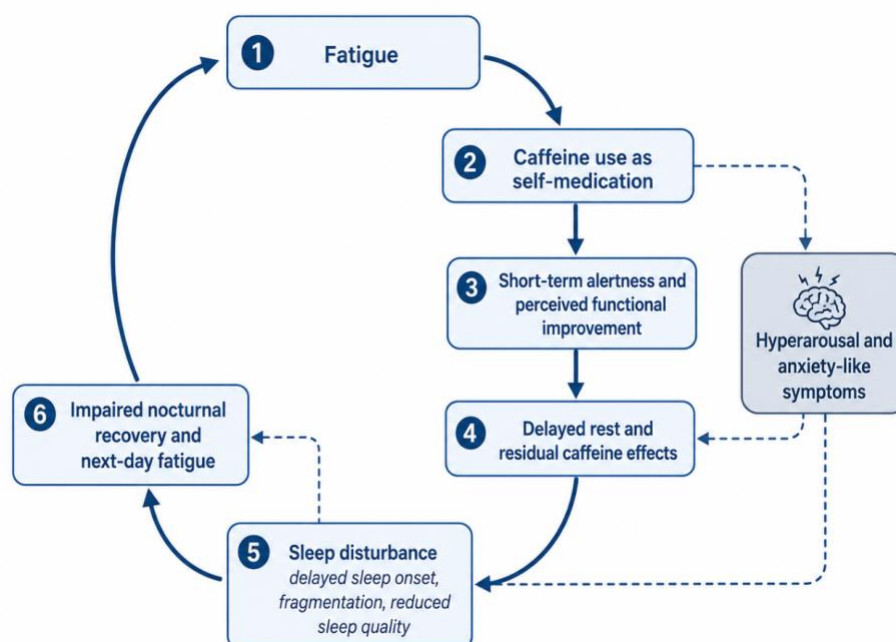
## Anxiety as a Reinforcing Component of the Fatigue–Caffeine Cycle

While caffeine is frequently used as an accessible, short-term strategy to counteract fatigue, caffeine-related hyperarousal may represent an important physiological and psychological cost [1,7,15]. Anxiety-like symptoms associated with higher caffeine intake should not be viewed merely as isolated side effects; rather, they may become reinforcing components within a broader behavioral loop involving fatigue, sleep disruption, and repeated caffeine use [4,19]. When caffeine consumption shifts from functional alertness toward overstimulation, the resulting psychological tension and autonomic arousal may make it more difficult for individuals to transition into restorative sleep [7,12,21].

As a result, heightened arousal may contribute to delayed sleep onset, sleep fragmentation, alterations in sleep architecture, and poorer subjective sleep quality, particularly when caffeine is consumed in higher doses or later in the day [21,22]. This caffeine-related sleep disruption may contribute to next-day fatigue and a reduced sense of recovery [3,21,22]. In response to this intensified fatigue, individuals may become more motivated to use caffeine again as a rapid countermeasure, thereby reinforcing the original behavioral pattern [1,15,19]. Importantly, anxiety-like symptoms may not always deter further caffeine consumption. Instead, by contributing to arousal and poorer sleep, they may indirectly perpetuate the fatigue that drives caffeine use, thereby contributing to a self-sustaining cycle of exhaustion, hyperarousal, and sleep disturbance [4,19,21,22].

## 4. Discussion: The Fatigue–Caffeine–Sleep Disturbance–Anxiety Cycle

The findings synthesized in the preceding sections suggest that fatigue-driven caffeine use may be best understood not as an isolated behavioral habit, but as part of a self-perpetuating behavioral and physiological cycle. Within this cycle, fatigue motivates caffeine consumption, which provides short-term relief; residual stimulant effects may interfere with sleep and recovery, and subsequent fatigue increases the likelihood of further caffeine use. Anxiety-like symptoms and hyperarousal may further amplify this process by worsening sleep initiation, subjective sleep quality, and emotional regulation. This discussion integrates these mechanisms into a unified fatigue–caffeine–sleep disturbance–anxiety model. The proposed conceptual model is presented in Figure 1.



**Fig. 1.** Proposed conceptual fatigue–caffeine–sleep disturbance–anxiety cycle. The model illustrates how fatigue-driven caffeine use may provide short-term alertness while contributing to sleep disturbance, impaired recovery, next-day fatigue, and further caffeine use. Hyperarousal and anxiety-like symptoms may amplify this cycle.

#### **4.1. Fatigue as the Entry Point into the Cycle**

In the proposed model, fatigue represents the entry point in the maladaptive behavioral loop. Physiologically and cognitively, fatigue signals a reduced capacity to sustain further physical or mental exertion and may indicate the need for rest, recovery, and restoration of biological resources [13,14]. Under ideal homeostatic conditions, this signal would naturally prompt rest and recovery. However, in demanding academic, occupational, or social environments, individuals may feel compelled to override this biological drive to maintain daily functioning despite fatigue [17,18,19].

Consequently, fatigue may function not only as a symptom of insufficient recovery but also as a behavioral driver that increases the likelihood of caffeine use. Within the proposed model, this is important because caffeine does not resolve the underlying need for rest; rather, it temporarily reduces the perception of exhaustion and allows continued functioning despite an unmet biological need for recovery [12,15]. This distinction helps explain how an initially adaptive coping strategy may become embedded in a self-perpetuating pattern of delayed rest, impaired recovery, and repeated caffeine use [12,15,19].

#### **4.2. Short-Term Reinforcement and Behavioral Maintenance**

Repeated reliance on caffeine as a self-medication strategy may be sustained by its relatively rapid and noticeable effects on alertness and perceived functioning. Following ingestion, caffeine may acutely enhance alertness, vigilance, and cognitive performance while temporarily reducing the subjective perception of fatigue and effort [15]. Particularly in states of pronounced fatigue or sleep deprivation, caffeine has been shown to partially mitigate specific cognitive deficits, providing individuals with tangible short-term relief [20]. Because this pharmacological intervention may allow individuals to continue functioning despite occupational or academic demands, they may learn to associate caffeine intake with restored functional capacity and successful coping [1,15,19].

This immediate positive feedback, in which caffeine is perceived as reducing the distressing sensation of exhaustion, may reinforce repeated use and consolidate caffeine as a preferred behavioral response to fatigue. However, while this short-term reinforcement may temporarily relieve the immediate experience of fatigue, it does not resolve the underlying physiological need for rest or recovery [12,15]. Instead, caffeine masks fatigue by temporarily blocking central adenosine signaling, thereby enabling continued wakefulness without providing true biological restoration [12]. Thus, the reinforcing value of caffeine lies not only in its pharmacological effects, but also in the behavioral learning that links caffeine intake with perceived coping success. Over time, this learned association may strengthen caffeine use as a default response to fatigue, particularly when rest or recovery is delayed [1,15,19].

#### **4.3. Sleep Disruption as a Central Maintaining Mechanism**

Sleep disruption appears to be a central maintaining mechanism in the proposed cycle because it links short-term caffeine use with renewed next-day fatigue. Although caffeine may provide daytime relief, residual stimulant effects during the intended sleep period may interfere with sleep initiation, continuity, and restorative sleep processes, particularly when caffeine is consumed in higher doses or later in the day [12,21]. In this way, caffeine may reduce the very recovery process needed to resolve the fatigue that motivated its use.

Importantly, caffeine may affect not only sleep duration and continuity but also restorative aspects of sleep architecture. Experimental evidence and quantitative EEG studies indicate that caffeine can attenuate slow-wave activity and reduce time spent in deep NREM sleep, particularly under conditions of higher-dose exposure or recovery sleep after sleep deprivation [5,21,23]. Because slow-wave activity is closely linked to sleep intensity and the dissipation of homeostatic sleep pressure, its attenuation suggests that caffeine may reduce the physiological depth and restorative potential of sleep [5,23]. Thus, even when total sleep duration appears subjectively adequate, sleep may be less restorative at the physiological level [5,21,22].

As a result of impaired nocturnal recovery, individuals may awaken with residual sleep pressure, reduced perceived recovery, and increased next-day fatigue [3,9,21]. Because individuals may not always accurately perceive the extent of caffeine-related sleep disruption, they may fail to attribute morning fatigue to prior caffeine intake, particularly when they are still able to fall asleep or when subjective sleep quality appears acceptable [21,22]. Instead, recurring fatigue may reinforce the perceived need for caffeine as a rapid countermeasure, prompting further use to maintain functioning the following day [1,15,19]. Consequently, sleep disruption may serve as a central maintaining mechanism of the cycle: by limiting full recovery, it can renew the biological and behavioral motivation for further pharmacological masking of fatigue [3,9,12,21].

#### 4.4. Hyperarousal and Anxiety as Amplifying Factors

As the proposed cycle progresses, some individuals may increase their caffeine intake to counteract accumulating fatigue, creating a secondary layer of disruption: central nervous system hyperarousal [2,7]. Higher caffeine consumption may contribute to anxiety-like symptoms, including psychological tension, jitteriness, restlessness, and signs of autonomic arousal [2,7]. Rather than functioning merely as isolated daytime side effects, these physiological and emotional responses may act as amplifying factors within the fatigue–caffeine loop [4,19].

When an individual approaches the intended sleep period in a state of caffeine-related hyperarousal, the natural transition into restorative sleep may be impaired. The combination of ongoing adenosine receptor antagonism and elevated psychological tension may increase the likelihood of delayed sleep onset, nocturnal fragmentation, and poorer perceived sleep quality [12,21,22]. Moreover, heightened anxiety-like symptoms and physiological restlessness may contribute to a state of hypervigilance that interferes with sleep initiation and reduces the subjective sense of nocturnal recovery [4,22].

Consequently, caffeine-related arousal and anxiety may amplify the sleep disruption that maintains the cycle. Poorer sleep may intensify next-day fatigue and emotional dysregulation, particularly in individuals already exposed to academic, occupational, or psychological stress [3,4,19,24]. In response to this combined state of fatigue and psychological tension, individuals may consume additional caffeine to restore functioning, thereby increasing the likelihood of further hyperarousal and subsequent sleep disturbance [19,21]. In this way, anxiety-like symptoms do not simply accompany fatigue-driven caffeine use; they may strengthen the self-perpetuating cycle by linking overstimulation, impaired sleep, next-day fatigue, and repeated caffeine consumption [4,19,21,22].

#### 4.5. Public Health and Behavioral Implications

From a public health and clinical perspective, the central issue highlighted by this cycle is not caffeine consumption itself. When used appropriately and at moderate intake levels, caffeine is generally considered a widely tolerated stimulant that may support alertness, vigilance, and short-term performance [1,2,15]. Rather, concern arises when caffeine becomes the primary or sole strategy for managing chronic fatigue, sleep restriction, or persistent psychological demands [17,18,19]. In such contexts, repeated reliance on central nervous system stimulation may reinforce a maladaptive loop involving delayed recovery, disrupted sleep, next-day fatigue, and increased hyperarousal [19,21,22].

Mitigating this cycle requires targeted behavioral education rather than a simplistic emphasis on caffeine avoidance. Public health and clinical recommendations should emphasize not only total caffeine intake, but also timing of consumption, cumulative daily dose, individual sensitivity, and sleep hygiene [17,18,21]. Consumers may not always recognize that late-day or high-dose caffeine intake can affect subsequent sleep, particularly when they are still able to fall asleep or when subjective sleep quality appears acceptable [21,22]. Educational efforts should therefore encourage awareness of dose- and timing-dependent effects, including the potential value of limiting caffeine intake later in the day and avoiding escalation during periods of fatigue or sleep loss [21].

Finally, recommendations should acknowledge substantial inter-individual variability. Genetic differences in caffeine metabolism, variation in adenosine receptor sensitivity, habitual use patterns, and baseline vulnerability to anxiety may all influence the strength with which caffeine affects sleep, arousal, and psychological well-being [4,7,8,10]. Universal guidelines may therefore be useful as general reference points, but they may not fully protect individuals who are especially sensitive to caffeine's sleep-disrupting or anxiogenic effects [8,10]. A more nuanced approach would frame caffeine not as inherently harmful, but as a tool whose benefits and risks depend on dose, timing, context, and individual susceptibility. Such an approach may help individuals move from maladaptive reliance on caffeine toward more sustainable fatigue management, improved sleep hygiene, and better recognition of the fatigue–caffeine–sleep disturbance–anxiety cycle [17,18,19,21].

#### 4.6. Limitations of the Proposed Model

Several limitations of the proposed model should be acknowledged. First, the fatigue–caffeine–sleep disturbance–anxiety cycle is an integrative conceptual framework derived from evidence across multiple research domains, rather than a directly tested causal pathway. Second, the strength of each pathway may vary substantially across individuals depending on caffeine dose, timing of consumption, habitual use, sleep opportunity, baseline anxiety, and genetic or metabolic susceptibility. Third, much of the available evidence addresses individual components of the cycle, such as caffeine and sleep or caffeine and anxiety, rather than the full dynamic interaction among fatigue, caffeine use, sleep disruption, and anxiety-like symptoms. Fourth, some of the dose- and timing-related findings discussed in this review are based on a randomized crossover trial involving only 23 young men. Consequently, the generalizability of these findings to women, older adults, and other populations remains limited. Future longitudinal and experimental studies are therefore needed to test the temporal and causal relationships proposed in this model.

#### 5. Conclusions and Future Directions

Caffeine remains one of the most widely consumed psychoactive substances worldwide, and when used appropriately, it can serve as an effective and accessible short-term countermeasure against fatigue [1,15]. By temporarily antagonizing central adenosine receptors, low-to-moderate caffeine intake may reduce the subjective perception of exhaustion, support cognitive alertness, and help individuals maintain functioning during demanding academic, occupational, or social obligations [12,15]. Within this context, caffeine may be understood as a useful behavioral and pharmacological tool that temporarily supports vigilance and perceived functional capacity without being inherently harmful.

However, the evidence synthesized in this review suggests that repeated fatigue-driven caffeine use may contribute to a maladaptive behavioral and physiological loop. When caffeine is repeatedly used to override the biological need for rest, its residual effects may interfere with subsequent sleep, particularly when intake occurs at higher doses or later in the day [12,21]. This disruption may affect sleep onset, sleep continuity, sleep architecture, and perceived sleep quality, thereby limiting nocturnal recovery and increasing the likelihood of next-day fatigue [3,5,21,22,23]. In turn, persistent fatigue may strengthen the motivation for further caffeine consumption, reinforcing the pattern of fatigue-driven caffeine use.

Beyond sleep impairment, this self-perpetuating cycle may be amplified by central nervous system hyperarousal and anxiety-like symptoms. Escalating caffeine intake in an attempt to counteract accumulating fatigue may contribute to psychological tension, jitteriness, restlessness, and autonomic arousal, particularly in susceptible individuals or at higher intake levels [2,4,7]. These physiological and emotional responses may further interfere with sleep initiation, subjective sleep quality, and emotional regulation, thereby intensifying the perceived burden of fatigue and reinforcing the maladaptive cycle [4,19,21,22,24].

Addressing this cycle requires moving beyond simplistic recommendations for caffeine avoidance. Future research and public health initiatives should focus on targeted behavioral education that emphasizes dose, timing of intake, cumulative daily consumption, sleep hygiene, and individual susceptibility [17,18,21]. Particular attention should be given to inter-individual variability, including genetic differences in caffeine metabolism, adenosine receptor sensitivity, habitual use patterns, and baseline vulnerability to anxiety [8,10]. A nuanced, personalized approach may help individuals use caffeine strategically while reducing the risk of impaired sleep, heightened arousal, and persistent fatigue. Such an approach may support more sustainable fatigue management and improve recognition of the fatigue–caffeine–sleep disturbance–anxiety cycle.

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