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Review Article

Physiology Section

Neurophysiological Consequences of Caffeine Consumption in Youth: A Narrative Review

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ABSTRACT

The last two decades have seen a notable rise in the consumption of Energy Drinks (EDs). Particularly, alcoholic ED for young individuals and adolescents. Caffeine is the most extensively used psychoactive stimulant that people of all ages consume. It is found in nature and may be obtained from cocoa beans, coffee seeds, leaves of tea, and kola nuts. There are no known safe amounts for kids to consume ED or caffeine. Furthermore, there are no appreciable advantages to these substances/products regarding how the brain, psychomotor abilities, or social development grow over the short- or long term. Adverse consequences, notably when correlated with acquiring excessive amounts of caffeine, have been reported in the literature. High levels of caffeine consumption have been found in more recent research to contribute to anxiety, insomnia, and cardiovascular irregularities among adolescents. In addition, mixing alcohol with caffeine has also been found to be related to higher levels of risk-taking and substance dependence. The World Health Organisation (WHO) has also warned against the use of ED among children based on these possible health hazards. Here, it is indicated that there is an immediate need for public health campaigns and regulatory action seeking to control energy drink use among youth populations. This study highlights key facts about the adverse effects of these drugs, their intensity, and the reasons behind their use.

Keywords: Cardiovascular effects, Cognitive development, Energy drinks, Neural processes, Substance dependence, Young adults

INTRODUCTION

Caffeine is a psychostimulant that is derived from a variety of plants and is widely used worldwide [1]. Liquids classified as ED are in a group that includes goods frequently made with caffeine and occasionally enhanced with additional nutritional ingredients. "Dr. Enuf" was the first energy drink offered in the U.S., introduced in 1949 [2]. Energy drinks first appeared in Europe in 1987, then spread to other parts of the world. After introducing Red Bull in 1997, its popularity increased significantly [3,4]. The energy drink market grew by 56% between 2002 and 2006, with an estimated overall value at retail of USD 12.5 billion in the United States in 2012 [5]. By 2013, each year, ED were consumed in more than 160 nations, more than 5.8 billion liters [6].

Presently, the most widely accepted explanation explains how caffeine prevents adenosine's harmful effects on neurotransmission [7-9]. Caffeine competes with adenosine receptors, primarily subtypes A1 and A2A, to lessen their effects and increase dopamine, glutamate, and noradrenaline release. Even at modest dosages, such as in coffee, caffeine's capacity to inhibit adenosine receptors is evident [10]. Strengthening can be achieved by reducing pain perception, enhancing force and sustainability, and maintaining or raising the speeds at which motor units fire during muscle contraction [7].

Exercise-induced energy substrate mobilisation may be impacted by caffeine. Because reduced glycogen utilisation leads to longer training durations, it is especially advantageous during aerobic exercise [11]. Several mechanisms are the foundation of athletic performance, including accelerated calcium mobilisation and repression of phosphodiesterase, even though muscle glycogen is essential for many aerobic and anaerobic sports [12]. Sarcoplasmic reticulum calcium release may be triggered by caffeine, which prevents its reabsorption by mobilising intracellular stores of calcium. These processes allow coffee to improve contractility during contractions below the submaximal level [10]. As a result, coffee is an ergogenic aid for various workouts, including weight training, combat, and endurance sports, as well as exercise attempts with high glycolytic demands [13]. The competitive inhibitor caffeine is nonselective of phosphodiesterases, inhibiting the breakdown of compounds such as cAMP or cyclic adenosine monophosphate by hydrolysing phosphodiester bonds. CAMP stimulates lipolysis [10].

Additionally, studies have shown how caffeine affects endothelial function by acting as an inhibitor of NO, a nitric oxide stimulant, and a second messenger of NO in the form of cyclic Guanosine Monophosphate (cGMP) [14,15]. Reactive Oxygen Species inactivation of NO (ROS), inflammation, increased vasoconstrictors, and other factors have been proposed as the processes behind endothelial and malfunction of vascular smooth muscle [16]. An imbalance in the inhibitor of asymmetric dimethylarginine, a rise in endogenous NO synthase (eNOS) in endothelial cells and an aberrant shear stress. It has been shown that caffeine reduces Cerebral Blood Flow (CBF), and cerebral blood velocity is measured using various methods [17,18]. Caffeine has repeatedly been found to speed up reaction times and increase alertness despite the reported CBF drop and, therefore, lower availability of metabolic substrates [19,20].

Young people have become the new target market for manufacturers, who formerly focused on athletes. Energy drinks are frequently advertised in places where young adults and teens like to visit. About two-thirds of energy beverage users are between 13 and 35 years, with boys making up the other two-thirds of the market [21]. Energy drinks rank second among youth supplements for nutrition in the US; over 30% routinely take ED [6]. Energy drinks are just as popular worldwide throughout the Kingdom of Saudi Arabia. When asked about their routine energy usage, about 50% of Students from the Saudi Academy who participated in the survey admitted to doing so [5].

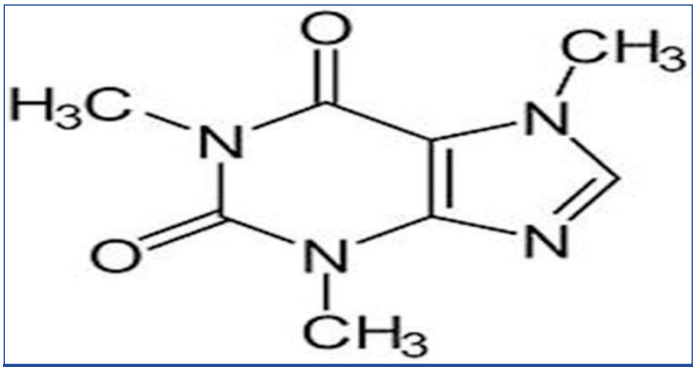
Recent Indian studies reveal a rising trend of caffeine and energy drink consumption among adolescents and young adults. In Delhi, 97% of school-going adolescents reported regular caffeine intake,

mainly through tea, coffee, and soft drinks [22]. Among medical students, around 62% consumed ED, mostly as occasional users [23]. Another study from Maharashtra highlighted high awareness but widespread misconceptions regarding the safety of such beverages [24]. These findings suggest that lifestyle pressures and limited awareness may be driving excessive caffeine use among Indian youth.

This review article seeks to explore the health hazards and neurophysiological impacts of caffeine and energy drink intake among adolescents. The aim was to evaluate the trends of energy drink and caffeine consumption among adolescents, to assess their effects on anxiety, sleep, and cardiovascular outcomes

BIOCHEMICAL CHARACTERISTICS

Caffeine, or 1,3,7-trimethylxanthine, reveals structural similarity with adenosine, xanthine, and uric acid. It appears naturally in cocoa, coffee beans, kola nuts and cherries. where it functions as an allelopathic and anti-herbivorous compound [25]. In humans, caffeine is quickly absorbed through the gastrointestinal tract, with about 99% absorbed within 45 minutes of ingestion. Hot beverages enable faster absorption than cold ones due to temperature and sugar-related effects on gastric clearing [26]. Once absorbed, caffeine crosses biological membranes, including the blood–brain barrier and placenta, and its half-life diverges with factors such as smoking, liver disease and pregnancy [26]. Chemical composition of caffeine is shown in [Table/Fig-1] [27].



[Table/Fig-1]: Chemical structure of caffeine [27].

TIMING OF CAFFEINE INGESTION

Caffeine enters the circulation system through the gastrointestinal tract and is rapidly absorbed [28] after consumption. One hour after intake, blood caffeine levels peak [13]; however, it is indicated that the highest plasma concentration occurs 30 to 60 minutes after consumption [29]. Additionally, presented are maximal plasma concentrations measured 15-120 minutes after ingestion. Inter-individual variations, as well as delayed stomach emptying and metabolism, are the causes of these detected time gaps [13,30,31]. Following its absorption, caffeine quickly permeates every bodily tissue and flows across the barriers between the blood and the brain, placenta, and testes [10,32]. In humans, the shelf life of caffeine may range from 2 to 12 hours (~3-5 hours on average) [29], and for adults, it is about 3 to 5 hours [31]. Absorption occurs in the gastrointestinal system when caffeine and ED are consumed in various quantities. The maximum amount of caffeine in the blood after absorption varies significantly across individuals and depends on several variables. The highest blood concentration of caffeine following absorption is highly variable from person to person, owing to several factors. They are age, weight, genetic variation in polymorphisms (particularly CYP1A2 enzyme, which metabolises caffeine), liver enzymes, smoking, use of other medications, and regular use of caffeine [33].

Consequently, the highest plasma time (typically between 30 to 120 minutes) and the actual caffeine concentrations vary considerably among individuals, resulting in changing physiological and pharmacological effects [34]. Since EDs include taurine and glucuronolactone, which enhance the effects of caffeine, their caffeine amount differs from what is listed on the labels. Moreover, guarana has caffeine. According to the container, it has taurine 1000 mg, glucuronolactone 600 mg, caffeine 80 mg, niacin 18 mg, pantothenic acid 6 mg, B6 mg, B2 mg, B12 mg, inositol, carbonated water, sucrose, glucose (27 g sugar), citric acid, and caramel flavour [35].

EFFECTS OF VARYING CAFFEINE INTAKE

Caffeine may be detected in the blood 5 to 15 minutes after consumption and its effects peak between 40 and 80 minutes later [28,36]. Caffeine at higher doses (9-13 mg/kg) would not stop impairing physical performance, but it may worsen its side effects [Table/Fig-2] [15,20,25]. When subjects consumed caffeine, they took substantial dosages (~10-13 mg/kg), which had negative effects on their stomachs, anxiety, disorientation, difficulty concentrating, and difficulty falling asleep [28,37,38]. Subjects who took lesser amounts (7-10 mg/kg) reported flushes, headaches, palpitations, tremors, chills, and nausea [38-40]. The physiological reactions and adverse effects decreased but did not go away when caffeine doses were lowered to a reasonable dosage of 5-7 mg/kg, maintaining the ergogenic benefits [28,38]. A person who ingests 200 mg or more of caffeine runs the danger of being toxicosed, which can result in symptoms such as anxiety, restlessness, upset stomach, muscular cramps, and periods of extreme alertness [41,42]. Consuming low to modest levels of 3-6 mg/kg of caffeine sixty minutes before exercise is advised to reap the benefits, per the research [7,12,43]. It was demonstrated that caffeine had an ergogenic effect at 3 mg/kg without influencing the levels of catecholamines, lactate concentration, glycerol, or FFA or exercise Heart Rate (HR) [36,44].

Caffeine consumption of up to 1000 mg/day caused severe side effects [30], which included headaches, vertigo, shaking, extrasystole, tachycardia, nausea, hyperactivity, and restlessness [45]. Hospitalisation was also possible after consuming about 2000 mg/day of caffeine, which also caused toxic symptoms and symptoms related to the metabolic, gastric, neurological, and cardiovascular systems [46]. Caffeine is the primary active ingredient in EDDs and sports snacks, which, when used in excess, can be poisonous and have adverse consequences, including tachycardia, vomiting, heart issues, shock, or even death. Excessive caffeine consumption can also produce anxiety and irritation [47].

System/Effect	Description	Reference
Cardiovascular and respiratory effects	Caffeine raises catecholamine levels in the blood. Increases diastolic and systolic blood pressure due to arterial stiffness and endothelium vasodilatation. Respiration rate increases depending on plasma caffeine levels.	[20,25]
Endocrine and metabolic effects	Caffeine raises circulating catecholamine levels, reduces baseline metabolic rate, and induces lipolysis releasing Free Fatty Acids.	[20]
Gastrointestinal and urinary effects	Caffeine stimulates the small intestine, leading to salt and water secretion. Causes diuresis as a pharmacological effect.	[20]
Other medical effects	Caffeine inhibits adenosine receptors, induces apoptosis in UVB-damaged cells, and acts as a psychoactive drug in Parkinson's treatment. Safety and efficacy remain key concerns.	[15]

[Table/Fig-2]: System-wise impact of caffeine on human physiology [15,20,25].

BENEFITS OF CAFFEINE TO THE HUMAN BODY

Energy drinks contain a high amount of caffeine, providing users with the benefits of improved recall, increased alertness, and a heightened mood. Alford C et al., conducted one of the most frequently referenced studies on this subject [48]. They analysed the responses of 37 people to a widely recognised

energy drink. [Table/Fig-3] presents the summary of selected studies on the cognitive and physical performance effects of energy drink consumption [48-52]. [Table/Fig-4] presents the benefits of caffeine to the human body [48, 50-52].

S. No.	Author [ref no]	Place/year of the study	Study objective	Findings/Outcome
1	Alford C et al.,	United Kingdom / 2001	To evaluate the effects of a commercially available caffeinated energy drink on mental (cognitive) and physical performance (aerobic capacity, psychomotor tasks, and subjective alertness) [48]	Study on 37 participants consuming a popular energy drink. Showed improved aerobic performance (max speed maintenance, 65-75% max HR endurance), enhanced mental skills (choice response, attention, recall), and increased subjective alertness
2	Erdmann J et al.,	Canada/2007	To investigate how consumption of a standard energy drink influences upper body muscular endurance and anaerobic performance in physically active young adults [49]	Wingate cycle test; consumption of the same energy drink brand improved upper body muscular endurance but no effect on anaerobic peak and average power
3	Chtourou H et al.,	Tunisia/2007	To assess the influence of energy drink ingestion on reaction time and anaerobic power output in the context of physical activity [50]	ED significantly improved reaction time during physical activity but did not affect anaerobic power production
4	Mwape RK et al.,	Zambia/2019	To determine the effects of ED on cognitive function and mood in individuals experiencing mild sleep deprivation in a controlled, randomised, crossover design [51]	94 volunteers in a double-blind, randomised, placebo-controlled, crossover study. Energy drink improved mood and cognitive function in mildly sleep-deprived individuals; attention levels maintained for six hours, unlike the placebo

[Table/Fig-3]: Summary of selected studies on the cognitive and physical performance effects of energy drink consumption [48-51].

ADVERSE EFFECTS OF CAFFEINE ON THE HUMAN BODY

Cardiovascular effect: Multiple studies have demonstrated a link between the consumption of ED and elevated HRs and arterial blood pressure [52,53]. The effects of caffeine on the ergogenic substance of the energy drink were the explanation for what occurred. Additionally, high-energy drink use has been linked to significant cardiac symptoms such as ventricular arrhythmias, ST-segment elevation, and QT prolongation [54]. Myocardial infarction has been associated with energy drink consumption in young, healthy men between the ages of 17 and 19 years [46,55]. It has been noted that using ED causes platelet aggregation through arachidonic acid, lowering endothelial function and increasing platelet activity in young, healthy individuals [56].

Neurological and psychological effects: Those who take it might experience a sodium imbalance in a warm environment, which could reduce the isometric strength of the legs and begin to show signs of alcohol consumption. Restlessness, twitching of the muscles, anxiety, sleepwalking, gastrointestinal issues, and sudden sleep deprivation are some of the symptoms [41]. Moreover, a high rise in these outcomes is linked to coffee drinking, cortical hyperexcitability that is pro-nociceptive, which is connected to both everyday headaches, both acute and chronic [57]. The classification system has identified four types of caffeine-induced mental disorders. DSM-IV is a comprehensive guide to disorders of the brain, Fourth Edition: excessive caffeine consumption, caffeine-induced anxiety, caffeine-induced sleeplessness, and inappropriate behaviour related to caffeine [58]. Epileptic seizures and ischaemic stroke may become more common in those who use energy beverages, according to many investigations [59]. People who consume more than the daily recommended amount of 300 milligrams of caffeine may experience hallucinations [60]. The elevated cortisol levels that accompany coffee use may help to explain this. When cortisol levels are high, stress has a more profound physiological effect, increasing the possibility of delusions [61]. Blending guarana, taurine, and caffeine may cause and enhance apoptosis by reducing catalase and superoxide dismutase activity, according to in vitro studies done on human brain SH-SY5Y cells [62].

Gastrointestinal and metabolic effects: Regular energy drink consumers may have higher sugar intake, usually between 21 and 34 grams per ounce. These beverages frequently include sugars in various foods, similar to high fructose corn syrup, glucose, and sucrose. As such, consuming an excessive amount of ED may increase your vulnerability to illnesses like obesity and type 2 diabetes [41]. Furthermore, the high sugar level in ED may be detrimental to gut health by reducing the variety, activity, and expression of genes in the gut flora. This may, therefore, increase the chance of acquiring

Study (Author & Year)	Place and year of the study	Participants/design	Parameters evaluated	Findings/effects reported	Reference
Alford C et al.,	United Kingdom/2001	37 healthy adults; cycle ergometer test	Physical endurance, psychomotor performance (memory, attention, response time), and subjective alertness	Significant improvement in aerobic endurance (maintaining 65–75% max HR), aerobic performance, and mental alertness, including attention and recall	[48]
Chtourou H et al.,	Tunisia/2019	12 elite cyclists (male and female); double-blind, randomised crossover study	Endurance performance, perceived exertion	Improved endurance performance compared with placebo; no change in perceived exertion	[50]
Mwape RK et al.,	Zambia/2019	94 volunteers; double-blind, randomised, placebo-controlled crossover	Cognitive performance (memory, attention) and mood (POMS, Bond-Lader, Chalder Fatigue Scale)	Improved mood and cognitive function under sleep deprivation; sustained attention for up to six hours post-consumption	[51]
Shah SA et al.,	United States of America/2019	22 untrained, healthy females; single-blind, placebo-controlled	BP, HR, time to fatigue, oxygen saturation, VO_2 max	No enhancement in any physical performance indicators following energy drink consumption	[52]

[Table/Fig-4]: Benefits of caffeine to the human body [48, 50-52].

diseases like metabolic syndrome and obesity [63]. Caffeine has been shown to reduce insulin sensitivity as soon as it is consumed; this may help to explain why many studies link energy drink usage to higher blood sugar levels [64]. According to Beaudoin M-S et al., research on dose-dependent effects, insulin sensitivity increases by 5.8% for every milligram of coffee consumed per kilogram [65]. According to a case study, a lady who drank too many ED developed symptoms such as jaundice, upset stomach, and noticeably elevated liver enzyme levels. This result was consistent with the results of Huang B et al., who reported a 36-year-old person in a comparable situation [66]. To determine the high-risk individuals and the underlying mechanism of energy drink-induced liver injury, further study is needed.

Renal effects: Research has shown that ED' caffeine content increases the production of urine or diuresis [67]. It is recommended to avoid drinks when working out for long periods in hot weather because they might cause dehydration. Studies have shown that prolonged exercise that leaves an individual 1.5% undernourished can raise body temperature, HR, and perceived exertion [68]. Additionally, coffee causes natriuresis, or the excretion of salt, which can alter plasma volume and have a major impact on cardiovascular performance when exercising [68]. Furthermore, prolonged physical activity may result in an imbalance in sodium levels in a warm environment, which might lower the legs' isometric strength [69].

Dental effects: One Swedish study identified a significant connection between the use of ED and tooth destruction [70]. Marshall TA et al., discovered comparable outcomes among American youngsters [71]. There has been a 2.4-fold rise in tooth erosion linked to energy drink consumption because of their low pH and high sugar content [72]. Pinto SC et al., also discovered that ED may result in cervical dentin hypersensitivity if they remove the smear layer from teeth [73].

CONCLUSION(S)

Coffee and caffeine exhibit significant short-term stimulating effects on the nervous system, but too much consumption can result in negative consequences like anxiety, panic attacks, memory loss, and addiction. Young adults, adolescents, and children are most at risk because of frequent consumption of ED, which can cause damage to long-term health despite offering short-term performance gains. Moderate to low levels of caffeine can be safe for healthy adults, but consumption among youths should be discouraged. More stringent controls and prudent marketing activities are called for to reduce risks and protect public health.

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