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Caffeine's Physiological and Psychological Effects

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## Introduction

The word “caffeine” was originated from the German term “kaffee” and the French expression “café” which both directly translate to “coffee.” Caffeine and coffee are both reflective of its spread through Europe by Arabia and Turkey where coffee trees were first cultivated in the sixth century. Caffeine’s chemical name is 1,3,7-Trimethylpurine-2,6-dione with the chemical formula  $C_8H_{10}N_4O_2$ . It was first extracted into its purest form via cocoa beans in the 1820s by German scientist Friedrich Runge (Helmenstine 2019). When purified, caffeine is extremely bitter and takes the form of a white crystalline powder. From then on its applications to everyday life has spread rapidly. Caffeine is a substance that is known and utilized on a global scale. Billions of people consume this substance every day as it is one of the most commonly used ingredients in the world. Caffeine is a naturally occurring compound that has been found in approximately 60 plant species. Caffeine is present in many of the drinks that people consume such as coffee, green and black tea, soft drinks, energy drinks, and cocoa. Not only is caffeine present in a variety of drinks, it is also included in some foods, including energy bars, chocolate bars, breakfast cereal, and ice cream. Caffeine falls under the category of psychoactive drugs and is scientifically categorized as a stimulant. It functions by stimulating important parts of the body like the brain and central nervous system and can facilitate alertness and impede the onset of fatigue. There are many benefits that caffeine can have on the body both physiologically and psychologically. However, as of recent there has been extensive research on not only caffeine as a whole but also on the negative effects that can be produced from caffeine. Since caffeine is naturally a stimulant, it can tend to be addictive. It is always recommended to take everything in moderation as too much of any substance can have debilitating effects.

## How Caffeine Works

In order to fully understand the effects caffeine has on the body, a discussion on what caffeine does to the body on a biochemical level is important. Research is still being conducted on caffeine's intricate mechanisms on the body as it is only partially understood. First, caffeine is absorbed rapidly after being consumed. It has a high rate of diffusion which means that it can travel throughout the bloodstream very quickly. From there it can access all organs and essentially every cell in the body. The reason caffeine can exhibit its effects rather fast is because it is fat soluble which allows it to easily pass through the cell membrane. It is then quickly and completely absorbed from the stomach and intestinal tract into the bloodstream ("Caffeine & Neurotransmitters"). Caffeine is also able to easily pass through the body because there are no physiological barriers that prevent its passage throughout tissues in the human body.

Caffeine's capability to work depends on a variety of factors. The first factor is its ability to enter the central nervous system. In order to successfully do so, caffeine must cross the blood-brain barrier. The blood brain barrier is a defensive mechanism that protects the central nervous system from biological or chemical exposure by preventing viruses as well as large and small molecules from entering the brain or its surrounding fluid ("Caffeine & Neurotransmitter"). Many drugs have difficulty at this stage. However, caffeine passes this barrier very easily.

Many drugs, including caffeine, can achieve their effects through altering or imitating the release or uptake of neurotransmitters, which are the chemical messengers that regulate how the neurons in the central nervous system interact with each other. These neurotransmitters are changed by drugs in a variety of ways. Some of the ways neurotransmitters can be altered are by increasing/decreasing synthesis, inhibiting or enhancing their transport, modifying their storage, release, or way they are degraded, by directly mimicking their activity, or by blocking their

action at the receptor site (“Caffeine & Neurotransmitters”). Caffeine is a stimulant which achieves its effects by actively blocking activity levels of adenosine. Adenosine is a compound that is found throughout all the body and is used for a variety of reactions. Adenosine can make a person feel tired or fatigued and has also been shown to dilate blood vessels in the brain. The reason caffeine is such a good inhibitor of adenosine is because a nerve cell cannot distinguish the difference between them since they are structurally very similar. Caffeine is able to block the A1 receptors, the receptors which adenosine binds to. This classifies caffeine as an adenosine-receptor antagonist. However, instead of slowing down intracellular activity like adenosine, caffeine does the opposite. The nerve cell speeds up because caffeine is taking up all the receptors that adenosine would normally bind to (“How does caffeine work in your brain?”). Similarly, caffeine also blocks A2A receptors which are responsible for the release of dopamine and glutamate. This is the reason many people feel better after they drink coffee. Other receptors that are also affected by caffeine include acetylcholine, serotonin, and norepinephrine.

The life cycle of caffeine is very short-lived in the body. In order to fully demonstrate how caffeine is flushed throughout the body, a circadian-like schedule will be described. To begin, when an individual awakens, their body has metabolized most of the adenosine molecules. They are still present, just not in a great quantity which explains why many people feel tired when they wake up. This is the time when people usually ingest caffeine via the form of a beverage like coffee. The caffeine gets absorbed through the intestinal tract, and within about an hour it becomes readily available throughout most parts of the body, especially the brain. This sudden influx of caffeine molecules is when peak concentrations are at its highest. At this time the caffeine molecules are actively blocking the adenosine receptors. During this period, many people experience high levels of alertness, wakefulness, and energy. After a couple hours, the

caffeine molecules unbind from the adenosine receptors. Caffeine is then metabolized through the enzyme CYP1A2 into various substances. Some of the substances caffeine is metabolized into include paraxanthine, theobromine, and theophylline. Paraxanthine is used in the mediation of caffeine and possesses anti-inflammatory effects. Theobromine has diuretic, stimulant, and relaxation effects. It has been shown to dilate blood vessels and can lower blood pressure. Lastly, theophylline is in medications used to prevent and treat shortness of breath, wheezing, and chest tightness. The half-life of caffeine is approximately 3-5 hours long and is greatly dependent on the individual's ability to metabolize it. This is contributed by levels of enzymatic activity as well as the available amount of CYP1A2 in the body. Fluctuations in the half-life may also be noticeable in specific populations such as pregnant women, smokers, and individuals with liver problems, as the liver is the major organ responsible for metabolic processes. Shortly after most of the caffeine is finished metabolizing, the adenosine molecules are able to bind to their appropriate receptors. This in turn promotes the functional purpose of adenosine and is the reason why many people start to feel drowsy and physically relaxed after their caffeine spike has depreciated.

### **Benefits of Caffeine**

Caffeine has been used as a tool to benefit the body in a variety of ways. It is used for medicinal purposes, improving cognitive and physical functioning, and much more. Although caffeine can have detrimental effects if taken in an improper manner, the benefits are far and wide when taken appropriately.

### **Enhancement in memory**

Caffeine has been shown to improve long-term memory. New research has shown that a dose of caffeine after learning can have the ability to boost memory consolidation. A study conducted by researchers at John Hopkins University and published by the journal *Nature Neuroscience* found that caffeine enhances certain memories at least up to 24 hours after it is consumed (Borota et al., 2014). The researchers conducted a randomized, double-blind, placebo-controlled trial in participants whose caffeine consumption was little to none. On the first day, participants were asked to study the images of objects, and after doing so received either a 200mg dosage of caffeine or a placebo. Salivary samples were collected at baseline, 1-hour, 3-hour, and 24-hour time periods after administration of caffeine or placebo to determine which of the two treatments was received via detection of caffeine metabolites. Twenty-four hours after the study session, participants were evaluated based on recognition performance. The items tested for recognition were either the same items seen from the previous day (targets), new items (foils), and items that were similar but not identical to the ones seen the day before (lures). Examples of lures would be two different picnic baskets or a different image of a seahorse. It was found that of the participants that had a significant increase in caffeine metabolites, these participants were more likely to call lure items 'similar' rather than 'old' compared to participants who received the placebo (Borota et al., 2014). Additional identical studies were conducted with dosages of 100mg and 300mg and found no significant change between 200-300mg but a noticeable difference between 100-200mg. Thus, it was concluded that a dose of at least 200mg is required to observe an enhancing effect of caffeine on memory consolidation. Furthermore, additional increases in dosages beyond 300mg demonstrated an inverted-U pattern.

According to the data presented, there is an optimal level of caffeine that aids in memory consolidation. A dosage that is too low or too high will have negligible effects.

### **Decrease energy intake in obese individuals**

There have been many claims that caffeine has a direct effect on one's basal metabolic rate and energy expenditure throughout the day. However, the research relating to these claims are vague and has not been fully understood. One study published in the journal *Obesity* analyzed the effects that different amounts of coffee had on dietary intake and appetite. The results found that no statistically significant difference was found for normal-weight individuals. However, there was conclusive evidence to claim that reduced energy intake was present in overweight/obese participants (Gavrieli et al., 2013). The study involved a randomized crossover design with 17 overweight/obese individuals. The volunteers took part in three daily trials which were separated by at least one week. They began with a standard breakfast supplemented with 200ml of coffee that contained either 3mg or 6mg caffeine/kg body weight, or water. Participants recorded their appetite feelings on a visual analogue scale for the 3 hours following. At 3 hours, participants consumed another meal and the next day recalled their food intake. Let it be noted that the meal consumed at the 3-hour mark was *ad libitum*, meaning that they consumed food until they felt satiated. The results revealed that although energy intake was relatively similar in the Caffeine 6 group (6mg caffeine/kg body weight) and water and actually higher in the Caffeine 3 group, total energy intake throughout the day in the Caffeine 6 group was significantly lower (550kcal lower) than that of water (Gavrieli et al., 2013). It was also noted that the Caffeine 3 group had higher levels of satiety at the 15 and 60 minute marks compared to that of water consumption. This suggests that there is some correlation between caffeine intake



and energy consumption. The mechanisms for why this may be are still being extensively researched.

### **Increase in muscle torque and activity**

It is well known that caffeine is a stimulant that is used by a variety of athletes in an attempt to enhance performance. Many athletes consume pre-workout supplements which are packed with caffeine. A study in 2014 published by *Muscle & Nerve* tested the effect that caffeine has on muscle torque and activity during resistance exercise in men. The double-blind, randomized cross-over study included 10 male semi-professional rugby league players who were all trained in strength with  $9 \pm 5.5$  years of training (Duncan, Thake & Downs, 2014). The individuals were asked to attend the laboratory on 3 separate occasions. The first occasion involved a briefing session, familiarization, and performance of maximal voluntary isometric contraction to provide baseline electromyographic data to normalize data gathered in subsequent testing sessions (Duncan, Thake & Downs, 2014). The next two laboratory experiments were randomized and separated by 3 days. Participants had one of two conditions, 250ml of artificially sweetened water with 6mg caffeine/kg body weight, or 250ml of artificially sweetened water (placebo). These solutions were consumed 60 minutes prior to the exercise trial. Participants then completed 6 repetitions of dominant knee extension on an isokinetic dynamometer at 3 angular velocities ( $30^\circ\text{s}^{-1}$ ,  $150^\circ\text{s}^{-1}$ ,  $300^\circ\text{s}^{-1}$ ) with 1 minute rest between sets (Duncan, Thake & Downs, 2014). This was used to measure torque in knee extensors. Furthermore, activation of the quadricep medialis was measured through surface electromyography. The results indicate that muscle torque was significantly greater in the presence of caffeine in comparison to the placebo ( $\sim 6.68\text{Nm}$ ). Not only was muscle torque facilitated through caffeine, but muscle activation also increased in all instances of angular velocity compared to the placebo (69.7%, 100.4%, and

103.8%, respectively). This experiment demonstrates that acute caffeine ingestion improves muscle performance during short-term maximal dynamic contractions in strength-trained men (Duncan, Thake & Downs, 2014).

### **Decreased risk of type 2 diabetes mellitus**

One of the many physiological benefits of caffeine is its reduction in many chronic diseases such as type 2 diabetes mellitus. A meta-analysis study published by the *European Journal of Nutrition* in 2013 found that coffee and caffeine have a linkage to type 2 diabetes mellitus. For dose-response analysis in women, data from 12 articles including 21,754 cases were used. The incidence of type 2 diabetes mellitus was shown to decrease by 15% for every 2 cups of coffee consumed per day (Jiang, Zhang & Jiang, 2013). The dose-response analysis for men included data from 7 articles with 14,806 cases used. Similarly, a decrease in type 2 diabetes mellitus by 8% was found for every 2 cups of coffee consumed per day. In comparison to caffeine intake, which was also conducted in the study, findings were relatively similar, with an overall decrease of about 14% in type 2 diabetes mellitus (Jiang, Zhang & Jiang, 2013). This study suggests that coffee and caffeine intake are directly correlated with incidences of type 2 diabetes mellitus. The study goes on to further describe that caffeinated coffee was found to be positively related to insulin sensitivity. Insulin sensitivity is important in regulating risks for chronic diseases like type 2 diabetes mellitus because it refers to how sensitive the body is in response to insulin. The higher the sensitivity to insulin, the greater the body's ability to use blood glucose more effectively. This in turn has an indirect relationship with blood sugar (higher insulin sensitivity results in lower blood sugar levels). This relationship between caffeinated coffee and insulin sensitivity was only found in habitual coffee drinkers, and other studies show there might be a negative effect associated with non-habitual coffee drinkers.

### **Decreased risk for liver disease**

As caffeine has been noted to decrease the risk of type 2 diabetes mellitus, it is also important to note that there are many other health problems that can be reduced with caffeine, including liver disease. This meta-analysis study published by *Liver International* was conducted by 4 researchers (Saab, Mallam, Cox II, and Tong) which aimed at determining if caffeine had a viable relationship with a decrease in liver disease. The study which was constituted by multiple different experiments showed that coffee had various positive benefits on the liver. To begin, various studies confirmed that coffee consumption and caffeine were associated with decreased levels of Alanine-aminotransferase (ALT) as well as Gamma-glutamyl transferase (GGT). These enzymes are critical enzymes that function in the liver. Elevated levels of these enzymes in the blood have been found to be present in people with liver disease or who have suffered damage to the liver. These decreases in enzymatic levels were found mostly in males and also in a subset of populations prone to damage to the liver, such as individuals who were overweight, had viral hepatitis, impaired glucose metabolism, iron overload, or excessive alcohol intake (Saab et al., 2014). In addition to a reduction in the risk for liver disease, this study also found that coffee can have positive effects with a decrease in cirrhosis (chronic liver damage leading to scarring and liver failure). Specifically, three studies demonstrated that coffee consumption had an inverse relationship between caffeine intake and cirrhosis. There are many reasons why coffee consumption may aid in the decrease of these variables, but paraxanthine is at the forefront. In addition to the benefits that paraxanthine offers (as described earlier), it can also suppress the synthesis of connective tissue growth factor (CTGF). This growth factor has a substantial impact on the progression of liver cancer, cirrhosis, and fibrosis.

### **Consequences of Caffeine**

Caffeine has many substantial benefits as previously described. It can enhance memory, reduce energy intake in obese individuals, increase muscle torque and activity, and much more. However, as much as there are benefits to caffeine, there are also equally as many negative effects that can accompany its intake. It is important to note that scientific research suggests there are likely to be no adverse health effects when taken in moderation. Most of the examples discussed are specific circumstances for when moderation is not considered and are the result of excessive caffeine consumption.

### **Caffeine's addictive properties**

As stated earlier, caffeine is scientifically classified as a psychoactive drug. It is a natural stimulant, which has the purpose of accelerating the central nervous system. Other stimulants which fall under the same classification as caffeine include cocaine, amphetamines, and nicotine. The world's obsession with caffeine has a lot to do with the series of chemical reactions that the body undergoes when consuming caffeine. According to the National Institute on Drug Abuse (NIDA), caffeine enhances dopamine signaling in the brain. Dopamine is described as a chemical that helps control movement, motivation, and emotions, therefore enhanced dopamine signaling makes an individual feel more alert and awake (NIDA 2016). However, addiction, as defined by NIDA, is an uncontrollable or compulsive use of a substance even when it is the source of negative consequences for the person using it. So, although caffeine can have addictive-like properties, it is more so described as a dependency rather than an addiction, as many people usually suffer from mild withdrawal symptoms like tiredness, headaches, and insomnia. One of the main reasons caffeine's addictive properties are substantially less than other psychoactive drugs like methamphetamines and cocaine is because of the sheer influx of

dopamine. Caffeine only produces a small rise in dopamine, and this small increase is not substantial enough to create an imbalance in the reward circuits in the brain necessary for it to be classified as addictive. Nonetheless, caffeine is classified as a psychoactive drug and when taken in mass quantity can have addictive-like properties.

### **Problems in pregnant women**

In terms of consuming anything that might be regarded as harmful or have negative implications while pregnant, caffeine is amongst the list. Caffeine has been believed to have an association with an increased risk of miscarriage as well as low birth weights in pregnant women. A meta-analysis study was published by *BioMed Central Medicine* in 2014 about maternal caffeine intake during pregnancy and its association with risks of low birth weight. This study included 13 prospective studies. 9 of those studies included low birth weight as a binary outcome variable (90,747 participants and 6,303 cases) and 6 studies (10,015 participants) with birth weight as a continuous outcome variable (Chen et al., 2014). The studies found that there was in fact an association between maternal caffeine intake and the probability of delivering a newborn with low birth weight. The results showed that low caffeine intake, which is between 50-149mg of caffeine a day, was associated with a 13% increase in low birth weight. Moderate caffeine intake (150-349mg/day) was associated with a 38% increase. Finally, high caffeine intake (greater than 350mg/day) was associated with a staggering 60% increase in low birth weight (Chen et al., 2014). These numbers were compared to minimal/no levels of caffeine intake. Furthermore, a dose-response relationship concluded that for every 100mg increase in caffeine per day a 13% increase in probability for low birth weight occurred.

### **Impairment of bone repair process**

Although caffeine can make one's emotional state slightly altered it is still considered stable. However, some of the physiological processes that can occur in the body during that time prove otherwise. In a 2015 study published by the *Brazilian Dental Journal* the experiments conducted were to answer the question of whether or not caffeine has a direct correlation to a variety of physiological processes such as increasing calcium excretion, inhibition of osteoblast proliferation, delay in the tissue repair process, and more. The study focused on 45 rats and was conducted under standard and controlled conditions. The rats were subject to tooth extraction and had either intake of coffee, intraperitoneal administration of the aqueous solution of caffeine, or nothing (control). After histometric analysis of the 42 days in which bone formation was monitored, it was found that the control group had the highest percentage of new bone formation for periods 7, 21, and 42 days when compared to other groups (Macedo, Brentegani & Aparecida de Lacerda, 2015). In fact, it was also discovered that the percentage of newly formed bone in rats that were given caffeine showed a decrease by 79.60% by the 7<sup>th</sup> day, 50.79% decrease by the 21<sup>st</sup> day, and a 52.28% decrease by the 42<sup>nd</sup> day in comparison to the control (Macedo, Brentegani & Aparecida de Lacerda, 2015). Further explanation of these findings indicates that in the rats which coffee was consumed, various large areas of blood clots around the dental socket were found as well as delayed production of granulation tissue compared to the control. Thus, this study as well as other studies represent the significance of caffeine on bone density and how chronic and excessive consumption of caffeine can have deleterious effects. Research is still being conducted on the actual mechanism of how caffeine can affect bone remodeling and is still not entirely clear.

### **Impairment in Hearing Recovery**

One of the more interesting and often surprising findings of caffeine's effect on the body is impairment in hearing recovery. A specific study published by *JAMA Otolaryngology Head and Neck Surgery* in April 2016 tested the effects of caffeine and hearing recovery after acoustic overstimulation events in guinea pigs. The study utilized 24 female albino guinea pigs divided into 3 separate groups. Groups were exposed to caffeine (Group 1), acoustic overstimulation events (Group 2), and both (Group 3). Acoustic overstimulation events (AOSEs) were introduced on days 1 and 8 for an hour long duration of 110-dB pure-tone sound. Results were recorded up to day 15 of the study. At the end of the study, groups 2 and 3 were compared and were found to have statistically significant differences. Group 3 had much greater impaired auditory brainstem response threshold shifts at frequencies of 8, 16, and 25 kHz (Daniel et al., 2016). Impairment in these frequencies was much greater in days 4, 8, 11, and 15. Furthermore, the study showed that damage to the outer hair cells of the guinea pigs exposed to both caffeine and AOSEs was significantly greater than group 2. Light microscopy revealed that changes in the composition of parts of the ear were also more aggressive in group 3 compared to group 2. The process of understanding why caffeine has an impact on hearing after an AOSEs is still being researched. In addition, further studies are needed to determine its effects on humans as this model was demonstrated through guinea pigs.

### **Increased cardiovascular risk**

Since caffeine is a stimulant, the central nervous as well as the sympathetic nervous system are both being activated. Increased activation in the sympathetic nervous system is expected under situations of stressful and dangerous situations. This area of the body is commonly referred to as our "fight or flight" response. An increase in this system has a variety

of physiological responses including a direct impact on blood pressure and cardiovascular health. A study published by the *European Society of Cardiology* in 2015 tested for the relationship between coffee intake and cardiovascular risk in young adults with mild hypertension. This study involved over 1,200 non-diabetic patients ranging from ages 18-45 years old who had untreated stage 1 hypertension. A linear relationship was found between coffee use and risk of hypertension needing treatment. Specifically, heavy coffee drinkers had a four-fold increase while moderate coffee drinkers had a three-fold increase in risk of cardiovascular problems (European Society of Cardiology). In addition to the effects that coffee had on cardiovascular health, it was also found that there was some correlation between coffee consumption and increased risk for prediabetes in young adults with hypertension who are slow caffeine metabolizers. The scientific reasoning behind this is that individuals with a slower caffeine metabolism will have longer exposure to the detrimental effects of caffeine on glucose metabolism, said Dr. Lucio Mos, a cardiologist at the hospital of San Daniele del Friuli in Udine, Italy (European Society of Cardiology). This is one of the many specific circumstances where caffeine intake can elicit more harm than good.

### **Special Considerations**

As described above, caffeine is a drug in which the situational purposes are far and wide and can have either beneficial or deleterious effects on the human body. There are many circumstances where it can and should be used and other situations where it should be heavily avoided. These special considerations may also vary from person to person and are simply recommendations on the general knowledge of caffeine's effects.



### **Time of day**

Knowing when the proper time frame for when caffeine intake is at its safest and most effective is one of the most important pieces of information people can have about caffeine. Something that is very underestimated and rarely discussed in the world of caffeine consumption is chrono pharmacology. This is defined as the study of the interaction of biological rhythms and drug action, according to Steven L. Miller, a postdoctoral research fellow at the Geisel School of Medicine of Dartmouth College. The so-called “biological clock” is essentially the human’s 24-hour clock. During this time period, our physiological and behavioral activity varies based upon the time of day. An important steroid hormone that is responsible for many regulations in our body is cortisol. Also known as a stress hormone, cortisol is released by the adrenal glands when the body perceives stress. This can cause an increase in heart rate and blood pressure as well as increase alertness. So, if cortisol levels are somewhat high, an individual should not consume caffeine because the body is fundamentally already in a heightened state of awareness. Various studies have concluded that cortisol levels are peaked around 8 to 9AM. This time of day just so happens to be when the majority of people consume their first cup of coffee. It is used by many as their “wake up call” and several cannot start their day without a nice cup of coffee. Cortisol is generally consistent on decreasing throughout the day, with slight additional spikes at noon to 1 and 5:30-6:30. Therefore, if caffeine consumption is best supplemented when cortisol levels are low, it is best to consume it between the hours of 9:30-11:30 (Miller 2013). It is also important to make sure caffeine consumption stays minimal throughout the evening, as too great of a dose can dramatically affect one’s sleep cycle. Examples of sleep problems caused by caffeine include insomnia and night terrors.

### **Unpredictability in products**

Caffeine is one of the most widely used and distributed drugs in the world. Consumption of caffeine on a daily basis is unrivaled by any other substance. What many people fail to understand is the fact that the amount of caffeine in many mainstream beverages is unknown. Caffeine in beverages can vary widely from product to product. According to an article titled "Sleep and Caffeine" by Thomas M. Heffron, scientists at the University of Florida bought a 16-oz cup of the same type of coffee from the same coffee shop for six days straight. The coffee was then analyzed to determine exactly how much caffeine it contained. The results concluded that caffeine variability in beverages is clearly present with the lowest amount of caffeine being 259mg and the highest amount being 564mg (Heffron 2013). This more than double range of caffeine in beverages should be enough to make people wonder exactly what is in their drinks. Caffeine is considered to be a "generally safe" substance and is not regulated by the Food and Drug Administration. Companies which serve caffeine in products must state that caffeine is in the product but do not necessarily have to state the exact amount.

### **Interactions with other drugs**

Drugs can not only affect the body in several ways, but they can also affect other drugs if taken simultaneously. This is commonly known as a drug-drug interaction, a change in a drug's effect on the body that can occur when taken with a second drug. These drug-drug interactions can enhance, inhibit, prolong, or delay the absorption of the other drug. Drug-drug interactions can also create adverse effects. Caffeine has many different interactions with a lot of conventional substances taken. To begin, the single commonly used drug that should not be taken in accordance with caffeine is ephedrine. Ephedrine is also classified as a stimulant and it functions to speed up the nervous system. This decongestant and bronchodilator can be used to

relieve shortness of breath, tightness in the chest, and wheezing. Since both of these substances are classified as stimulants, it is highly advised not to take both substances at the same time.

WebMD clarifies that taking both could cause overstimulation of the nervous system and cause serious side effects such as heart problems, vomiting, changes in mood, and anxiety. There are many other substances that exhibit a moderate interaction with caffeine, including adenosine, antibiotics, and anticoagulants. Adenosine, which is commonly known as the brand name Adenocard, is often used by physicians to conduct heart tests like a cardiac stress test. Caffeine and adenosine have the same receptors as stated before, so caffeine's ability to block the effects of Adenocard are extremely high. It is best recommended to stop consuming caffeine at least 24 hours prior to a cardiac stress test ("Caffeine"). In addition to adenosine, another substance which should not be taken with caffeine is antibiotics, specifically, quinolone antibiotics. These antibiotics decrease the body's ability to break down caffeine allowing it to stay in one's system for a longer duration. Side effects can include jitteriness, headaches, and increased heart rate. Common antibiotics that have this effect include ciprofloxacin, enoxacin, and norfloxacin ("Caffeine"). Anticoagulants are another substance which can cause adverse effects when supplemented with caffeine. Caffeine can have the ability to slow blood clotting. If taken simultaneously with anticoagulants such as Heparin and Warfarin, this can increase the chances of bruising and if wounded can cause severe and uncontrollable bleeding.

### **Caffeine sensitivity**

Caffeine sensitivity is something that varies from person to person and the biggest determinant of how sensitive one is to caffeine involves their genetic makeup. According to an article published by *Caffeine Informer*, Ted Kallmyer states that there are three genetic links to caffeine. The first link is in the CYP1A2 gene, which regulates the ability to produce the

CYP1A2 enzyme discussed earlier. Slight changes in an individual's DNA sequence will code for how efficiently they can metabolize caffeine. The vast majority of individuals produce a moderate concentration of this enzyme and therefore lie somewhere in the middle. The next link which contributes in determining caffeine sensitivity is the aryl hydrocarbon receptor (AHR) gene. This gene regulates the activity of the CYP1A2 gene, allowing it to turn on and off. It does this by binding to the region of DNA between CYP1A1 and CYP1A2. The third genetic link involved is the specific type of adenosine receptors in someone's brain. If a person does not possess the correct adenosine receptors then caffeine cannot bind to those receptors in the proper orientation. If caffeine does not bind then the awakening effects that caffeine possesses will be rendered inactive. The structural differences in genetic material allows for classification of caffeine sensitivity. Generally speaking, most people fall under the normal sensitivity levels. This category can usually intake 200-400mg of caffeine on a daily basis without showing any signs of adverse effects. If consumed earlier in the day, caffeine should not hinder sleep patterns. A small portion of the population, roughly 10%, are hyposensitive to caffeine (Kallmyer 2019). This group of individuals can consume upwards of 500mg of caffeine with little to no effect on the nervous system. They are able to metabolize caffeine at an exceptional rate and therefore can consume caffeine later in the day while still maintaining a proper night's sleep. The last classification one can fall under is being hypersensitive to caffeine. These individuals have extreme reactions to very slight amounts of caffeine (less than 100mg). Just in a dose of 100mg alone, people can experience overdose symptoms such as insomnia, jitters, and increased heartbeat (Kallmyer 2019). It is important to understand the level of caffeine on a person to person basis and knowing how much the body can handle at any given time.

## **Regulation of Caffeine**

It has been discussed throughout this research article that caffeine has the potential to be hazardous when consumed in substantial dosages. Although caffeine can be considered safe in certain quantities, it is unregulated and can therefore be a dangerous substance. It is important that precautionary measures as well as the possibility of implementing restriction on caffeine be examined and understood.

### **Reducing caffeine intake**

There are many ways to deal with a consistently high daily consumption of caffeine. In order to successfully soothe the desire for caffeine, the first step is to keep tabs. Paying close attention to the daily consumption of caffeine, whether it be from foods, beverages, or both, is an important step in the process. This can be done by reading and recording the labels of the products consumed. After caffeine consumption is recorded and understood, there are a few ways to combat the crave. One of the ways to cut back on the caffeine is to reduce the overall intake gradually. A slightly smaller cup of coffee, avoiding highly caffeinated beverages, or even diluting drinks with water is a great way to lessen consumption. This is also beneficial because slight reductions in caffeine over the course of a few weeks can dramatically lessen potential withdrawal effects. A rapid decrease may be necessary in some circumstances; however, the employment of this strategy can result in minor withdrawal symptoms such as headaches, irritability, fatigue, etc. Another way to cut back on caffeine is to go decaf. As many people get their means of caffeine through coffee, decaffeinated beverages have a similar appearance and taste as their counterparts. Decaffeinated beverages also have the ability to be a placebo. As many people recognize their coffee drinking habits are to obtain a "caffeine buzz," some research has shown that replacing a cup of coffee with decaf can result in similar effects due to

the placebo effect. As coffee is not the only beverage that is consumed in mass quantity with caffeine, shortening the brew time of tea can also reduce caffeine content. These are just a small fraction of the countless ways caffeine consumption can be reduced.

### **Education on caffeine**

One of the best ways to further education on the dangers of caffeine is in the classroom. “The American Academy of Pediatrics recommends that adolescents do not consume energy drinks, yet between 30-50% reported consuming energy drinks” (Centers for Disease Control and Prevention). As caffeine has no particular place in an adolescent’s diet, it is important that education by teachers and other school staff be implemented in schools. Not only do students pose a threat to the potential dangers of caffeine, but athletes even more so, as it can cause for dehydration and heart palpitations while practicing or in a competition. Athletes can be further educated outside the classroom by their coaches and mentors about important situational circumstances like the differences between sports drinks and energy drinks. Education on topics like these can let children make better decisions on what to put in their bodies, as a staggering amount of schools across the country have vending machines filled with highly caffeinated drinks. The Education Resources Information Center states, “Nationwide, 75% of school districts do not have a policy in place regarding these types of beverages that contain high levels of caffeine for sale in high school vending machines, school stores, or a la carte in the cafeteria” (Center for Disease Control and Prevention). Allowing children to know the difference between these types of things can help them lead healthier lives.

**Discussion**

This research paper examined and discussed the physiological and psychological effects of caffeine on the body. This research paper included an introduction on caffeine as well as how it interacts with the body. Discussion of the benefits of caffeine, which included examples like enhancement in memory, decreased energy intake in obese individuals, and increased muscle torque and activity were observed. Additionally, the consequences of caffeine were considered, which included caffeine's addictive properties, implications in pregnant women, effects on the bone repair process, and more. Finally, special considerations as well as an emphasis on the education of caffeine were studied.

### References

- Borota, D., Murray, E., Keceli, G., Chang, A., Watabe, J. M., Ly, M., ... Yassa, M. A. (2014). Post-study caffeine administration enhances memory consolidation in humans. *Nature Neuroscience*, *17*(2), 201–203. doi: 10.1038/nn.3623
- Caffeine & Neurotransmitters. (2017, February 6). *World of Caffeine*. Retrieved from <http://worldofcaffeine.com/caffeine-and-neurotransmitters/>
- “Caffeine: Uses, Side Effects, Interactions, Dosage, and Warning.” *WebMD*. Retrieved from <https://www.webmd.com/vitamins/ai/ingredientmono-979/caffeine>
- Chen, L.-W., Wu, Y., Neelakantan, N., Chong, M. F.-F., Pan, A., & Dam, R. M. V. (2014). Maternal caffeine intake during pregnancy is associated with risk of low birth weight: a systematic review and dose-response meta-analysis. *BMC Medicine*, *12*(1). doi: 10.1186/s12916-014-0174-6
- Coffee linked with increased cardiovascular risk in young adults with mild hypertension. (2015, August 29). *European Society of Cardiology*. Retrieved from <https://www.sciencedaily.com/releases/2015/08/150829123701.htm>
- Duncan, M. J., Thake, C. D., & Downs, P. J. (2014). Effect of caffeine ingestion on torque and muscle activity during resistance exercise in men. *Muscle & Nerve*, *50*(4), 523–527. doi: 10.1002/mus.24179
- “Energy Drinks.” (2019, May 29). *Centers for Disease Control and Prevention*. Retrieved from <https://www.cdc.gov/healthyschools/nutrition/energy.htm>
- Examine.com. (2020, March 10). How does caffeine work in your brain? *Examine.com*. Retrieved from <https://examine.com/nutrition/how-caffeine-works-in-your-brain/>



- Gavrieli, A., Karfopoulou, E., Kardatou, E., Spyreli, E., Fragopoulou, E., Mantzoros, C., & Yannakoulia, M. (2013). Effect of different amounts of coffee on dietary intake and appetite of normal-weight and overweight/obese individuals. *Obesity*, *21*(6), 1127–1132. doi: 10.1002/oby.20190
- Heffron, T. M. (2013, August 1). “Sleep and Caffeine.” *Sleep Education*. Retrieved from <http://sleepeducation.org/news/2013/08/01/sleep-and-caffeine>
- Helmenstine, A. M. (2019, June 2). Do You Know How Caffeine Works in Your Body? *ThoughtCo*. Retrieved from <https://www.thoughtco.com/chemistry-of-caffeine-608500>
- Is Caffeine Really Addictive? (2016, May 10). *National Institute on Drug Abuse*. Retrieved from <https://teens.drugabuse.gov/blog/post/caffeine-really-addictive>
- Jiang, X., Zhang, D., & Jiang, W. (2013). Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies. *European Journal of Nutrition*, *53*(1), 25–38. doi: 10.1007/s00394-013-0603-x
- Kallmyer, T. (2019, December 10). “Caffeine Sensitivity.” *Caffeine Informer*. Retrieved from <https://www.caffeineinformer.com/caffeine-sensitivity>
- Macedo, R. M., Brentegani, L. G., & Lacerda, S. A. D. (2015). Effects of Coffee Intake and Intraperitoneal Caffeine on Bone Repair Process - A Histologic and Histometric Study. *Brazilian Dental Journal*, *26*(2), 175–180. doi: 10.1590/0103-6440201300219
- Miller, S. L. (2013, October 23). “The best time for your coffee.” *NeuroscienceDC*. Retrieved from <https://neurosciencedc.blogspot.com/2013/10/the-best-time-for-your-coffee.html>

Saab, S., Mallam, D., Cox, G. A., & Tong, M. J. (2013). Impact of coffee on liver diseases: a systematic review. *Liver International*, *34*(4), 495–504. doi: 10.1111/liv.12304

Zawawi, F., Bezdjian, A., Mujica-Mota, M., Rappaport, J., & Daniel, S. J. (2016). Association of Caffeine and Hearing Recovery After Acoustic Overstimulation Events in a Guinea Pig Model. *JAMA Otolaryngology–Head & Neck Surgery*, *142*(4), 383. doi: 10.1001/jamaoto.2015.3938