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# Caffeine as Cause or Cure?

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Abstract

Everyone has experienced a migraine or headache at some point in their life. In the United States alone, over 3 million people struggle with recurring migraines every year. Recently, the correlation between migraines and caffeine intake has been a rising topic among researchers and healthcare professionals. However, there is much disagreement on whether caffeine has been a cure or a cause of migraines. In this paper, we will analyze an recent international clinical trial focused on the immediate effects of caffeine withdrawals as posted by the scientific journal, *Frontiers in Neurology*. While this study was not completed as originally proposed, it will give us a little insight as to the effects of a neurostimulant withdrawal. We will also find that the structure of a caffeine molecule is very similar to that of adenosine, which is a natural, neural metabolite, relating to sleep and drowsiness. When caffeine is more concentrated than adenosine, it inhibits the effects of adenosine (Nowaczewska et al).

Introduction

One of the most common "household health problems" to date is the headache. It has become the most popular excuse for missing class or work. It comes as a side effect to most drugs, therapy, and illnesses. At some point in their life, and for whatever reason, everyone has experienced a headache. The Mayo Clinic estimates that over 3 million people per year, in the United States alone, suffer from headache migraines.

We know that most people within the United States and all throughout the world enjoy the effects of caffeine, whether it be through drinking coffee or other caffeinated beverages. "The use of caffeine to stay awake and alert is a long-standing habit. Coffee is the most popular beverage after water and is consumed worldwide in daily amounts of approximately 1.6 billion cups" (Cappelletti et al). Along with coffee addiction, comes coffee withdrawals; avid coffee drinkers will often experience something called the caffeine headache which occurs as the result of a sudden decrease in caffeine. Is it true that we can become so addicted to caffeine that our bodies go through physical withdrawals when we no longer have it flooding our system? Is the caffeine headache real? Let's find out.

The first step in understanding the caffeine headache is understanding what the presence of caffeine does to our bodies. Research has shown that the structure of caffeine is actually very similar to that of adenosine. Adenosine is a naturally occurring signaling metabolite within the body that acts as a neural inhibitor, leading to effects of sleepiness and drowsiness.

How do two wildly similar molecular structures lead to very opposite effects? Basically, caffeine competes with adenosine in binding to the same receptors. When caffeine is flooded at a high concentration, it binds to more receptor sites than adenosine, essentially blocking adenosine and blocking the effects of sleepiness and drowsiness. Adenosine receptors, A1 and A2A, are known as G protein-coupled receptors (GPCR). GPCRs are folded, single polypeptides that are embedded within the plasma membrane as transmembrane proteins. They bind a ligand on the outside of the cell, which signals a nucleotide (GTP) to bind on the inside of the cell, dismembering its three subunits, and creating an amplified effect within the cell. One of the unique characteristics of the GPCR is that, with the binding of

the proper ligand, such as adenosine, hundreds or thousands of secondary signals can be processed (source: GPCR).

Discussion

Now that we understand how caffeine blocks the amplified effects of adenosine, how does this lead to the cure or cause of headaches? In a study presented by the scientific journal, *Frontiers in Neurology*, the Norland Hospital Trust, and others, designed an experiment to test and understand the effects of caffeine withdrawal as a migraine trigger. This study was designed with no prior background information, because limited knowledge is available on the direct effects of caffeine on the CNS. This study was meant to include eighty test subjects with pre-existing chronic migraines, and a daily intake of 300-800mg of caffeine. And while the original study actually failed as a consequence of low recruitment, we were able to obtain limited exposure to the idea through the remaining nine subjects. The revised test consisted of the participants substituting their average caffeine intake with placebo capsules for 5 weeks and then switching back to their normal caffeine intake for the following 5 weeks (Alstadhaug et al). This was done, primarily, to test whether the caffeine headache was psychological, or physical, and to see if it ever was triggered.

Out of the nine subjects, withdrawal triggered severe migraines in seven of the participants, while the remaining two suffered from less severe headaches. While the study failed to express the effects of caffeine withdrawals over time, it did show us the more immediate effects of a caffeine withdrawal on the central nervous system (Alstadhaug et al).

**Cure?**

While there are virtually no studies that actually test if caffeine can directly *treat* migraine attacks, there is some evidence suggesting that caffeine may be effective in long-term migraine treatment. One negative aspect of surplus adenosine is that it acts as a neuromodulator in migraine pathophysiology. An adenosine uptake inhibitor, dipyridamole, has been shown to increase the frequency of migraine attacks. Since caffeine is known to block the effects of adenosine, it may help block this pathway (Nowaczewska et al.). A recent study by González et al. also suggested that changes in intestinal microbiota could be positively affected by regular coffee consumption. Since migraines and the gut-brain axis are related, and if probiotics have shown to help mitigate migraines, then caffeine could also possibly impact migraines in this same way.

**Cause?**

On the other hand, caffeine may act as a trigger for migraines; There are many triggers for migraines, including stress, dehydration, fatigue, and sleep (Peroutka et al.). As a result, caffeine withdrawal, which also produces many of these symptoms, may contribute to more frequent migraines. Caffeine also causes urinary loss of magnesium, which is essential to neuromuscular conduction and nerve transmission. As such, magnesium is known to play a beneficial role in muscle aches and headaches. Therefore, by reducing the level of magnesium, high levels of caffeine might induce migraines. High doses of caffeine also cause “an acute diuretic effect”, which can lead to dehydration and subsequently, headaches (Nowaczewska et al.). One study showed that consuming 3 or more caffeinated beverages a day is correlated with more frequent headaches (Mostofsky et al.). However, there are no studies to date that have established and proven a direct cause between caffeine consumption and headaches.

Conclusion

In the United States alone, it is estimated that over 3 million individuals struggle with chronic migraine, many of which are reported to be caffeine induced. The correlation between migraines and caffeine intake has become a rising topic in healthcare, as more individuals present these problems. Considering the evidence, it is not conclusive whether caffeine is more a cure or a cause of headaches.

However, it is advised for those who suffer from frequent headaches and migraines to limit the amount of caffeine they consume daily to avoid possible triggers. People who suffer from chronic migraines should always be cautious of the amount of caffeine that they consume. The suggested daily limit, according to the Mayo Clinic, for the human body should not exceed 400mg. The most important factor is consistency as to avoid it as a headache trigger.

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