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# Migraine Triggers

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## Abstract

*Migraines are a painful and life-interrupting disease which strikes around 23 million Americans every year (Goadsby et al., 2017). Not enough studies have been done to help the public fully understand migraines. Details regarding the causes and pathophysiology of migraines continue to be analyzed by physicians and scientists, as no theory has been fully confirmed regarding a migraine's concrete path. The goal of this scientific review is to provide an overview for the main triggers of migraines, in reference to recent clinical investigations, and to understand why they might cause patients to be more prone to having a migraine attack upon encountering these triggers. Additionally, topics including the uncertainty whether migraineurs should avoid their triggers or learn to live with them, and the pathophysiology behind the triggers will be explored in this review. Some physicians suggest staying away from known triggers, while others say to allow one's self to be exposed, as a means of getting the sensitized central nervous system (CNS) used to the triggers and to make the CNS aware that these stimuli are, in essence, not harmful.*

*Migraines have been affecting people's lives for over two thousand years and are said to be the 6th leading cause of disability, according to the World Health Organization (WHO) (Goadsby et al., 2017). Of the 23 million Americans that suffer from migraines, women are predominantly affected (Silberstein et al., 1999). The ratio of 3:1 women versus men getting migraines is most likely due to hormonal changes and leads to an understanding of the reason migraines usually begin in females at puberty and can last until the age of 35-45, according to the WHO. Migraineurs claim that their daily lives are impacted by their frequent migraines, with 50% of them having 1 or more migraines per month (Silberstein et al., 1999).*

## Methods

Through the usage of databases such as Google Scholar, Touro Library, and the National Center for Biotechnology Information (NCBI), scholarly articles and peer-reviewed journals were obtained and reviewed for inclusion purposes. Each article was analyzed and verified, before assuming validity. Some key phrase searches included "migraine triggers," "hormonal migraine triggers," and "caffeine as a migraine trigger."

## Introduction

Migraine is a neurological disease that is not understood very well. It is more than just a headache and can be debilitating and life-altering at times. According to the International Classification of Headache Disorders, a headache is only classified as a migraine if it fits the description of a "recurrent headache manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia."

Many scientists have tried taking a deeper look into what exactly causes a migraine, what transpires in the brain while a migraine is occurring, why some people are more prone than others, and how to successfully treat migraine patients. From the studies that have been done to relate what can trigger a migraine, very few have been successful and completed in their entirety. However, scientists have gained some knowledge over the past century based on diary studies, clinical questionnaires, and patient surveys. The most common triggers are known to be caffeine, stress, sleep deprivation, a woman's menstrual cycle which involves hormonal changes, and some foods (Marmura, 2018). This review will give an overview of those triggers and explain some possible reasons why these triggers will cause a migraine headache.

## What is a Migraine?

Migraines can be broken down into 4 phases. A migraine begins with the premonitory phase, followed by aura (if present). It then proceeds into a migraine headache, and finally, the postdrome phase. Although there is a listed sequence of events, most migraineurs say that many of the phases overlap each other. For example, although exhaustion is associated with the premonitory phase, a migraine patient typically feels tired throughout the duration of the migraine (Goadsby et al., 2017).

The first phase is named the premonitory phase, and this occurs around 24-48 hours prior to the headache. Many people, including some doctors, believe that the migraine begins with a headache. However, contrary to the public's belief, some scientists admit that the headache phase of a migraine is already well into it. The premonitory phase notifies the patient of an upcoming headache. It can be observed as tiredness and having a hard time concentrating, as well as a feeling of irritability. The hypothalamus, which controls homeostasis, is said to be involved in this phase, due to altered homeostatic functions such as thirst, nausea, and frequent urination, which are observed during this phase. Studies done using positron emission tomography (PET) have shown increased blood flow to the hypothalamus during the premonitory phase, indicating a connection between the two. Seventy two percent of migraineurs can recognize when a migraine is coming, according to these premonitory symptoms (Goadsby et al., 2017).

Aura, which is found in one of three migraineurs, can present itself in numerous ways- mainly sensory and visual. Although symptoms play out differently in each patient, a sensory aura usually involves a patient feeling numb in one body part or limb. A visual aura can be characterized as visual hallucinations with flashing lights. Aura is correlated with cortical spreading depression (CSD), as

a result of experimental discussion. CSD is defined as a depolarization of glial cells across the visual cortex, followed by an electrical or chemical wave spreading across the brain (Goadsby et al., 2017). Animal studies have shown that CSD causes changes in blood flow as well as a release of neuropeptides involved in vasodilation and inflammation which is linked to migraine pain. CSD is also known to activate the trigeminal nociceptive pathways (Cui, Kataoka, & Watanabe, 2014).

The migraine phase is characterized, as stated above by the World Health Organization, as unilateral pulsating pain accompanied by photophobia or phonophobia, and very often nausea. Migraineurs report this pain as moderate to severe and tend to crawl into bed at this point.

The postdrome phase is very similar to the premonitory phase. It involves neck stiffness, drowsiness, and difficulty concentrating. In fact, scientists are unsure whether these symptoms persist throughout the entire migraine malady, or if they reappear after the headache phase. Interestingly, many migraineurs attribute these symptoms to the medication they took to relieve their headache (Goadsby et al., 2017).

### Trigeminal Path

The trigeminal nerve is one of twelve cranial nerves. Its function is to supply sensation to parts of the head including the face and mucous membranes. This nerve is connected to many blood vessels throughout the brain, and it originates in the brainstem. Upon receiving signals from the meninges, which in turn releases neuroinflammatory mediators, the trigeminovascular system is activated and can cause a migraine headache (Goadsby et al., 2017). Scientists do not know why this signal occurs, and they continue to investigate its source. The release of inflammatory substances such as prostaglandins or serotonin, can cause the blood vessels near the end of the nerve to swell, which causes head pain (Professional, 2018). These inflammatory substances cause the surrounding tissue to be sensitive to otherwise normal activities, and therefore pulsations, which under normal circumstances are not felt, are perceived as throbbing pain in a migraine. In turn, anything that would cause one's heart rate to climb, and increase the rate of blood flow, will be perceived as pain during a migraine. Examples include exercise and physical activity (Amin et al., 2018). This may be the reason why migraineurs avoid daily physical activities during their attacks.

### Symptoms

One of the countless symptoms related to migraine headaches, is known as allodynia. This refers to having

pain from regular daily activities, such as brushing their hair, laying their head down on a pillow, scratching their scalp, or wearing contact lenses. This pain is perceived as a result of these small stimuli, through sensitization of migraine pain pathways (Moy & Gupta, 2020). Two thirds of migraine patients experience this symptom together with migraine attacks. This aspect of migraine pain is usually attributed to the more severe headaches and can be a pointer leading to the diagnosis of chronic migraines. Proven by studies that measure the brain signals during a migraine, sensitized thalamic neurons are said to be the cause of this overreaction towards normally harmless stimuli (Goadsby et al., 2017).

### Photophobia

Photophobia is described by patients when light becomes bothersome and too bright. When most people are not bothered by this light, migraineurs can become aggravated by it. For example, in a study done, non-migraineurs were able to endure light until it reached the intensity of a sunny day, yet the migraineurs already reported pain and discomfort at the level of an overcast, rainy day (Rossi & Reuber, 2015). Studies show that light can activate nociceptive thalamic neurons and worsen migraine pain. This is true even if the patient is blind yet has an intact optic nerve (Goadsby et al., 2017).

### Triggers

Many ideas and hypotheses have been reported regarding the connection between migraine pain and triggers. A trigger is anything that causes a migraine to be more likely to occur. Migraines can be brought about by anything that directly or indirectly initiates vasodilation, activation of the trigeminal pathway or the brainstem, and cortical spreading depression. Dietary triggers can cause migraines by releasing norepinephrine and serotonin, which can act as vasodilators. Additionally, migraine attacks are more likely to occur when the migraine threshold is diminished by a trigger, which makes it easier to initiate an attack (Nowaczewska et al., 2020).

Many migraineurs cannot point to one specific thing that most likely causes their migraines, but rather a combination of a few factors (Nowaczewska et al., 2020). In fact, when asked what a possible cause of their migraine is, migraineurs most often cannot answer that question point blank, and are only able to identify some triggers when given a list of options. Confirming migraine triggers is almost impossible with the methods used most often such as diary studies, surveys, and questionnaires. This demands participants to think retrospectively and they very often confuse their thoughts with common migraine

misbeliefs, as opposed to actual symptoms that they've had. Electronic diaries seem to be the best method of recording data, as contributors can mark down their symptoms as they are experiencing them, and it is less likely for them to get confused (Nowaczewska et al., 2020).

Although some scientists believe that there are actual triggers that can bring on a migraine, others say that this is only a confusion of premonitory symptoms. They claim that a migraine has already begun 24-48 hours before the onset of pain (during the premonitory phase), and factors that others believe to be triggering the migraine, are only a consequence of premonitory symptoms. Some of these symptoms include food cravings, inability to stay focused and to concentrate, and fatigue. So, for example, when one feels tired as a result of this premonitory symptom in his already existing migraine, he is inclined to drink coffee or another caffeinated drink, and later feels the pain that is characterized as a migraine headache. This causes the patient to believe that coffee, or any other caffeinated food item, generates migraine headaches for him, when, in reality, it was only a cause and effect of his premonitory symptom. In the face of this confusion and difference of opinion amongst the scientists, the general public still believes that some factors, whether endogenous or exogenous, can cause one to be more prone to migraines (Goadsby et al., 2017).

A study was done in the Headache Outpatient Department of the University Medical Center at Hamburg-Eppendorf that proves this point, in which around 1000 participants were asked to highlight their so-called triggers and to relate the time interval in which it took to perceive head pain. While analyzing the results, 38.5% of the migraine patients claimed to have symptoms starting at the earliest 6 hours before the headache, and many of the presumed triggers were very closely related to leading premonitory symptoms. For instance, those who claimed flickering or bright light was a trigger for their migraine, also mentioned having photophobia during their premonitory phase. It is very likely that the flickering and bright lights were confused as a trigger and were in fact only early signs of a looming migraine. Researchers say that some 'migraine triggers' do have the ability to prompt a migraine, depending on which phase it is perceived (Schulte, Jürgens, & May, 2015).

If a migraine is said to be due to sensory neurons malfunctioning, then each individual's trigger threshold can be different, and even within one individual there can be different threshold levels during independent migraine attacks. It would therefore be clear, that triggers will only cause a migraine to materialize if the trigger reaches the sensory threshold. So, an external stimulus like an

environmental factor or stress will only induce a migraine if it is above the threshold level during that specific time (Schulte, Jürgens, & May, 2015).

### **Caffeine**

Caffeine has a dual job in migraine headaches. On one hand, caffeine is said to be beneficial to many migraineurs as it can lessen their symptoms or the length of their migraine headache. In fact, many migraineurs will choose their medication based on whether or not caffeine is included in its makeup. Yet, on the other hand, caffeine is said to be a migraine trigger, as well as being reported to cause headaches upon withdrawal. Coffee, tea, and other soft drinks all contain caffeine and have been listed as migraine triggers in around 10% of the population (Nowaczewska et al., 2020).

According to the Association of Migraine Disorders, when people enjoy consuming this substance to boost their energy, they tend to overdose. Their bodies then become dependent on having their daily coffee and no longer produce the same results as they have gotten accustomed to. They then try to consume more caffeine, hoping that a larger dose will increase the benefits, and run into a nasty cycle. If one day, they miss a coffee, they will most likely experience a caffeine withdrawal headache. This can occur after drinking coffee for as little as seven days. Caffeine withdrawal must be done gradually to avoid a migraine headache. Therefore, migraine patients are advised to be consistent with their amount of caffeine intake, and not to drink beyond 200 mg a day, about two servings of a coffee (this amount varies depending on how one makes their coffee) (Nowaczewska et al., 2020).

In a recent caffeine withdrawal study done in Norway, 80 participants were told to terminate their daily caffeine intake and replace it with either a capsule filled with caffeine or a placebo, identical looking. This study was randomized, and participants did not know which capsule they received. They divided the capsules of caffeine/placebo into smaller doses, to enable the participants to continue their way of life (i.e. having a few cups of coffee scattered throughout the day). Many of the participants dropped out before the end of the study due to withdrawal headaches. The study ended with nine participants, of which seven had intense migraines upon withdrawal from their usual intake of caffeine. When these participants continued with this daily dose for some time, they ceased to have migraines. However, one participant chose to reintroduce caffeine into his diet and consequently suffered from a migraine attack (Alstadhaug, Ofte, Müller, & Andreou, 2020).

Caffeine reduces the amount of urinary magnesium

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by acting as a reabsorption minimizer. Magnesium is important in managing chronic pain as well as migraines. Therefore, if someone has a reduction of magnesium in their urine due to excess intake of caffeine, they will be more prone to having a migraine attack. Additionally, caffeinated drinks such as coffee can cause a person to need to urinate which can lead to dehydration, another well-known migraine trigger (Nowaczewska et al., 2020).

### Sleep deprivation and Malnourishment

When looking at nuclei in the hypothalamus before and during a migraine attack, scientists noticed that they were more active than usual. These nuclei are involved in activating the trigeminovascular system and are recognized as migraine triggers. The hypothalamus regulates homeostasis regarding food and energy systems, circadian rhythm, and salt balance. Therefore, if someone skips a meal or is malnourished, or if they have constant interrupted sleep or reduced amounts of rest, they can be more likely to have a migraine attack. A study done on fasting revealed that 50% of fasting participants had a migraine headache (Goadsby et al., 2017). In fact, during Ramadan and on Yom Kippur, many fasters report having migraine headaches. An additional reason why fasting can cause a headache is due to caffeine withdrawal, as fasters miss their daily coffee.

A person's diet causes them to intake different amounts of needed vitamins and elements. Some foods will cause inflammation, release of nitric oxide, and vasodilation. A study conducted in Rome reported that increased consumption of whole-grain bread and pasta, thereby decreasing one's intake of white bread, was associated with fewer migraines and a significantly smaller amount of people needing medication to help with migraine pain (Hindiyeh et al., 2020).

### Stress

Stress is another factor of disrupted homeostasis that can trigger a migraine. It seems that migraineurs are more susceptible to changes in the environment. When a migraineur who has enhanced sensitization of brain stem pathways experiences stress, it can be misinterpreted as an unwanted intruder and can cause a migraine attack (Goadsby et al., 2017). A study reviewed a migraineurs stress levels over a period of time, and indeed, stress levels were high in the days leading up to the migraine (Schulte, Jürgens, & May, 2015).

### Menstrual Cycle

There is a 3:1 ratio of women getting a migraine versus men. This is most likely due to a woman's menstrual

cycle, which is reported to be the cause of more than 60% of migraines in women (Silberstein et al., 1999). By their early 50's, almost half of the world's women will have experienced at least one migraine headache (Moy & Gupta, 2020). Although it is unconfirmed due to lack of successful studies, menstrual migraines seem to be due to estrogen withdrawal at the end of the menstrual cycle. Results of studies done, in which women were given estradiol, shows that their migraines were delayed until their estrogen levels dropped. In addition, women who were given gonadotropin-releasing hormone to help with in-vitro fertilization reported migraines as an aftereffect of a rapid estrogen level descend. When looked at from the other side, high levels of estrogen are shown to lessen the likelihood of migraines, like in women who are post menopause or in their second or third trimester of pregnancy (Sacco, Ricci, Degan, & Carolei, 2012). Towards the end of a woman's menstrual cycle, she has low levels of estrogen and serotonin. This causes her trigeminal nerves to stimulate the production of substance P and calcitonin gene-related peptide (CGRP). These two substances cause vasodilation and sensitization to the trigeminal nerve, both of which are thought of as migraine triggers (Moy & Gupta, 2020).

### Genetics

While an average individual will not be affected by triggers, migraineurs, because of their sensitive protein receptors, will see these triggers as an enemy and cause an attack. The fact that some people are more prone to migraine headaches leads doctors to believe that there is some genetic factor (Nowaczewska et al., 2020).

Those who are taking medications like a hormonal contraceptive, can be more prone to migraines as their estrogen levels fluctuate drastically. (Moy & Gupta, 2020) Other medications that can cause migraines are those that contain high doses of caffeine and can lead to a caffeine withdrawal migraine (Nowaczewska et al., 2020).

### Treatments

Although caffeine is most often known as a migraine trigger, it can also be used to treat migraines. Caffeine can act as a vasoconstrictor which can lessen the migraine's effect and is said to relieve head pain by 40% when combined with other drugs like acetaminophen and aspirin. However, patients should be sure not to overuse this method as it can lead to a caffeine withdrawal headache if one consumes too much over a short period of time (Martin, 2019). Additionally, during a migraine, it is understood that adenosine binds to specific receptor molecules, causing a widening of blood vessels. Caffeine, as a

vasoconstrictor, can help bring the blood vessels back to their original size, thereby reducing the risk of having a migraine (Shapiro & Cowan, 2017).

Sleep is another well known treatment. Patients report sleep as having a therapeutic effect on headache pain. Therefore, doctors try to choose sedative medication when deciding what to give the patient to aid in healing the migraine (Vgontzas & Pavlović, 2018). Other treatments include taking analgesics like acetaminophen, aspirin, and Excedrin. Treatments are specific to each patient and their distinct migraine symptoms and should be discussed with a physician.

### Discussion

Many migraineurs have been advised by physicians or by medical personnel to steer clear of objects or situations that usually cause them to experience a migraine. However, studies have shown that avoiding common triggers can cause sensitization and an increased likelihood to have a migraine when one is later, perhaps unwillingly exposed to those triggers. Additionally, when people are constantly avoiding certain situations or specific foods, it can get frustrating and induce stress. This can be detrimental as stress is considered to be a migraine trigger as well. Furthermore, if we believe that migraines can be a consequence of sensory signals in the central nervous system overreacting to so-called 'triggers', getting the CNS used to these triggers and teaching it that they are not harmful, can be beneficial to those who suffer from migraines. Therefore, the public is recommended to continue their usual lifestyle, with these 'triggers' included in their daily living, so long as one does not yet feel the beginning of a migraine (Nowaczewska et al., 2020). However, all physicians will agree, that once a migraine patient feels the onset of the ailment, he should immediately do anything he can to avoid more pain, including staying away from things he knows can exacerbate his pain. Additionally, each individual is recommended to follow his/her migraine adventure with their physician, as each case is unique in its own way.

### Conclusion

Scientists have not come across enough information regarding migraines to know if it is better to avoid triggers, or to learn to live with the pain. More investigation needs to be done before a clear decision can be made. Researchers should try to find migraineurs who will not drop out of the study before the end (due to headache pain), as a means to discovering more information on migraine headaches and their pathophysiology. To avoid the bias of migraineurs reporting triggers through

a questionnaire, more investigations should be done via electronic diary, so the patients can report triggers as they are happening. This report includes data that helps the public better understand migraine triggers and their side effects.

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