EXPLORATION OF THE RELATIONSHIP BETWEEN STRESS, DIET AND/OR CAFFEINATED DRINK CONSUMPTION AND MIGRAINES

By

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Abstract

A vast amount of research shows that migraines affect many people around the world. It has been suggested that stress, caffeine and artificial sweeteners are three of the many factors that can cause migraines. Caffeine, ironically, has been shown to be both a trigger and a treatment. Pre-med students have been shown to be prone to migraines as their future goals require high/successful involvement in both the community and academics. This study provides insight into whether consumption of diet drinks, caffeinated drinks and/or stress is/are correlated with the intensity or frequency of migraines by surveying pre-med students near beginning and towards the end of their undergraduate career. While there was no correlation with consumption of either artificially sweetened or caffeinated beverages, stress was found to be the most common migraine trigger for this population. Rigor of major and post-graduation plans were among the highest sources of stress. Considering the influence stress had on migraine experience and these sources of stress, learning and utilizing stress reduction methods such as Cognitive Behavioral Therapy (CBT), Stress Inoculation Therapy (SIT), and Mindfulness Based Stress Reduction (MBSR) might be the most effective way to reduce intensity/frequency of migraines.

Introduction

Migraines are considered to be the third most common disease according to the Global Burden of Disease Survey 2010 by the Institute for Health Metrics and Evaluation. It is estimated that about 14.7% of the world's population suffers from migraines (Carod-Artal, 2014). The biological basis of migraines is hypothesized to be primarily a disorder of the central nervous

system (CNS). This hypothesis is supported by two observations: that migraines are often preceded, sometimes several hours before, by problems with speech, reading, emotional responses and sensory hypersensitivity, and that some typical triggers such as stress, hunger, and sleep disorders have a CNS origin. Moreover, it has been shown that patients show abnormal neurophysiological (EEG) patterns in the time before, during and between attacks (Panerai, 2013).

Although there have been many factors which serve to trigger migraines, according to Peroutka, stress was the most common cause sufferers listed for experiencing a migraine (Peroutka, 2014). Caffeine was another modifiable factor that was found to influence migraine experience (Carod-Artol, 2014). Especially in individuals that consume it in excess. The migraine is triggered as one of the potential withdrawal symptoms the migraine sufferers experience in response to decreased consumption of caffeine (National Headache Foundation, n.d.). Moreover, caffeine has been shown to have vasoconstriction properties (Matthew, 1985) and the auras that are often associated with migraines have been proposed to be caused by cerebral vasoconstriction (Silberstein, 2004). Therefore caffeine is thought to be both a trigger of migraines and their precursor symptoms. Conversely, caffeine paired with aspirin and acetaminophen has been shown to be about 40% successful at reducing migraine pain. And finally, the diet drink sweetener, aspartame, has also been shown to cause headaches. A study by Lipton et al (1988) found that individuals suffering from migraines were 3 times more likely to rate aspartame as a headache trigger. Given the evidence that stress, caffeine and aspartame separately affect the frequency/intensity of migraines, it was of interest to see how these factors might interact with one another to produce migraines. By further exploring the

role of these factors in producing migraines in pre-med college students, it is hoped the results from this study may provide insight into how reducing diet or caffeinated drink consumption and stress might benefit those experiencing migraines.

Background

Prevalence

The prevalence of migraines alone emphasizes the importance of addressing migraines and attempting to effectively decrease their intensity/frequency. Interestingly it has been observed that patients are very unlikely to seek treatment for migraines. It is estimated that over two-thirds of migraine sufferers have not seen a doctor about their symptoms or have since stopped receiving treatment (Ferrari, 1998). Recent reports approximate that about 29.5 million Americans suffer from migraines, and about half of these individuals have not seen any professionals to treat their symptoms ("Understanding Migraine: Understanding Migraine," n.d.). These statistics illustrate just how prevalent migraines are in the U.S. and why it is important that efforts be made to learn more about migraines and treatment. Though as of now, much of the public does not see the symptoms of migraines as significant enough to treat or eliminate.

The epidemiology of migraines is important to better understand who should be the target population for migraine research. It should be noted that there is a noticeable difference between genders on the occurrence of migraines. The statistics indicate that the overall experience of migraines occurs in 43% of women while only 18% of men report having migraines. The difference in gender experience of migraines is not obvious until individuals reach puberty, at which point women begin to report more migraines than men. Migraines without auras became most prevalent during puberty and peaked around 30-40 years old

(Finocchi & Strada, 2014). Whether these individuals are men or women, these studies show that college students comprise a significant part of the groups afflicted with migraines. Sex hormone differences between men and women are credited with some of the differences seen and can even be seen in differences in intensity, duration and frequency of migraines. A study done in the UK found that, on average, migraines not treated with medication lasted 28.4 hours in men, but in women these migraines lasted 36.7 hours. Furthermore, prevalent migraine symptoms differ as well, with women being more likely to have the following symptoms than men: light sensitivity, sound sensitivity, and nausea. Women apparently not only have longer migraine pain, but they also seem to have an increased risk to experience particular symptoms. Women were also found to be more susceptible to developing co-morbid diseases associated with migraines than men. These co-morbid diseases include but are not limited to: arterial disease, hypothyroidism, asthma, and endometriosis, depression, anxiety, irritable bowel syndrome, and fibromyalgia (MacGregor, Rosenberg, & Kurth, 2011). Looking at the migraine experience in its entirety, it appears that women are significantly more effected by migraines than men. This time frame of migraine experience emphasizes that our study's population is at the perfect age to talk about their experience of migraines.

Now that we have confirmed that there is an apparent inconsistency in migraine experience between the sexes, it is important to explore the possible explanations for these differences. High estrogen levels have been associated with the migraines particularly if they are preceded by auras (Finocchi &Strada, 2014). Transgender individuals who began taking anti-androgens and estrogen to become more feminine showed similar migraine prevalence (26%) as women. (Pringsheim &Gooren, 2004). It is apparent from these statistics that the

biochemical nature of the hormone estrogen plays a crucial role in migraine prevalence differences between genders. While, estrogen has been shown to not directly influence calcitonin gene-related peptide (CGRP) or 5-HT receptors in trigeminal system estradiol does appear to influence migraine formation by affecting neuropeptide release or receptor coupling. In the trigeminal nucleus caudalis (TNC) the presence of estradiol stimulates extracellular signal-regulated kinase (ERK). When ERK is stimulated increased nociception is seen, while bradykinin B2 receptors and interluekine-1b receptors, which activate release of CGRP, are decreased. Similarly progesterone appears to affect neurotransmission in TNC by reducing accidental plasma release (Finocchi &Strada, 2014). These findings further suggest that hormonal differences have a greater blame in women's higher susceptibility to migraines.

Furthermore estrogen is responsible for allowing glutamatergic and serotonergic systems to function properly and is responsible for activating/inhibitory effects on the GABAergic and noradrenergic systems. Progesterone has been shown to initiate GABAergic systems. Finally it has been shown that hormones progesterone and estradiol have opposing effects on neuronal excitability. Estradiol stimulates excitability, which increases the likelihood of cortical spreading depression, while progesterone has hindering effects (Finocchi &Strada, 2014). All these findings provide a strong argument that much of difference in migraine experiences between the sexes are due hormonal variances.

There have been no significant research findings that confirm or deny the influence genes on gender differences in migraine susceptibility. However, differences in brain function and structure have been credited for causing a difference between the sexes in migraine experience. It has been noted that disease-related structural changes in females are commonly

found in the insula and precuneus regions, while in males disease-related structural changes are usually in the parahippocampal gyrus. Thickening of dorsal and ventral parts of the precuneus, which is involved in sensorimotor filtering and reasoning and correlative handling, has been found to occur in females more than in males. Additionally significantly higher activation of parts of the brain, specifically amygdala and parahippocampus, which mediate emotional interpretation is seen more in females. This increased stimulation is also seen in the contralateral main sensory nucleus and spinal trigeminal nucleus located in the brainstem (Finocchi &Strada, 2014). These are just some of the mechanisms by which differences in brain structure between the genders may play a part in their differences in migraine experience. As we can see there are numerous mechanisms by which the differences in migraine frequency/intensity between genders are thought to arise.

Burden of Migraines

Due to the negative impact on productivity at work and life, there is a significant need to reduce migraines either by medicinal or alternative therapy these detrimental effects on productivity can occur as they often require individuals to rest, which of course inhibits them from working and results in unanticipated sick-leave for employers to address. . It is estimated that migraines are responsible for about 112 million days off in the United States (Hu X, Markson LE, Lipton RB, Stewart WF, & Berger ML, 1999). This signifies that migraines not only effect the individuals that suffer from them, but they also damage other aspects of the individual's life because they cause the individual to be bed-ridden. "Among all sufferers, over 3 million days per month were spent bedridden due to migraines (Stang &Osterhaus, 1993)." This statistic alone has huge ramifications for a nation as a whole and demonstrates the

importance of research into both treatment and prevention of migraines. . Furthermore migraines increase medical costs by increasing the need for doctor's office visit and prescriptions. "Assuming 29% male and 41% female patients were medically diagnosed, we estimated that close to $100 were spent per diagnosed patient per year "(Hu X, Markson LE, Lipton RB, Stewart WF, &Berger ML, 1999). Migraines not only cause individuals to work less, but also hike up their medical spending leading to sufferers bank accounts being hit in two different ways. Furthermore, migraines are also responsible for decreasing the efficiency of workers. With the assumption that the percentage of the working population is the same for migraine sufferers as the general population, males and females suffer from $690 and $1127 costs due to decrease in efficiency , respectively (Hu X, Markson LE, Lipton RB, Stewart WF, & Berger ML, 1999). It was found that the most frequent cost was due to days out of work and accounted for about 8 billion dollars of the cost. Furthermore workers aged 30 to about 50 years had a higher frequency of these kinds of costs compared to younger and older workers (Hu X, Markson LE, Lipton RB, Stewart WF, & Berger ML, 1999). These individuals are most likely in the middle of their careers, so it is interesting that they are most effected by bedridden days. It appears that if this is the case, it should be important not only to workers but also employers to find effective treatments of migraines, to reduce the negative impact to their workforce. Finally it was found that the average productivity of workers that choose to work with a migraine was found to be 42% for men and 34% for women (Hu X, Markson LE, Lipton RB, Stewart WF, & Berger ML, 1999). This is further disconcerting for employers because it seems to suggest that even when individuals are not bed-ridden by the migraine the migraine still has detrimental effects on the work they do. Again it appears that migraines not treated

effect many individuals from the employer, to the worker, to the individual that is receiving the work/product of migraine workers.

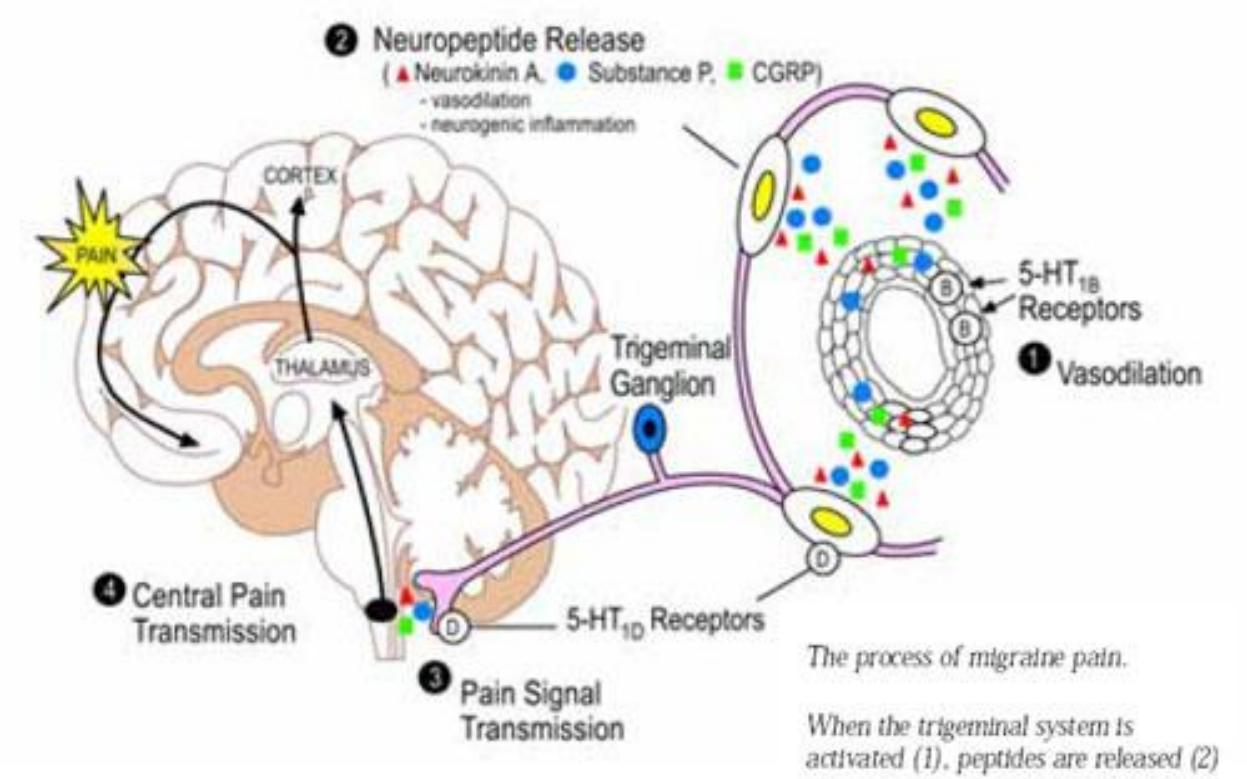
Thus far the burdens of migraines have focused on what they defined as indirect costs such as loss of production, but some research has been done on direct costs of migraines. The direct costs have not been assessed on the basis of money, but instead based a managed care claims computer system. Using this measurement it was found that migraine sufferers spent about $145 on average member-month enrollment compared to $89 spent by non-migraine sufferers (Hu X, Markson LE, Lipton RB, Stewart WF, & Berger ML, 1999). While this may not be the most accurate method to estimate the direct costs of migraines it does suggest that migraines do raise the healthcare spending significantly. This study highlights the effects that migraines have outside of their pain on the sufferer, thus it emphasizes why attempts to understand the triggers and treatments of migraine is of importance.

Interestingly these studies on the drains migraines pose to society found that very few migraine sufferers have pursued medical help to treat migraines. A study looking at migraine frequency in the United States estimated that about 16% of migraine sufferers have visited the doctor regarding their migraine experience (Lipton et al, 2001). It appears that migraine awareness not only needs to be promoted to society, but also to migraine sufferers. Migraine sufferers will only be benefited by more focus on treatment and causes of migraines, if they are persuaded to make efforts to receive medical treatment. Overall, these studies illustrate the importance of promoting migraine awareness to society not only to improve societal experience, but also to improve the quality of prevention and treatment available for migraines.

Biological Mechanisms of Migraines

The biological basis of migraines primarily involves the central nervous system. Migraines are classified as either being with or without auras. One study found that their participants represented this demographic: 33% reported have migraines with auras, 75% reported migraines without auras, while 33% claimed to have both. Migraines have been thought to be the result of a few different pathologies. A few of the pathologies thought to cause migraines are defective mitochondrial oxidative phosphorylation, low intracellular magnesium, increased concentrations of neurotoxic amino acids, hereditary dysfunction of calcium channels, or any of these factors combined (Ferrari, 1998).

It was found that the brainstem was the site of increased blood flow during migraines, suggesting that this area may be where the migraine is originated (Ferrari, 1998). The Trigeminovascular system is thought to be a component of migraine because during a migraine the trigeminal afferent secretes peptides that cause inflammation leading to head pain. Inflammatory reaction also causes a decreased sensory threshold in trigeminal afferents, which can initiate increased sensory information to the chief pain perception areas: thalamus, brainstem and cerebral cortex. The stimulation of this system can help explain the facial, head, and neck pain migraine sufferers often experience ("Understanding Migraine: Understanding Migraine," n.d.). These two theories emphasize that the brainstem plays a role in development of migraine. Furthermore the theory about the role of trigeminovascular system in migraine development explains pain that is associated with migraines. The figure below visually illustrates the role that the trigeminovascular system in the development of migraines:



The process of migraine pain.

When the trigeminal system is activated (1), peptides are released (2) prompting an inflammatory reaction. This increases flow of sensory traffic through the brain stem (3), the thalamus and ultimately the cortex (4).

Nitric oxide has also been found to cause migraines without auras by causing expansion of the middle cerebral artery, but given that it took between 3 and 10 hours for the migraine to set in suggests that another intermediate mechanism needs to be activated first prior to the onset of a migraine. Migraines with auras are associated with cortical spreading depression (CSD) which is characterized by a depolarization wave that disseminates across the brain cortex at a rate of 2-3mm/min. CSD initiates intense failure of brain ion homeostasis and a movement of excitatory amino acids out from nerve cells (Ferrari, 1998).

Changes in serotonin (5HT) levels have also been thought to be a component of migraine physiology. Particularly, it has been seen that serotonin (5HT) levels are low prior to

the onset of a migraine, but high once the migraine occurs. The actual changing in serotonin (5HT) levels is thought to be a self-defense tool of the body and not the reason for the development of migraines. The best treatment for migraines resulting from this condition is activation of certain 5-HT receptors (Ferrari, 1998). This finding seems to suggest that 5-HT receptor is modulated by what causes migraines.

Familial Hemiplegic Migraine (FHM) occurs as a result of mutation to chromosome 19p13 in about 50% of families. This mutation causes a disruption of 2.1 (P/Q) type voltage-gated calcium channels. The obstruction of P/Q type voltage-gated Calcium channel in periaqueductal gray matter (PAG) allows trigeminovascular nociceptive processing. Conversely, PAG will block sagittal sinus evoked trigeminal neuronal activity. Pain in the trigeminocervical complex travels by way of caudal cells. Calcitonin gene-related peptides (CGRP) is contained in the trigeminal ganglion emanating from trigeminal fibers. CGRP is in high concentration during migraines; it thought the vascular pain is the result of Superior sagittal sinus (SSS) increases cerebral blood flow (CBF) and increase in jugular vein CGRP concentrations (Goadsby, 2005). Calcium channels control serotonin (5-HT) secretion within the midbrain. Thus the malfunctioning in channels is hypothesized to reduce serotonin release which can make individuals vulnerable to migraine. It is interesting that calcium and magnesium are proposed to interact considering a decrease in magnesium is thought to relate to the development of migraines (Migraine Pathophysiology, n.d.). Again the trigeminovascular system is credited for producing the common symptoms of migraines. This interrelates the idea that this system releases peptides that cause inflammation, with the increased blood flow in the brainstem, and how these peptides modulate the release of serotonin (5HT). These theories seem to suggest

that the trigeminovascular system should be the focus of pharmaceuticals developed to treat migraines. Also if this system is heavily involved in migraine development it would be interesting to see if migraine triggers affect and influence the trigeminovascular system.

All these migraine theories relate central nervous system and trigeminocervical complex to development of migraines and migraine pain. Considering the vast amounts of research about migraine pathophysiology, it would appear that migraine pain is extremely complex. As a result of the complexity of migraine pain it has been contemplated that perhaps a better way of treating migraines is to eliminate the external source responsible for triggering these pain mechanisms (Ferrari, 1998). This relates to the goal of our study since rather than focusing on pharmacological treatments of migraines, we hope to work on minimizing the effects of external migraines triggers. Specifically, this study addresses the possibility of reducing specific drink consumption or utilizing stress-reducing methods are effective or related to decrease intensity/frequency of migraines.

Migraine Triggers

Now that the pathophysiology of migraines has been established, it is of interest to determine what triggers migraines. Research on precipitating factors of migraines have found that there are many migraine triggers. For instance, research found that the top ten triggers of migraines are: stress, noise, tiredness, and fasting, hormonal, lack of sleep, weather, light sensitivity, smells, and alcohol. Specifically, stress was listed as the number one trigger to migraines. Interestingly, it was noticed that in most of the common migraine triggers it was a decrease in a specific stimuli that made that the trigger of a migraine. This was noticed

particularly in hormonal, weather, food consumption, sleep, and stress triggers (Peroutka, 2014). These findings seem to suggest that perhaps the best prevention/treatment of migraines would be to focus on minimizing the influence of triggers. According to a study exploring triggers for migraines and tension-type headache found that both are often caused by the same triggers. In this study, they talked about the effectiveness of determining migraine triggers. Learning about what causes an individual's headache or migraine can help determine the best treatment (Haque et al., 2012). This seems rationale because if your migraines are tied to lack of sleep, knowing this information could enable you to get more sleep every day and thus have a positive impact on migraine experience. With these study findings it is believed that this can be used to manage the influence caffeine, stress, and artificial sweeteners on migraine experience.

Artificial Sweeteners as a Trigger

Diet drinks that are commonly available at grocery stores are known to contain artificial sweeteners in attempt reduce calories by reducing the sugar content of drinks. These diet drinks include sugar free energy drinks, diet soda, diet juice, and diet tea. Research on aspartame, a commonly used artificial sweetener in diet drinks, has been conflicting about whether or not it really causes migraines. For instance, one study found that migraine sufferers were three times more likely to report aspartame as a migraine/headache trigger. Studies revealed that consumption of aspartame was associated with lower levels of serotonin (Lipton, Newman, Cohen, & Solomon, 1989). As stated previously one of the theories of migraine formation noted that low levels of serotonin often preceded the migraine. Furthermore, it was noted that this observation suggests that the serotonin is a self-defense mechanism. This

suggests how aspartame contributes to the creating the cellular environment leading to migraine materialization.

Furthermore the physiological effects of aspartame is increased levels of plasma phenylalanine and tyrosine in the body (Schiffman et al, 1987). Phenylalanine, tyrosine, and L-tryptophan were found to be precipitating migraine factors (Shirley M. Koehler, 1988). However some research suggests that there is no clear difference in susceptibility to developing a migraine between individuals who consume or do not consume aspartame. Moreover it has been contemplated that migraines are the result of a neurological mechanism and that individuals with a low threshold to reach migraine are more likely to develop a migraine after consumption of aspartame (Shirley M. Koehler, 1988). These findings seem to suggest that aspartame has not definitively been linked to migraines. Instead it seems that there is a possibility that aspartame only increases the likelihood of migraines in already vulnerable individuals. This leads us to believe that perhaps stressed migraine- prone individuals are likely to report migraine after aspartame consumption, not because it is the true initiator but because their susceptibility of migraine was already high and aspartame just increased those odds. The lack of conclusive findings of aspartame directly influencing migraine experience is one of the reasons our study will try to see if stress is the common denominator between increased diet-caffeinated drink consumption and migraine experience and the diet-caffeinated drinks wrongfully take the blame for some migraines.

Caffeine as a Trigger/Treatment

Caffeine is paradoxically known to be a trigger and a treatment of migraines. Caffeine as a trigger of migraine is able to complete this action by being a vasoconstrictor. Migraines can also be attributed to withdrawal effects that individuals have when the suddenly stop consuming caffeine that they once consumed in excess. Conversely caffeine is also common component of treatment of migraines. These are just a few of the ways that caffeine has been shown to interact and effect migraines.

One of the theories of how migraines develop is due to vasoconstriction in the cerebral blood vessels (Mathew &Wilson, 1985). Vasoconstriction result in decrease blood flow in these vessels as stated above decreased blood flow in the brain is commonly seen in migraines (Silberstein, 2004). Therefore helps contribute to the decreased blood flow in the brain by being a vasoconstrictor furthering migraine development. Caffeine could be attributed as the precipitating factor if the development of a migraine is thought to be the result of vasoconstriction in the brain.

Furthermore caffeine can trigger a migraine due to caffeine withdrawals. Individuals that drink caffeine in excess develop an addiction to it, which leads to dependency on caffeine. These addicted individuals develop withdrawals when they abruptly cut back on their caffeine intake (National Headache Foundation, n.d.). A study on migraine triggers revealed that caffeine withdrawal was one of the most common nutritional precipitating factors of migraines (Mollaoğlu, 2013). Thus it appears that caffeine is a trigger of migraines in individuals that consume caffeine in excess and have dependence on it. Therefore caffeine as a trigger of

migraine is limited to regular caffeine consumers and is not as common in the rest of the population. According to Dr. Hunter, another way caffeine can cause migraines is if pain relievers for migraines are taken more often than needed. This abuse of treatment can elicit a dependence on the painkillers so when the individual stops taking the medication the body develops withdrawals. This phenomenon is known as "rebound" headache and is thought to occur because caffeine is so easy to become addicted to (Crooks, 2003). These are important mechanisms by which caffeine can cause migraines because in our study we believe that pre-med students consume caffeine in excess as a way to keep up with rigor of their course work.

Caffeine as a treatment of migraines is possible by utilizing caffeine's vasoconstrictive properties. As previously stated some migraines are thought to be due to increased blood flow and vasodilation of blood vessels in the brain. In these types of migraines, caffeine can be an effective treatment because of its ability to cause vasoconstriction of blood vessels and subsequently decreased blood flow. Many of the treatments of migraines have properties of vasoconstriction and some of them contain caffeine; some of these treatments include: dihydroergotamine, triptans, paracetamol, and non-steroidal anti-inflammatory drugs (NSAIDS) (Da Silva & Tepper, 2012). The characteristic of decreasing blood flow helps reverse the formation of a migraine. A study compared the changes of cerebral blood flow in individuals that were either administered caffeine or a placebo and it was determined that there was a significant decrease in blood flow in the caffeine group (Mathew & Wilson, 1985). Caffeine used as treatment of migraines utilizes its ability to decrease blood flow, which is advantageous in migraines that are onset by an increase in blood flow.

Stress as a Trigger

Stress, a migraine trigger, cannot be completely eliminated from individual's lives, but perhaps the effective treatment/prevention of these migraines is stress reduction therapy. A population that is prone to stress is medical school students. A recent study of medical students found that the most common cited triggers of migraines were: stress (24.9%), irregular sleep (20.08%), excessive reading (18.5%), examinations (11.1%), smoking (5.8%) and fasting (5.8%) (Al-Hashel et al, 2014). These triggers are very similar to the top ten that the general population of migraine sufferers listed, except for such factors as excessive reading and examinations which are specific to medical school students. It was also found that as the years of medical school progressed, so did the frequency of migraines (Al-Hashel et al, 2014). These findings are interesting because it does emphasize that stress is a crucial factor in migraine control in that stress does not necessarily ever disappear; in fact, it seems, at least for medical students, that the stress worsens with time. All of this suggests the importance of teaching stress reducing therapy to the public. Migraine sufferers have also reported that stress was not only a trigger, but also influenced the length of the migraine and could negate the effectiveness of migraine drug treatments (Sauro and Becker, 2009).

Some of the physiological effects of stress help explain why it might have such an influence on migraine experience. These physiological effects of stress include: release of adrenaline/epinephrine and cortisol. The first, in particular, result in increased muscle tension, blood vessel dilation, more frequent breathing, etc. (Tovian et. al, n.d.). Thinking back to the different biological mechanisms of migraines, the fact that stress causes blood vessel dilation relates to the scenario of trigeminal nerve migraines. This dilation allows for more blood flow

through brainstem, cortex, and thalamus which aids spreading/initiation of the pain of migraines. Research suggests that stress stimulates the immune system allowing pain to occur on a neuronal level. Specifically it has been found that stress causes inflammatory cytokines or intermediaries (i.e. TNF-alpha, IL-1beta, IL-6, and nitrous oxide) to be released which act as pain mediators that alert pain medium (Sauro &Becker, 2009). These studies not only establish that stress does influence migraine experience, but it also supports the focus on medical students, or in our study pre-med students, as an appropriate population to introduce and measure the effectiveness of stress reduction methods on migraine intensity/frequency.

Stress Reduction Methods

Since stress not only triggers migraines but also affects their duration and treatment effectiveness, it is important to learn how to minimize stress, using one of the several different methods that have been developed and researched (Sauro & Becker, 2009). One of the ways suggested to increase your resistance to stress is to exercise on a regular schedule. Exercise serves as a dual purpose activity: it not only makes us physically healthier but it can also help make us mentally healthy which decreases our susceptibility to stress. Deep breathing is another method of reducing stress as it helps relax the neuro-muscular system. This is accomplished by affecting the reticular activating system (RAS) that is responsible for modulating neuromuscular function. Another stress reducing method is progressive muscle relaxation (PMR). PMR is a variation of deep breathing that involves relaxing different muscle groups one at a time. This method has been found to help release emotional strain associated with stress. This program is usually prescribed for 15-20 minute sessions twice a day. Meditation also decreases stress as it allows individuals to better focus on the task at hand.

Yoga is another method in which individuals learn how to relieve tension in the body, which can also aid in enabling individuals to focus better on individual tasks. Cognitive-behavioral therapy (CBT) has also been used as a method for reducing stress experienced. The basis of CBT is to make an individual aware of the stressor and how bad the stressor is given the scenario. This method can also involve individuals recognizing that they attribute their feelings to others and outside events, but that they actually hold control over their own feelings. Ultimately many of the method of stress reduction involve having a healthy lifestyle that includes an adequate diet and well-round involvement of activities (Treven S., 2010). It appears that many of these methods involve utilizing pent up stress in a more productive manner and learning how to relax and focus. This method of stress reduction seems useful as it enables individuals to channel their stress energy towards something they can control, which is more effective than accumulating lots of stress. Another method of stress reduction is Mindfulness-Based Stress Reduction (MBSR). This method emphasizes acknowledging and accepting reality. It was found that this method was effective in work places as it increased life satisfaction, and lowered job burnout/distress (Sharma & Rush, 2014). Another study found a 65% decrease in total mood disturbance and 35% decrease in stress symptoms in individuals undergoing MBSR treatment (What Do We Really Know About Mindfulness-Based Stress Reduction, n.d.). In this study, the MBSR was measured with 17 interventions over a five year period and was found to be successful at decreasing stress levels (Sharma & Rush, 2014). It seems like MBSR is a treatment that goes a little further than CBT in establishing a healthy way of dealing with stress. All these methods seem to have potential for reducing stress, but they all need practice as one trains their mind to deal with stress more effectively. These are just a few of the many methods of

reducing stress, but the methods that will be explored in our optional follow-up interview will be cognitive behavioral therapy (CBT), Stress inoculation therapy (SIT), and mindfulness, and thus will be expanded on a bit further here.

CBT has been shown to be a very successful treatment among college students for managing stress. CBT focuses on the idea that individuals are not the victims of their stress and that if they worked to change their irrational beliefs their stress would greatly reduce stress. Beck, a CBT founder, believed that many individuals have involuntary illogical thoughts that their individual problems often stemmed from these thoughts. Beck believed that therapy should not be spent dwelling on the past to determine why these thoughts occurred, but instead it should be spent on training the individual to alter their thoughts (Beck, 1976). The mental issues that arise from these irrational thoughts can be a multitude of things including stress. Given the fact that CBT attempts to identify and change illogical thoughts, it seems like a plausible method of reducing stress.

Another pivotal player in the development of CBT is Albert Ellis who incorporated another component into CBT: rational emotive behavior therapy (REBT). Ellis believed that patients contributed to their development of psychological issues by the way they reacted to occurrences. He said that the best way to combat these thoughts is to identify them, change them, and move forward. Ellis approached therapy in an A-B-C process, A is the activating event, B is the client's belief, and C is the client's reaction to the event (Dryden & Still, 1998). Corey, another CBT analyst, theorized that A did not stimulate C, but instead B, the belief, is what resolved C (Corey, 2012). At the heart of CBT, is that it is these thoughts that causes problems not the random occurrences. Therapy of CBT and REBT are believed to strongly

overlapping and in both cases the therapist's role is to aid the patient in altering their beliefs. Stress can be one of these mental health problems that can be decreased with the use of CBT.

Having defined the process of CBT it is of interest to look at data demonstrating its effectiveness of treating stress. Considerable research investigating CBT has implied that it does reduce stress skillfully, with many of these analyzing CBT's ability to reduce stress, depression, and anxiety since these are often experienced together. A randomized control study was conducted on Jordanian students to determine the success of CBT in decreasing depression and stress levels. The authors found that individuals that participated in CBT had lower levels of stress and depression when compared to individuals in the control group (Hamdan-Mansour, Puskar, & Bandak, 2009). In summary, CBT is relatively effective in treating general stress because it attempts to deal with the real issue associated with stress, such as irrational thoughts.

Stress Inoculation Training (SIT) has also been shown to be an effective way to manage stress. SIT can be defined in three parts. The first part is considered to be the concept-based learning. This part emphasizes the psychological theory 'Schacter Two Factor Theory' that states that it is not enough to just have an emotion, you must also identify the source of it in order to completely have the feeling. In stressing this theory, SIT states that it is important develop both coping skills to decrease anxiety and also to change the thoughts igniting the anxiety. The patient is also advised that these anxiety provoking thoughts are not singular, that instead they are the result the patient's own actions and thoughts. Furthermore these thoughts are an accumulation of many thoughts and actions, and not the result of what happened in one event. The second part of SIT involves developing these needed skills and

practicing applying them. These skills demonstrate the importance of identifying and clarifying the anxiety. Then the patient is taught to think of ways to alleviate the anxiety. In addition, the patient is taught how to take these anxious thoughts and change them to less self-destructive thoughts. In doing so, SIT also focuses on the benefits of goal-driven self-guidance, problem solving, behavioral attempts to cope, and finally treating yourself for using your management skills. The third prong to SIT involves not learning new things, but polishing learned skills, practicing using these skills in real life. This period of time is filled with scenarios in and outside of therapy where the patient is pushed to use their coping skills. This is done with hopes that the skills are reinforced and improved for future anxiety/stressful situations (Meichenbaum & Deffenbacher, 1988).

Now that we understand the process and ideas behind the use of SIT, it is important to evaluate its success specifically with stress management. A study of first year law-students, a group commonly put under high amounts of stress, assessed the success of SIT. It was found that the students that were given the SIT treatments had the most improvement with their stress levels. Furthermore it was found that over half the students that were exposed to SIT were successful in improving their class rank (Sheehy, R., & Horan, J.J., 2004). Although the sample size of people exposed to SIT was very small (7), this study does seem to give promise to the possibility of SIT being useful for stress reduction. Like most of these studies on evaluating effectiveness of psychological treatment it is difficult eliminate other factors that could explain decreased stress, but even without that ability this study displays the possible benefit of SIT. A pilot study was conducted looking at nurses in school and the effectiveness of implementing stress inoculation therapy in order to reduce stress. This study found that SIT could be an

efficient program to better enable student nurses to deal with stress. An after completing stress inoculation therapy, the nurses had increased their use of positive coping skills and decreased negative coping skills (Foley & Stone, 1988). Another study analyzed the usefulness of SIT in treating individuals with severe anxiety found that this method does help reduce anxiety. The group treated with SIT had the lowest levels of state and trait anxiety in post testing (Holcomb, 1986). All these studies, although they are with small sample sizes, seems to suggest that SIT has positive aspects when it comes to reducing stress. It appears that it not only has promise of helping individuals with daily stresses of school, life, and work, but also people with severe anxiety disorders. This also suggests that SIT is an efficient way to manage stress because it requires the patient to acknowledge and attempt to change the counterproductive thoughts. As a result of this being the focus of SIT, we plan on asking individuals with migraines and stress in the voluntary follow-up interview if they have used this method. We hope to not only measure if it is a common method utilized, but also to see in our population of stressed physiology students if stress inoculation therapy is successful. These research findings suggest that our study should show that SIT was successful at reducing stress, which will give us another method of stress reduction to suggest to reduce migraine frequency/intensity.

The third stress reduction method to be discussed here is Mindfulness-Based Stress Reduction or Mindfulness. Mindfulness is the process by which one focuses on living in the moment and taking in the present without judgement. The importance of mindfulness is that you are not only aware of the present but are also open to experiencing it. In mindfulness the patient is told to have deep meditation where emphasis on all aspects of the presence are

stressed (Kabat-Zinn, 2003). There are many techniques to helping individuals be mindful these include: purposeful breathing, meditation, yoga, and becoming better at realizing life as it develops. Dr. Kabat-Zinn is the founder of MBSR he created it originally as an 8-week course that would aid an individual with mental health or chronic pain that had not been successful with other treatments. This course involved all the techniques listed above in order to emphasize the importance of relaxation and mindfulness. Furthermore, patients were also given homework to keep a gratitude journal or positive thoughts journal in order to help the person stay mindful. A study comparing individuals who underwent MBSR vs. no treatment should much better psychological results and decreased pain, suggesting that MBSR might be an effective treatment for better management of stress (Noonan, 2014). Mindfulness seems to attempt to not alter thoughts like SIT and CBT attempt to do, but instead focus on altering perception and consciousness of our thoughts, feelings, and body as a whole. Mindfulness is an alternative approach that focuses less on the thoughts and more on the moment and experiencing that moment to the fullest.

Given the significant differences between mindfulness and CBT and SIT in their approach their approach, it raises the question of how effective is it at reducing stress, and is it a better treatment? And does it work with healthcare professionals or those in training, such as our study population? A randomized control study of MBSR was done with medical and premedical students and showed a large decrease in depression and anxiety levels in students that underwent the eight week MBSR course (Shapiro, Schwartz, &Bonner, 1998). Another study was done to assess the effectiveness of MBSR in pre-med and medical students actively participating in clinical work. The participants of this study included 38 health care workers

ranging in age from 18-65, who were randomly assigned to MBSR group (i.e., the traditional 8 week MBSR course) or control group. Several tests were used to assess anxiety, depression, and burnout rates in the participant's pre and post experiment. Although eight of the eighteen individuals in the MBSR group were not able to complete the experiment the results still showed significant differences ($p=.04$ and .004, respectively) between the scores on perceived stress and self-compassion scales. With the MBSR group scoring much lower stress perception and higher compassion levels. Reports on the other tests showed a decrease in MBSR group, but these differences when compared to control group were not found to be significant. An interesting insight in this study was that the individuals that dropped out the study said that it was more due to a lack of time than anything else. The authors suggest that if MBSR could be taught without adding additional time to someone's already hectic schedule that perhaps it would be more used and helpful to health care professionals (Shapiro, Astin, Bishop, & Cordova, 2005). Taken together, these studies show promise for MBSR as an effective way to reduce stress in pre-med undergraduates. Furthermore, these findings suggest that not only would it help reduce stress, but that it would increase compassion which is a benefit to anyone pursuing a career in healthcare.

In order to determine whether CBT or MBSR was more effective at reducing stress, a study was done where individuals were assigned to CBT OR MBSR groups, and their pre/post scores were compared for several measures of depression, perceived stress, well-being, etc. The most significant positive changes were seen in the MBSR group compared to the CBT, including MBSR increases in mindfulness, well-being, and energy and decreases in perceived stress, depression, neuroticism, binge eating, and pain. Conversely CBT only showed noticeable

differences in three of the eight measures: increase in well-being and decreases in perceived stress and depression. These results were significant, but it should be noted that since the participants were not randomly assigned to treatment that some of the findings could be confounded. Although given the large changes observed, it is not likely that this was the sole reason for the difference (Smith et al., 2008). This seems to suggest that perhaps MBSR is more effective at reducing stress, although both treatments show success. Comparing the difference in the procedures of each treatment it seems that perhaps it is more effective to focus on increasing mindfulness rather than altering thoughts. It would be interesting to comparing long lasting effects of each treatment. I wonder if in a short amount of time CBT is not as effective because it takes more time to change thoughts, but with more time, it could be as effective as or more effective than MBSR. Furthermore it would interesting in these studies to see the personal view of the participant if they were exposed to both what they felt was more effective. Although our study will not be able to accomplish this, I think our study will attempt to get that personal take on at least one the stress reduction methods. It is likely our participants will only have experience with one, but it will still be good to get a personal view that is separate from the physical measures that have already demonstrated the effectiveness of both treatments.

Methods

Migraine's ties to stress and artificial sweeteners has been identified, but it is of concern that perhaps it is stress that is initiating the migraine and the consumption of diet caffeinated drinks are misattributed to causing the migraine. In order to better understand the interaction between stress, diet caffeinated drinks, and migraines, a study assessing the migraine

experience of pre-medical students will be conducted. It is hypothesized that this study will show that stress more greatly influences the migraine experience than diet caffeinated drinks because these drinks are consumed by stressed individuals in order to keep up with the demands of their coursework. This study was conducted by having pre-med students at the University of Arizona early on and towards the end of their undergraduate careers fill out a survey. This is an online anonymous survey that was distributed through the online course management system using survey Qualtrics software to four physiology classes: PSIO 485, PSIO 404, PSIO 380, and PSIO 201. Recruitment in these courses was done by either delivering in person or online a recruitment speech (Appendix 1). There are 770 students total enrolled in these 4 classes. This survey investigated the students' personal view of their own experience of migraines and triggers and the effects these triggers have on their migraine experience. This survey will investigate the student's personal view of their own experience of migraines and triggers and the effect these triggers have on their migraine experience. See Appendix 2 for Survey Questions. Furthermore it was planned that a follow-up interview for 10-12 people to further investigate detail about these specific triggers, use of stress reduction methods, and effectiveness of these methods on migraine frequency/intensity. . See Appendix 3 for interview questions, however due to lack of response no interviews were held. The data from the online anonymous survey was collected on Qualtrics, where it was collated, synthesized and analyzed.

Results

Of the 770 students enrolled in these physiology classes, 88 of them filled out the survey. Although this sample size is somewhat small, these responses will provide detailed

insight into the relationships between these variables in pre-med students enrolled in these classes at the University of Arizona.

Drink Preference

The first result to be discussed addresses what these students most often consumed. This question allowed us to assess if these students consume caffeinated drinks, artificially sweetened diet drinks, or both in excess. Fig 1 below displays these results.

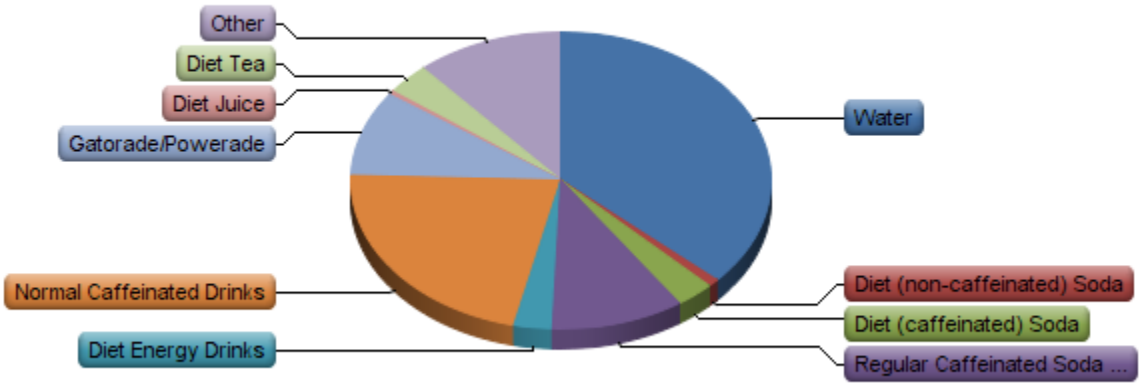


Figure 1. Drinks Normally Consumed: *This data includes responses to the question: During a normal week, what do you normally drink (check all that apply)?*

This graph displays that this population most frequently consumes water with 99% (87 out of 88) of the sample noting they consume water. Second to water the most frequently consumed drinks were normal caffeinated drinks with 86% (76 out of 88) choosing caffeinated drinks. This establishes that this population might be susceptible to over consumption of caffeinated drinks, but not of diet drinks. Totaling all sources of diet drinks together that individuals reported

normally consuming yielded only 28% (25 out of 88). In this study "diet" was defined as 'artificially sweetened'. At this point in time, the predominant artificial sweetener used in drinks is Aspartame. Therefore, these findings suggest that there is a less likelihood that artificial sweeteners are trigger for migraines in this population.

Drinks Consumed Most Often

Of the drinks that they consume normally, we wanted to determine which one was consumed the most. Fig 2 shows these results.

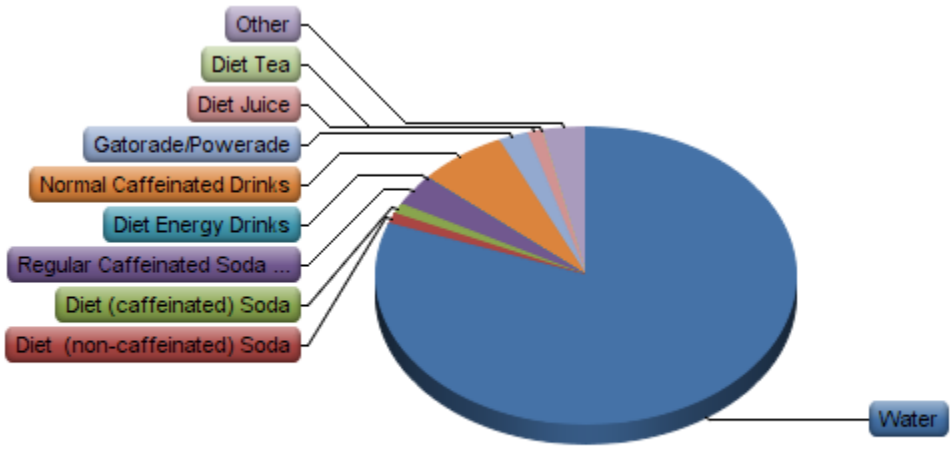


Figure 2. Drinks Frequently Consumed: *The data includes responses to the question "Of these drinks, which do you consume most?"*

It appears that water is drunk most often in this population as evidenced by 81% (71 out of 88) choosing this drink. (See Fig 2) This seems to suggest that most people do not actually consumed diet or caffeinated drinks regularly. Normal caffeinated drinks in total were reported to be drunk most often by 10% (9 out of 88) of the sample. Thus despite individuals reportedly

drinking caffeinated drinks during a normal week, it does not appear that caffeinated drinks are what they drink most. Diet drinks were chosen to be consumed most frequently by only 3% (3 out of 88). This finding reaffirms that this population does not seem to be at risk of overconsumption of artificial sweeteners.

Frequency of Consumption of Drinks Ingested Most Often

To evaluate which drinks might be consumed in excess we questioned respondents about the number of drinks they consume most. The results can be seen in Fig 3.

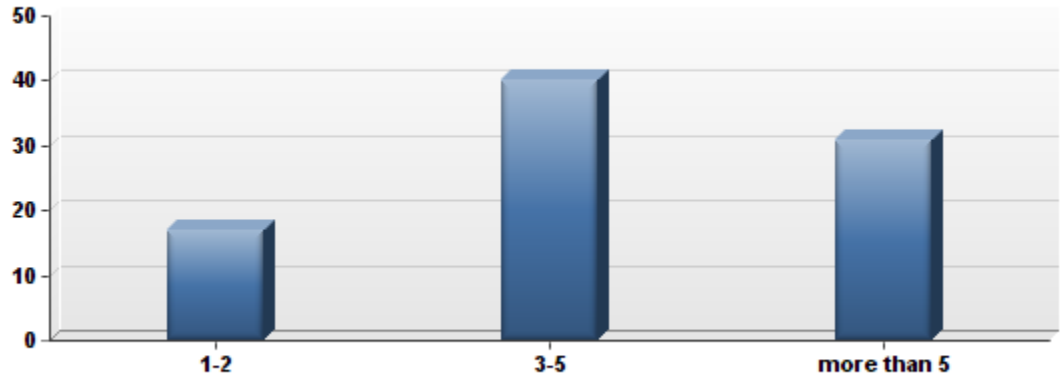


Figure 3. Daily Consumption of Most Regularly Consumed Drinks: *The data above includes response to this question: Of the one you drink most, about how many do you consume per day?*

The most common response was 3-5 drinks per day with 45% (40 out of 88) the sample selecting this choice. Only 35% of the sample (31 out of 88) reported drinking more than 5 drinks per day. This data was arbitrarily assigned to three categories: Low consumption (1-2 drinks/day), moderate consumption (3-5 drinks/day), and high consumption (more than 5

drinks/day). Thus it seems that the majority of this population has a moderate or high consumption rate of their most commonly consumed. Comparing this with Figure 2, water is the drink most likely to be consumed in excess. With such low percentages of people choosing caffeinated or diet drinks, it is hard to determine if some people in this population consume these drinks in excess or close to it (refer to Figure 2).

Incidence of Migraines

The next important component of this survey was to determine the number of students in this population who have migraines. It was found that about 36% (32 of 88 students) of the students reported having migraines. This finding does seem to suggest that this population has a higher susceptibility to developing migraines. In fact, this percentage is a little over double the reported global migraine susceptibility (14.7%). Despite this relatively small sample it certainly suggests a trend in this particular pre-medical school population.

Common Migraine Triggers

For the 28 of the 32 students who reported having migraines, the next important step was identifying the triggers. The results are displayed in Fig 4:

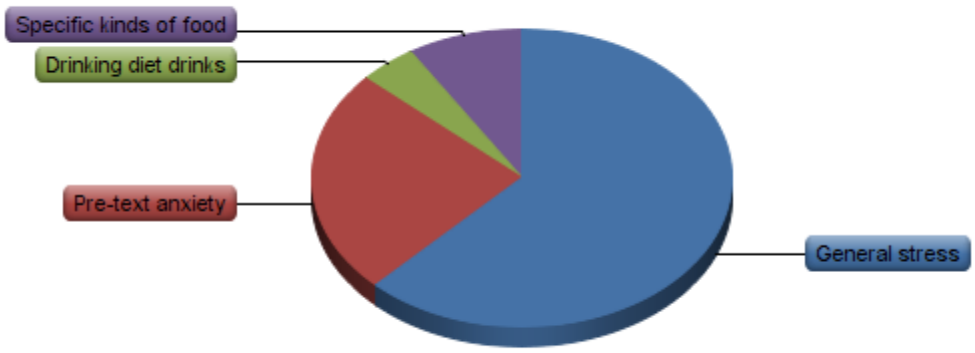


Figure 4. Most Common Triggers for Migraines. *This date includes responses to the question: Which of the following typically causes your migraines (select all that apply)?*

As is apparent in this figure, the most common trigger of migraines was general stress: 100% of theses migraine sufferers chose general stress as one of their migraine triggers. Furthermore it established that very few (only 2 out of 28) of these migraine sufferers claimed diet drinks as being a potential trigger of migraines. This seems to be congruent with previous research that found that stress is the most common precipitating factor (Peroutka, 2014).

Artificial Sweeteners as a Trigger

In order to further investigate artificial sweeteners as a major migraine trigger for this population, those who acknowledged having migraines were asked about consumption of artificial sweeteners and migraine experience. When questioned about whether artificial sweeteners caused or intensified their migraines, most of these migraine sufferers seemed uncertain. In fact 62% (16 out of 26) of these individuals responded that they were unsure if

diet drinks intensified their migraines. These findings seem to suggest that for this population, it is unclear if there is an association between migraines and artificial sweeteners.

Stress as a Trigger

To begin our research on this, we questioned the migraine sufferers about whether they considered themselves to be stressed individuals. The results to this question are shown in Fig 5.

Figure 5. Migraine Sufferers Perception of Being a Stressed Individuals: *These are the responses to this question: Do you consider yourself a stressed individual?*

As is illustrated, many of these students, 89% (25 out of 28), considered themselves to be stressed, which coincides with the fact that so many of them reported stress as a trigger. These findings seem to suggest that, at least for pre-med migraine sufferers, stress certainly seems to be an issue. The level of stress was rated on a scale from 1-10, with 1 meaning little stress and 10 being excessively stressed. These results are given in Fig 6.

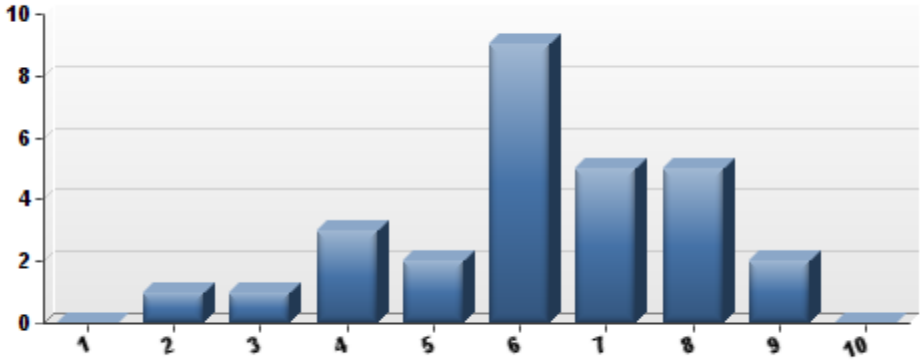


Figure 6. Perception of Daily Stress Level: *The data comprises the responses the question: On a scale 1-10, how would you rank your daily stress? 1 meaning little stress to 10 indicating excessive stress.*

As is obvious by the graph a level six of daily stress (32 %, or 9 out of 28) was the most common response. We arbitrarily divided the data into three categories: not very stressed (stress level (SL) of 1-2), mildly stressed (SL of 3-4), very stressed (SL of 6-10). Only 5 of the 28 responses ranked their daily stress less than 5. This seems to suggest that not only are these students stressed, but their actually heavily stressed. The sources of stress in these pre-med migraine students were of interest to us. Thus, we asked migraine sufferers which of the following were their sources of stress. Their responses are shown in Fig 7.

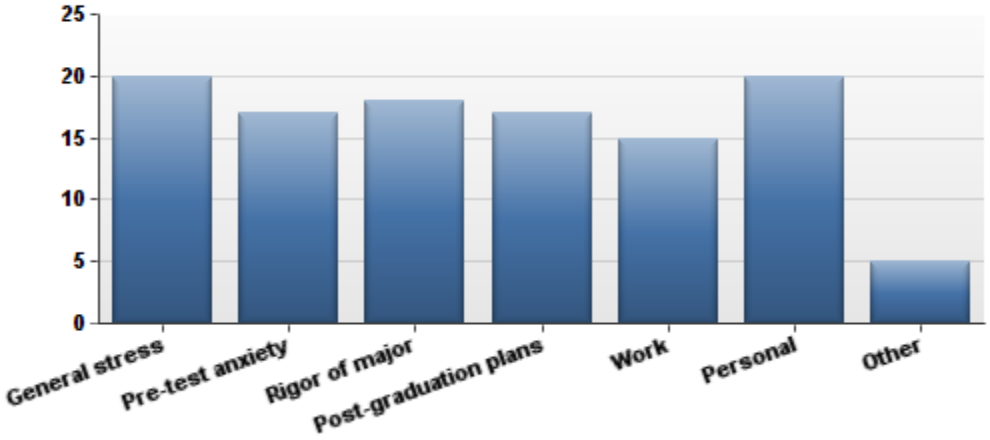


Figure 7. Sources of Stress: *Responses of students to this question: What are your sources of stress (select all that apply)?*

The most common sources of stress were general stress (71% or 20 out 28) and rigor of major (64% or 17 out of 28). Since general stress is a broader category it is difficult to identify specific details on what causes the stress. On the other hand, rigor of major (64% or 18 out of 28) and post-graduation plans with 61% (17 out of 28) reporting it as a source of stress are much more specific about what is causing the stress. This is an important finding in that it further affirms that perhaps pre-med students are more prone to stress than others.

Conclusion

Our hypothesis was that stress, caffeine, and artificially sweetened drink consumption relate influence migraine experience. The survey indicated that caffeine and artificial sweeteners did not appear to considerably influence migraine experience in this population. Artificial sweeteners not being clearly identified as a trigger of migraines is congruent with previous research on Aspartame. Despite the lack of definitive evidence that aspartame causes

migraines, it is still thought by many consumers that it is harmful to the body. These individuals' opinions are actually initiating many companies like Pepsi to move from using aspartame to sucralose (Choi, 2015). These sorts of action most likely further the concerns of consumers about aspartame's potential drawbacks, but this survey seemed to suggest that consumers' beliefs mimic the research: in other words they are unsure if aspartame does intensify/cause migraines. Similarly the findings that caffeine's relation to migraine development is uncertain coincides with previous research. It displays that the enigma surrounding whether caffeine is a cause or cure makes it difficult to definitively say it triggers migraines. Conversely the survey did suggest that stress is a chief trigger of migraines in these pre-med students. Stress not only seemed to be present in migraines sufferers, but it also seemed to be relatively high on a day to day basis.

Determining the triggers of migraines is important because if an individual knows what is causing their migraines they can try to modify or eliminate that trigger. Eliminating the trigger is obviously much easier to do in the cases of caffeine or artificial sweeteners, than it is for stress. Thus this is where the importance of learning and using stress reduction methods comes into play. Although we are unable to eliminate the stress in our lives, it is better to modify/reduce stress experience in hopes of decreasing the frequency/intensity of migraines. Stress reduction methods could also be beneficial to health and personality as was established with previous research. The three stress reduction methods we focused on all had positive influences on stress experience. The survey results for the sources of stress indicate that one of the major sources is post-graduation plans. Mindfulness which emphasizes living in the moment would appear to be very helpful in dealing with post-graduation plans stress. It would

appear that this type of stress probably is exacerbated by focusing too much on the future, so perhaps mindfulness's emphasis on being in present would help decrease this stress.

Stress was established to be an issue for this subset population, migraine sufferers, but it would be interesting in future studies to establish if these stress characteristics are true for pre-med students as a whole. It would seem that if the two of the major sources of stress for migraine sufferers were related to pre-med studies/goals that this stress level might also be true for non-migraine sufferers. If this were to be established as true for pre-med students as a whole it may be beneficial for programs of pre-med students to make stress reduction methods more known and available. Especially since as pre-med students the stress is unlikely to reduce anytime in the future, it may be beneficial to put more of an emphasis stress reduction methods.

As mentioned previously the prevalence rate for migraines in this sample was 36% which is much higher than the global prevalence of 14.7%. This is alarming in that it may pose that migraines are much more prevalent in pre-med students than in the regular population. This would make sense if stress is top precipitating factor of migraines and stress is high in pre-med students. Although it is important to note that with a small sample of 88 students it is difficult to say that these findings can be generalized to all pre-med students. Thus future studies with much larger populations should explore if the trend is still higher than the global prevalence in order to assess pre-med students susceptibility compared to others. If migraine prevalence is higher in pre-med students it would be advantageous to health professions if more was done to inform people about the nature and effects of migraines. I say this because previous research shows us that the amount of people that seek treatment for migraines is

relatively low, so perhaps one way to increase the number of people seeking treatment is to increase awareness. Studies have shown that migraine prevalence is higher amongst medical students (Al-Hashel, Ahmed, Alroughani &Goadsby, 2014). Since pre-med students may go on to medical school their susceptibility will only rise, thus awareness early may benefit their present and future health. Furthermore this awareness would emphasize the detrimental effects migraines have on ability to function efficiently in a job, which would not only stress the importance of treatment for migraines in employers but also in migraine sufferers. Treatments such as those focused on in this paper can involve identifying your migraine activators and doing something to either eliminate or manage their intake in the body.

Although the survey did provide some insight into migraine experience in pre-med students, there were some limitations to what can be ascertained from these results. For instance although research shows that there is a difference between migraine experience and different sexes, this cannot be confirmed or denied in our study because we did not ask specifically about gender. However, we know that population of physiology students at University of Arizona includes more females than males, so more females likely filled out the survey/had migraines than males. There was no question regarding the class designation of the respondents, thus it is difficult to know how stress changes as you proceed further along in major. In future studies it would interesting to ask this question in order to see how stress and migraine experiences change throughout the years of college. Given the fact that the second most common sources of stress were rigor of major and post-graduation plans, one can hypothesize that we might have seen stress increase as one got further along in schooling. We anticipate this to be the case because we also know that the major becomes harder and post-

graduation plans become more relevant with time. Moreover the survey had 88 respondents, but only 84 of them finished the whole survey, which accounts for the slight difference into total responses depending on the question. Despite a progress bar included and all the questions being on one webpage interface there were still some that did not finish filling out the survey. In future, maybe the survey should force each question to be answered before you can submit the final copy. These are just some problems with the survey that limit the generalizability of these findings.

Furthermore another potential limitation of this study is the fact that it was a small sample due to difficulty recruiting students in these classes (only 88 subjects). Data was quite convincing that diet and caffeine drinks are not the trigger of migraines in this population; however, because the sample was small it is hard to generalize to the average pre-med student. Therefore because the sample was small it is hard to generalize these findings to all pre-med students. Future studies that gain more participants will have a better assessment of migraine's relationship with these variables.

Reflection

My honors thesis experience has taught me a lot about my topic, my major, and myself. I feel walking away from this thesis that I am much more knowledgeable about migraines and the mechanisms by which they are triggered. This is very beneficial to me because I feel like I now better understand the root of migraine pain. Through my thesis I was able to understand that many different things can cause migraines, which is what contributes to the difficulty of treating them. I felt that in my thesis I was able to take all the different aspects of body

function I learned throughout the years and apply it to understand my real life health issues. I liked that the thesis allowed me to choose a topic of my own interest it made putting together all the parts much more fun. Furthermore, I liked the flexibility of the thesis in that I could also add parts like stress reduction methods because it allowed me to include my minor, psychology, in my thesis as well. I felt that incorporating my minor into my thesis allowed me to see how the psychology and physiology of the body work together. I have a newfound appreciation for just how psychological stress can negatively impact not only the mind but also the body. I really felt that this poster presentation allowed me to research my interests and kind of let those interests finally come together.

Furthermore my thesis taught me a lot about the steps involved in research. I do not think I quite appreciated IRB approval till I saw just how much paperwork is involved in getting approval. The survey component of my thesis was also a learning moment for me because it taught me how hard it is to get individuals to fill out your survey. I realized that in order to be successful you have to be persistent in pleading to fill out the survey. Furthermore by realizing that I did not include questions about demographic in my survey, I realized the value in trying to review surveys over and over to make sure that you have all interests covered.

Finally I thoroughly enjoyed doing the poster session as a component of my thesis. Although originally I was nervous about having to present in front of a group of people, it turned to be quite fun and I think pretty successful. It was great to share my knowledge with others because it made me feel like all my work on the thesis was worth it. It was worth it in that moment I felt like I had really learned a lot from my research. Moreover, the poster session was great because I got to hear someone else's perspective on my research which I felt

made me more objective in my analysis. In conclusion, my honors thesis was a great addition to my education and I am really glad I was able to do it.

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Appendix 1

Got Headaches or Migraines?

Reviewed and Approved by University of Arizona IRB and found acceptable for human subject research.

Whether yes or no-
would love to have your help:

- **WHAT:**
  - Senior PSIO honors project
  - Studying relationship between migraine, diet drinks, & stress.
- **HOW:**
  - An anonymous online survey
  - Click Here to Access Survey: https://uarizona.co1.qualtrics.com/SE/?SID=SV_8weXGisKaLBHF8p
  - Optional follow-up interview for 10-12 people
- **WHEN:**
  - Please complete by April 10
- **Author:** Claire Birch Yeoman. Contact at tbirchyeoman@email.arizona.edu. **THANKS!**

Appendix 2

Anonymous Online Survey

1. During an average week, what do you normally drink? (Check all that apply). **(Note: For this and all following questions diet refers to artificially sweetened drinks.)**

    - ☐ Water
    - ☐ Diet (non-caffeinated) Soda
    - ☐ Diet (caffeinated) Soda
    - ☐ Regular Caffeinated Soda (ie. Non-diet)
    - ☐ Diet Energy Drinks
    - ☐ Gatorade/Powerade
    - ☐ Diet Juice
    - ☐ Diet Tea
    - ☐ Other

2. Of those drinks, which do you consume most?

- ☐ Water
- ☐ Diet (non-caffeinated) Soda
- ☐ Regular Caffeinated Drinks (ie. Non-diet)
- ☐ Diet Energy Drinks
- ☐ Normal Caffeinated Drinks
- ☐ Gatorade/Powerade
- ☐ Diet Juice
- ☐ Diet Tea

- Other

3. Of the one you drink most, about how many do you consume per day?
   - 1-2
   - 3-5
   - more than 5
4. Do you suffer from migraine headaches?
   - Yes
   - No

If yes, continue the survey. **If no, discontinue filling out survey. Thanks for your participation!**

5. Which of the following typically triggers your migraines? (select all that apply)
   - General stress
   - Pre-test anxiety
   - Drinking diet drinks
   - Specifics kinds of food
   - I am not aware of any specific triggers
6. What is the approximate number of headaches you experience per week?
   - 1
   - 2
   - 3
   - 4
   - More than 4

7. When do you generally consume diet drink products relative to the onset of a migraine?
   - Before
   - After
   - Unsure

8. If you consume them, do the diet drinks intensify the migraine?

   - Yes
   - No
   - Unsure

9. If yes, how would you rate the migraine pain after compared to before consuming diet drink? 1 being very little pain and 10 being extremely painful.

   - 1
   - 2
   - 3
   - 4
   - 5
   - 6
   - 7
   - 8
   - 9
   - 10

10. Do you consider yourself a stressed individual?

    - Yes
    - No

11. On a scale 1-10, how would you rank your daily stress?
    1 meaning little stress to 10 indicating excessive stress.

    - 1
    - 2
    - 3
    - 4

- ☐ 5
- ☐ 6
- ☐ 7
- ☐ 8
- ☐ 9
- ☐ 10

12. What are sources of your stress? (select all that apply)
    - ☐ General stress
    - ☐ Pre-test anxiety
    - ☐ Rigor of Major
    - ☐ Post-graduation plans
    - ☐ Work
    - ☐ Personal
    - ☐ Other

Thank you for your participation! If you are interested in participating in a follow up interview, please send an email to tbirchyeoman@email.arizona.edu

Appendix 3

Questions for Voluntary Follow-up Interview

All the following questions refer to non-alcoholic drinks and 'diet' refers to artificially sweetened drinks

- Do you drink diet or regular drinks?
- Specifically, what kind of diet drinks do you consume most?
- Do you notice a difference in drink consumption during stressful times? If yes, what difference(s) do you see?
- Does the intensity and frequency of your migraines increase during stressful periods of time?
- Do you know of any specific triggers for your migraines?
- What are your post-graduation plans?
- Do you think your post-graduation plans are a source of your stress?
- Do you find that methods to reduce stress decrease the intensity of migraines? Do these methods reduce the frequency of your migraines?
- If you have had success with stress reducing methods, which methods have been successful?
- Do you have medical/behavioral therapy for migraines? If so, what have you used?