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THE EFFECTS OF MIGRAINE HEADACHE AND PHYSICAL ACTIVITY ON COGNITIVE FUNCTION

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THE EFFECTS OF MIGRAINE HEADACHE AND PHYSICAL ACTIVITY ON COGNITIVE FUNCTION

By

Marguerite Theresa Moore

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THE EFFECTS OF MIGRAINE HEADACHE AND PHYSICAL ACTIVITY ON COGNITIVE FUNCTION MEASURED BY IMPACT

ABSTRACT

By

Marguerite Theresa Moore

Migraine headaches are a common and often debilitating neurological disorder affecting between 18-25% of the female population and 6-13% of the male population. There has been no universal agreement on the long or short-term effects of chronic migraine headaches on neurocognitive function or on the cognitive recovery patterns following a migraine. Research has also been inconclusive on the effects physical activity may have on the intensity and frequency of migraine attacks. The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur a migraine.

One hundred twenty-two (122) individuals completed baseline testing with 44 migraineurs incurring a migraine and completing all testing. They were matched to 44 non-migraine controls for sex, education level and age. A pre-test / post-test design was used with the following independent variables: migraine status, physical activity, testing occasion sex, exercise, sleep, and diagnosis status. The dependent variables were the four composite scores of ImPACT (verbal memory composite score, visual memory composite score, reaction time composite score, and motor processing speed), level of pain, and impact of headache scores. Descriptive statistics and several analyses using MANOVAs, ANOVAs and t-tests which were performed with the alpha level set a priori at .05.

Repeated measures one-way ANOVA revealed declines in neurocognitive function of migraineurs in verbal memory (ρ=.045), visual memory (ρ=.041), and reaction time (ρ< .001) at 24 hours. When compared to non-migraine controls MANOVA tests revealed a main effect for group x time for visual memory (ρ=.036), motor processing speed (ρ=.044) and reaction time (ρ=.002) composite scores. Post hoc Univariate ANOVAs revealed that migraineurs experienced the largest declines between baseline and 24 hours with verbal memory (ρ=.005), visual memory (ρ=.001) motor processing speed (ρ=.003) and reaction time (ρ=.002) worse than controls. Reaction time (ρ=.028) and motor processing speed (ρ=.022) remained impaired at 48 hours, and motor processing speed (ρ=.009) was significantly impaired at 7 days. Physical activity levels did not significantly affect neurocognitive function in migraine or non-migraine groups (ρ-values range 0.232-0.933). Females reported higher pain levels than males (ρ=.028). Sleep, exercise, and type of medication did not significantly affect neurocognitive function scores in migraineurs. Physical activity levels significantly decreased the HIT (Headache Impact Test) overall scores (ρ=.020) with results approaching significance in both migraineurs (ρ=.080) and non-migraineurs (ρ=.094).

Conclusively, migraineurs neurocognitive function is affected in the postdromal phase of migraine, with cognitive decline reversible within a few days of onset. Physical activity had no impact on neurocognitive function scores; however, collegiate students who performed physical activity rated their HIT scores lower than those not physically active. Further research is warranted to determine the degree of cognitive deficits the general population may incur after a migraine, and ways to minimize postdromal effects.

ACKNOWLEDGEMENTS

First and foremost, I need to thank my family. My husband, who has seen me through the frustration, gave me unending encouragement and support and pushed me to complete each step to the best of my abilities. I want to thank my kids, who have given up much of their mommy summer time and have gone with me on many "study trips" both downstate and around the area to collect data. And, of course my mom who has spent hours taking care of my kids, often on short notice when someone had a migraine or some other "emergency" came up. My family, both extended and immediate has supported my educational process through its entirety and I sincerely appreciate all of the comments of support from aunts and uncles, cousins, brothers and sisters and my parents. Thank you for listening to me on countless occasions reason my way through and supporting my decisions.

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A thank you needs to be offered to my friends both at MSU and in Marquette. Thank you for your support and guidance through these last few years. Thank you for not allowing me to give up! A thank you also to my students, I have learned through you how to be a better person, better educator and advisor. I need to say a big thank you to my volunteers, both migraineurs and controls. Without your dedication to research, the completion of this paper would not have been possible.

So many people have helped me and supported me through these last six years, through the move, both kids, and to a new full time position. Thank you all for everything you have done for me and my family. I never could have completed this with out the support of my community of family and friends. I am so lucky to have such a wonderful foundation of support.

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CHAPTER 1

Introduction

Overview of the Problem

Migraine headaches are a common and often debilitating neurological disorder affecting between 18-25% of the female population and 6-13% of the male population (Lipton, Scher, Kolodner, Liberman, Steiner, & Stewart, 2002; Lipton, Diamond, Reed, Diamond, & Stewart, 2001; Launer, Terwindt, & Ferrari, 1999; Lipton, Stewart, Celentano, & Reed, 1992). There has been no universal agreement on the long or short-term effects of chronic migraine headaches on neurocognitive function or on the cognitive recovery patterns following a migraine. Individuals suffering from migraine headaches report lower visual processing speed (Wray, Mijovic-Prele, & Kosslyn, 1995), verbal ability (Waldie, Hausmann, Milne, & Poulton, 2002), and decreased reaction time (Zeitlin & Oddy, 1984). Researchers suggest migraine headaches may produce structural and functional brain dysfunctions (Elkind & Scher, 2005; Swartz & Kern, 2004; Kruit, et al., 2004). Specifically, MRI studies on migraine subjects suggest asymptomatic subcortical (Swartz & Kern, 2004) and deep white matter changes (Swartz & Kern, 2004; Kruit, et al., 2004), and abnormalities in the cerebellar region of the posterior circulation (Swartz & Kern, 2004). Research has also been inconclusive on the effects physical activity may have on the intensity and frequency of migraine attacks. Physical activity either exacerbates or diminishes a migraine headache (Folkins & Sime, 1981; Rooke, 1968; Lambert & Burnet, 1985). To date, no research (to my knowledge) has examined the effect(s) physical activity and migraines have on neurocognitive function.

Migraine headaches affect individuals differently and are associated with a variety of symptoms. Classifications have been developed to differentiate "migraine without aura," often called the common migraine, and, "migraine with aura," often called classic or classical migraine. Aura commonly manifests as visual disturbance, verbal difficulties, and sensory disturbances. Migraine headaches may occur only on one side of the head, with pulsating or throbbing pain. The quantity/quality of pain either stops or limits the individual performance of daily activities (Society I. H., 2005). In addition, patients suffer from nausea or vomiting, photophobia or phonophobia. Aura classically manifests as visual disturbances, sensory disturbances, or as difficulty with speech (Society I. H., 2005).

College students are subject to many of the common triggers for migraine headaches in their daily lives. Students studying for tests often skip meals, study through the night, under sleep or oversleep, or suffer from post-crisis letdown when they cram prior to exams. Many female college students use oral contraceptives. Oral contraceptives worsen migraine headaches in some patients, but are also used to moderate migraines in others (Granella, Sances, Pucci, Nappi, Ghiotto, & Nappi, 2000). The general onset age for migraines is during and following the pubertal years, often putting college students early in the disorders course. Migraineurs with a shorter onset history are often unaware of what triggers their migraines and consequently suffer needlessly. Most triggers are inconsistent and are associated with migraine on one occasion but not on another (Robbins, 1993). This makes it more difficult for many patients to begin a preventative program because they cannot determine their personal migraine triggers.

Migraine headaches have a prodromal phase and a postdromal phase. The phase of the migraine occurring prior to the main migraine attack is referred to as the prodromal phase. This warning phase can be operative eight to 48 hours prior to an attack. It often manifests as common signs of discomfort, such as dizziness or cervical neck pain, and can go unnoticed by the migraineurs (Waelkens, 1985). Triggers associated with migraine headache include stress, anxiety, fatigue, post-crisis letdown (the stress relief following a crisis), depression, irregular sleep patterns (under or oversleeping), menstruation, ovulation, physical and intellectual effort, environmental factors (exposure to heat or cold), weather changes, missing meals and oral contraceptives (Turner, Molgaard, Gardner, Rothrock, & Stang, 1995). Edibles such as cheese, chocolate, and alcohol are also known triggers for migraines (Robbins, 1993; Wacogne, Lacoste, Guillibert, Hugues, & Le Jeunne, 2003; Puri, et al., 2006). A large percentage of migraineurs are unable to identify their triggers, making it idiopathic in nature.

Postdrome phase refers to the phase of the migraine after the main migraine attack. The average postdrome phase lasts 25.2 hours. The quality and breadth of postdromal symptoms suggest involvement of the whole brain, specifically the frontal lobe and hypothalamus areas (Blau, 1991). Postdrome symptoms may be used to diagnose migraine in the absence of aura. Blau (1991) reported on the most common symptoms in a group of 40 migraineurs who completed a questionnaire on the day following their most recent attack. These symptoms were physical and mental tiredness, impaired concentration, subdued or depressed mood, and reduced physical activities. Many migraineurs experience low-grade headaches or a feeling of "hangover" during this phase (Kelman, 2005b). The postdrome phase has a significant effect on a college student

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with migraines. While the severe headache may be gone, lesser, but still debilitating, symptoms continue and are not commonly recognized by teachers, parents and even the student. Anecdotal evidence suggests students feel they do not perform to their potential and report lower grades on tests, quizzes and other modes of testing following a migraine attack. Difficulties arise in determining duration of time from completion of the attack due to the postdromal phase. Therefore, most studies determine time from initiation or start of the migraine. Overall, the postdromal phase has a significant impact on the individual's level of daily activities the day following a migraine headache.

Scientific evidence confirms health benefits are seen with moderate-intensity physical activity (U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition and Physical Activity, 1999). The U.S. Department of Health and Human Services defines how physical activity recommendations are met as moderate-intensity for at least 150 min per week, or vigorous-intensity for at least 75 min per week, together with muscle strengthening activities on two or more days of the week. Moderate physical activity is defined as some increase in breathing or heart rate, while vigorous physical activity is defined as a large increase in breathing or heart rate where conversation is difficult or broken (U.S. Department of Health and Human Services, 2008). Previous research has examined physical activity relating to cardiovascular fitness.

There is contemporaneous but conflicting research on the relationship between physical activity and migraine. Stress, or post-crisis letdown, is a known trigger for migraine, while mild to moderate physical activity is known to diminish stress (Turner,

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Molgaard, Gardner, Rothrock, & Stang, 1995). Logically, exercise is frequently promoted as a method of migraine management (Folkins & Sime, 1981). Some individuals use vigorous exercise successfully to abort a migraine headache at the first signs of onset (Darling, 1991). Conversely, exertional exercise without proper warm-up can be a trigger for migraine headaches (Lambert & Burnet, 1985; Rooke, 1968).

The relationship between migraine and exercise has been explored by researchers. Data indicate pain intensity and frequency of migraines decrease after a regular exercise program was initiated (Lockett & Campbell, 1991; Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003). The results of these studies strongly suggest an ongoing exercise program is essential for decreased migraine frequency. However, previous researchers stopped short of examining neurocognitive function of migraineurs meeting physical activity recommendations and those not meeting physical activity recommendations in a collegiate population.

Several studies examined cognitive function and migraine headaches; however, research is inconclusive whether migraine headaches lead to cognitive dysfunction over time (Jelicic, van Boxtel, Houx, & Jolles, 2000; Magnusson & Becker, 2003; Gaist, et al., 2005; Launer, Terwindt, & Ferrari, 1999; Waldie, Hausmann, Milne, & Poulton, 2002). Direct comparison can be difficult due to the methodological problems of selection bias (convenience sample or hospital sample) and small sample size (Hooker & Raskin, 1986; Leijdekkers, Goudswaard, Menges, & Oriebeke, 1990; Le Pira, Zappalà, Giuffrida, Lo Bartola, Morana, & Lanaia, 2000; Le Pira, et al., 2004; Haverkamp, Hönscheid, & Müller-Sinik, 2002; Zeitlin & Oddy, 1984). Consequently, it is difficult to determine the long-term effects of migraine headache on cognitive function.

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A number of studies found migraine is not associated with cognitive decline (Lipton et al, 2002; Hu, Markson, Lipton, Stewart, & Berger, 1999; Schreiber, Hutchinson, Webster, Ames, Richardson, & Powers, 2004; Bell, Primeau, Sweet, & Loftland, 1999). A Danish twin study concluded that lifetime diagnosis of migraine health was not associated with cognitive deficits, which is an epidemiological gold standard (Gaist, et al., 2005). Similarly, Haverkamp and colleagues found children with migraines and their unaffected sibling also reported no cognitive dysfunctions differences (Haverkamp, Hönscheid, & Müller-Sinik, 2002). However, subjects are often recruited from a local migraine group, which may contribute to reporting bias. Prior research has focused on long-term cognitive function following a migraine; however, very few studies have examined short-term cognitive function and the recovery pattern following a migraine headache in a collegiate population.

Research has found a reversible cognitive decline in the recovery pattern following migraine headache (Meyer, Thornby, Crawford, & Rauch, 2000). A reversible cognitive decline is defined as a cognitive decline during the headache interval which completely subsides during a measured period after the individual is headache free. Meyer and colleagues (2000) found a reversible cognitive decline 30 hours after recovery from headache and nocturnal sleep. This is after the postdrome phase is complete in most individuals. Cognitive decline can also be reversed by migraine medication. Specifically, two prescription drug studies utilizing sumatriptan (injection and nasal spray) determined cognitive dysfunction was reversible 15 minutes after medication administration (Farmer, Cady, Bleiberg, & Reeves, 2000; Farmer, et al., 2001). A limitation to these studies was not monitoring the subjects beyond 45 minutes. In both studies, cognitive function

(simple reaction time, sustained attention/ concentration, working memory, visual-spatial processing) and alertness/fatigue were adversely affected during a migraine headache. However, results of these studies may be skewed by the lack of a comparison to a control group as well as small sample size.

Migraine studies have reported long-term or permanent cognitive decline in information processing, reaction time, verbal ability and visual processing (Hooker & Raskin, 1986; Zeitlin & Oddy, 1984; Waldie, Hausmann, Milne, & Poulton, 2002; Wray, Mijovic-Prele, & Kosslyn, 1995). Hooker and Raskin tested 29 migraineurs who exhibited poorer free recall of semantic material and diminished ability to discriminate forms and analyze spatial relationships in the tactile modality. Five subjects reported not feeling as "bright" since migraines started. Zeitlin and Oddy's 19 migraineurs, recruited through a migraine clinic, showed consistently poorer performance on a series of memory and information-processing tests. While many studies found long-term neurocognitive deficits in migraineurs, the two primary limitations of these studies are the lack of a control group and the use of diagnosed migraine patients only. Furthermore, no previous research specified college-aged patients or examined short-term recovery patterns from migraine headaches compared to a control group. Conclusively, it is relevant and significant to determine whether neurocognitive effects of a migraine resolve in a short period of time in a college population.

Significance of the Problem

Migraine headaches are an episodic and progressive disorder affecting a significant portion of the population, more than asthma and diabetes combined (Lipton et al, 2002; Lipton et al, 2001; Launer, Terwindt, & Ferrari, 1999; Lipton, Stewart,

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Celentano, & Reed, 1992). During a migraine attack, progression is seen in aura development (if present) and intensity of pain, with prodromal and postdromal symptoms typically leaving migraineurs performing at a decreased capacity for up to one week surrounding a migraine attack. With frequent attacks, migraine is a direct cost to the individual and the economy as a whole. From a collective perspective, direct and indirect costs relating to migraine headaches are estimated at 13 billion dollars, impacting society in many venues, including work productivity, absenteeism and social functioning (Lipton et al, 2001). Ninety one percent (91%) of individuals who suffered from migraine headaches reported functional impairment, with 53% of respondents indicating their headaches cause severe impairment or require bed rest. Another 51% reported a reduction in their school or work productivity of at least 50% during a migraine episode (Lipton et al, 2001). With the average migraineur experiencing one migraine per month, and 25% debilitated by at least two episodes per month, how does this affect college students with migraine headaches (Launer, Terwindt, & Ferrari, 1999)? It is widely held that lost time due to migraine headaches is the result of short-term effects. However, few studies have examined the relationship between migraine headache and short-term cognitive function.

College students are expected to be ready on a daily basis for pop quizzes, tests or practical skills tests. Students may study for months for a licensure, board or certification test where the outcome determines their future standing and status in their profession or job. From ages 18-28 the prevalence of migraine increases yearly, and the life of the college student is full of migraine triggers, making it important to determine if migraines affect cognitive function following an attack.

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Researchers have produced inconsistent results on long-term cognitive function following a migraine headache and the effect(s) of physical activity on migraines. From individuals who suffer exertional migraines to those that ward off migraines through physical activity, no research study has captured the effects of physical activity under an observational approach. Furthermore, no prior research examined the effects of migraine and physical activity on cognitive function within 24-hour, 48-hour, and one-week intervals after a migraine and compared the data to a control group. Finally, prior research did not contrast neurocognitive function following a migraine headache with an individual's baseline neurocognitive test scores.

Statement of the Problem

The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur migraines.

Need for Study

The postdromal phase of migraine has yielded inadequate results for the public in general and suffering migraineurs specifically. This phase of the migraine affects migraineurs significantly post migraine and may last for days. Little and limited research has explored the neurocognitive deficits following a migraine, and no prior research determined whether physical activity has any effect on migraine and neurocognitive function. The hypotheses and research questions of this study are listed below.

Hypotheses and Research Questions

Primary Hypotheses.

The primary focus of this study is neurocognitive function as it relates to migraine headaches and individuals who meet or do not meet physical activity recommendations. The independent variables were:

A. migraine status — migraine (M), non-migraine (NM)

B. physical activity — met physical activity recommendations PA; did not meet physical activity recommendations (NPA)

C. testing occasion — baseline (B), 24 hours (24h), 48 hours (48h), and one week (7d)

The dependent variables were neurological function defined as the four composite scores of ImPACT. The four composite scores of ImPACT are verbal memory composite score, visual memory composite score, reaction time composite score, and processing speed composite score. The ImPACT composite scores were collectively referred to as neurocognitive function. All subjects in this study were college students between the ages of 18 and 28. Specific hypotheses include:

Effects of Testing Occasion on Neurocognitive Function

H1a. Baseline neurocognitive function scores will be higher than 24 hours post-migraine scores for migrainous college students.

H1b. Neurocognitive function scores at 24 hours will be lower than 48 hours post-migraine scores for migrainous college students.

H1c. Neurocognitive function scores at 48 hours will be lower than 7 days post-migraine scores for migrainous college students.

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H1d. Neurocognitive function scores at baseline will exhibit no difference than 7 days post-migraine scores for migrainous college students.

H1e. Neurocognitive function scores at baseline will exhibit no difference than 24 hours, 48 hours or 7 days post-baseline scores for non-migrainous college students.

Effects of Migraine Status on Neurocognitive Function

H2a. The migraineurs and non-migraineurs will exhibit no difference in neurocognitive function at baseline.

H2b. The migraineurs will exhibit lower neurocognitive function scores than the non-migraineurs at 24 hours post-migraine.

H2c. The migraineurs will exhibit lower neurocognitive function scores than non-migraineurs at 48 hours post-migraine.

H2d. The migraineurs will exhibit lower neurocognitive function scores than the non-migraineurs at 7 days post-migraine.

Effects of Physical Activity by Testing Occasion on Neurocognitive Function

H3a. Physically active migraineurs will exhibit no difference in neurocognitive function scores than non-physically active migraineurs at baseline.

H3b. Physically active migraineurs will exhibit higher neurocognitive function scores than non-physically active migraineurs at 24 hours.

H3c. Physically active migraineurs will exhibit higher neurocognitive function scores than non-physically active migraineurs at 48 hours.

H3d. Physically active migraineurs will exhibit no difference on neurocognitive function scores than non-physically active migraineurs at 7 days.

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H3e. Physically active non-migraineurs will exhibit no difference in neurocognitive function scores than non-physically active non-migraineurs at any testing interval.

Exploratory Hypotheses

The purpose of the exploratory hypotheses was to examine the relationships between additional variables collected throughout the study. The independent variables were:

A. migraine status	migraine (M) and non-migraine (NM])
B. sex	female and male
C. diagnosis status	physician diagnosed (PD) and self-diagnosed (SD)
D. testing occasion	24 hours only
E. physical activity	met physical activity recommendations (PA)
	did not meet physical activity recommendations (NPA).

The dependant variables are level of pain and impact of headache scores. The Headache Impact Test (HIT) score was referred to as impact of headache scores.

H4. Female migraineurs will rate their pain higher than male migraineurs at 24 hours post-migraine.

H5. Physician diagnosed migraineurs will rate their pain higher than self-diagnosed migraineurs at 24 hours post-migraine.

H6a. Physically active individuals will score lower than non-physically active individuals on their impact of headache score.

H6b. Physically active migraineurs will score lower than non-physically active migraineurs on their impact of headache scores.

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H6c. Physically active non-migraineurs will score lower than non-physically active non-migraineurs on their impact of headache scores.

Exploratory Research Questions

The purpose of the exploratory research questions was to examine the relationship between additional variables previously not researched in the literature. The independent variables were migraine status (migraine only), exercise (yes and no), and sleep (none, a little to 4 hours, 4-8 hours, more than 8 hours). The dependant variables were pain, and the four composite scores of ImPACT. The four composite scores of ImPACT are verbal memory composite score, visual memory composite score, reaction time composite score, and processing speed composite score, which were referred to as neurocognitive function.

RQ 7. Is there a difference in pain reported at 24 hours post-migraine for college students who use prescription medications, over-the-counter medications, or no medications for their migraine headaches?

RQ 8. Is there a difference in pain reported at 24 hours post-migraine for college students who did or did not exercise during the 24 hours immediately following onset of a migraine headache?

RQ 9. Is there a difference in neurocognitive function at 24 hours post-migraine for college students who did or did not sleep during hours immediately following onset of a migraine headache?

Assumptions, Limitations and Delimitations

Assumptions of the Study.

The assumptions of this study included: the subjects answered all questions honestly, were aware of a physician diagnosis of migraine, that they physician diagnosis was correct, and that tried their hardest on all occasions when taking the ImPACT test. Another assumption of the study was that the subjects were honest about the onset of their migraines and contacted the investigator in a timely manner following migraine onset.

Limitations of the Study.

A limitation of this study was related to the participant population. The population of the Upper Peninsula of Michigan is not ethnically diverse, making the sample primarily Caucasian. Generalizing the results to the broader population was difficult, although results may be generalized to a similar population of college-aged individuals 18 to 28 years of age. Sex representation was not equal due to the prevalence of migraines in females, occurring at a rate three times that of males.

Delimitations of the Study.

One of the delimitations of the study was that the 24 hour questionnaire asked about the past 24 hours of their migraine headache, which may not capture prodromal symptoms. Another delimitation of the study was that the research focused on ImPACT's ability to detect neurocognitive function following a migraine, but the subjects were not administered any other tests to establish neurocognitive function. A final delimitation was that subjects offered subjective information throughout the study, which was not verified with a physician.

Operational Definitions

Exercise. Bodily exertion for the sake of developing and maintaining physical fitness (www.nlm.nih.gov/medlineplus/mplusdictionary.html). For the purpose of this study, exertion is measured in minutes over a one-week period and determined whether it is moderate-intensity or vigorous-intensity physical activity.

Impact of headaches. The impact an individual experiences related to their headaches in their daily lives. This may include sleep quality, level of pain, length of post-dromal features, and frequency of migraine.

Migraine. A migraine is a headache satisfying the following criteria. The migraine may or may not occur with aura. The headache has at least two of the following characteristics: 1) unilateral location, 2) pulsating quality, 3) moderate or severe pain intensity, or 4) aggravation by or causing avoidance of routine physical activity. During the headache, at least one of the following is present: 1) nausea and/or vomiting, or 2) photophobia and/or phonophobia.

Neurocognitive function. For the purpose of this study, the ImPACT composite scores were collectively referred to as neurocognitive function. The four composite scores of ImPACT are verbal memory composite score, visual memory composite score, reaction time composite score, and processing speed composite score.

Onset of a migraine. The onset of the migraine is the time (hour) the individual starts to develop either headache symptoms or any aura they recognize as the start of a migraine headache.

Over-the-counter medications. Any medication utilized by an individual and is recognized by the American Medical Association as a medication to treat migraine headaches which is available without a physician prescription.

Pain. A state of physical, emotional, or mental lack of well-being or physical, emotional, or mental uneasiness ranging from mild discomfort or dull distress to acute, often unbearable agony. It may be generalized or localized, and is the consequence of being injured or hurt physically or mentally or of some derangement of or lack of equilibrium in the physical or mental functions (as through disease). It usually produces a reaction of wanting to avoid, escape, or destroy the causative factor and its effects (National Institute of Health Dictionary through Med-Line).

Physical Activity. Moderate-intensity physical activity or vigorous-intensity physical activity, self reported and measured over a one-week span in minutes.

Physician diagnosis. An individual who has obtained a migraine diagnosis by a physician. Individuals self-report their physician diagnosis.

Prescription medication. Any medication prescribed to the individual specifically intended to treat migraine headache acute symptoms or any medications utilized to prevent migraines.

Self-diagnosis. Any individual who meets IHS criteria for migraine with aura, migraine without aura, or menstrual migraine, and has not been diagnosed formally by a physician.

Testing occasion. A testing occasion is the time frame an individual completes any surveys and one of the four ImPACT tests (baseline, 24h, 48h, and 7d) post-migraine.

Sleep. The natural periodic suspension of consciousness during which the powers

of the body are restored (National Institute of Health Dictionary through Med-Line).

Definitions

Aura. Occurs prior to a migraine headache. Auras may be in the form of visual disturbances, unilateral paresthesias (pins and needles feeling) and/or numbness, unilateral weakness, or aphasia or unclassifiable speech difficulty. Visual disturbances may be in the form of loss of vision, seeing stars, zigzag lines or sparkles (Society I. H., 2005).

Adila and Sanchez (1988) described aura symptoms as consisting of any of the following listed in Table 1:

Table 1: Aura Symptoms

Aura Symptom	Explanation of symptom
Anomia	Forgetting the name of things
Difficulty speaking	Difficulty forming words/ knowing the right word
Depersonalization	Feeling as if another person
Seeing the world as strange	Seeing the world as strange
Macropsia	Increase of apparent object size
Micropsia	Decrease of apparent object size
Simultaneous agnosia	Only the full or partial object is recognized
Automatic behavior	Disassociating from a task, performing tasks automatically
Inability to understand language	Difficulty comprehending the words and their meanings
Olfactory hallucinations	A hallucinations involving the sense of smell
Achromatopsia	Disappearance of colors
Chromatopsia	Modification of object colors

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Table 1 Continued	
Palinopsia	Visual perseveration- reports seeing figures or images repeatedly
Pelopsia	The object seems to become larger and approach the patient
Gustatory hallucinations	A hallucination involving the sense of taste
Alexia	Inability to read
Acalculia	Calculation disturbance
Telopsia	Objects seem small and far away
Transient global amnesia	A passing episode of short-term memory loss without other signs or symptoms of neurological involvement
Hemisomatognosia	Unilateral misperception of one's own body

Cognition. A term referring to the mental processes involved in gaining knowledge and comprehension, including thinking, knowing, remembering, judging, and problem solving. Cognition involves higher-level functions of the brain and encompasses language, imagination, perception, and planning.

ImPACT. Immediate post-concussion assessment and cognitive testing (ImPACT) is a computer-based program used to assess neurocognitive function and migraine symptoms.

Incidence. The number of new cases of a specific disease occurring during a specified period of time, divided by the population at risk for developing the disease. These do not include already diagnosed cases.

Migraine without aura. An individual who has experienced at least 5 headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) with at least two of the following characteristics:

(1) Headache is only on one side of the head

(2) Pulses or throbs

(3) It is of moderate to severe intensity (stops you or limits you in performing daily activities) or

(4) The pain is aggravated by walking stairs or similar routine activities.

In addition, at least one of the following accompanies the headache attack:

(1) Nausea or vomiting or

(2) Photophobia or phonophobia (Society I. H., 2005).

Migraine with aura. An individual who has had at least two attacks with at least three of the following four characteristics:

(1) One or more fully reversible aura symptoms

(2) At least one aura symptom develops gradually over 4 minutes, or two or more symptoms occur in succession

(3) No single aura symptom lasting more than 60 minutes, or

(4) Headache interval follows aura within 60 minutes (Society I. H., 2005).

Motor processing speed. It is a measurement of the speed that an individual completes a specified task in units of time.

Phonophobia. The fear of sound. Individuals with phonophobia during migraine may desire to be in a quiet room, and state that sounds increase the intensity of their migraine.

Photophobia. The fear of light. Individuals with photophobia during migraine may desire to be in a dark room, and state that light increases the intensity of their migraine.

Physically active. Moderate-intensity physical activity for at least 150 minutes per week or vigorous-intensity physical activity for at least 75 minutes per week. For the purpose of this study, individuals meeting this definition of physically active (PA) are in the PA group, and individuals not meeting this definition of physically activity are in a not physically active (NPA) group.

Prevalence. The number of affected persons present in the population at a specific time divided by the number of persons in the population at that time.

Reaction Time. The measurement of the time it takes to recognize and respond to a designated response.

Tinnitus. Ringing in the ears.

Verbal Memory. A measurement of reaction time to the recognition of words previously viewed by the individual.

Visual Memory. A measurement of reaction time to the recognition of symbols previously viewed by the individual.

CHAPTER 2

Literature Review

The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur migraines. In order to gain insights from previous research conducted on migraine headaches, this review of literature is divided into eight major sections: (a) Migraine symptoms and management, (b) pathology of migraine; (c) differential diagnosis for migraine headache; (d) epidemiology of migraine; (e) neurocognitive function of migraine patients; (f) physical activity and migraine; (g) instrument validity; and (h) summary of the literature.

Migraine Symptoms and Management

Migraine headaches are documented throughout history. Hippocrates described the visual aura and the relief of the headache by vomiting (Unger, 2005) in 500 AD. Important historical figures like Charles Darwin, Thomas Jefferson, and Robert E. Lee among many others, consistently reported the recurrent disability from headaches. Jefferson reportedly did not meet with Congress for one month following a terrible bout with a chronic migraine (Unger, 2005).

Historical remedies have varied from binding an orange half or applying black plaster to the temple (and allowing either the orange half or the plaster to drop off in time), to sleep and solitude (Loder, 2002). Traditional practices culminated with the more modern technique of sumatriptan, a nasal spray that can be administrated within minutes

of a migraine attack (Farmer, et al. 2001). Despite historical documentation and the accumulated knowledge of migraine through centuries, migraines are still somewhat a mystery because of their varying presentation of signs and symptoms.

Migraine headaches affect each individual differently and are associated with a myriad of symptoms. Different classifications have been identified to differentiate "migraine without aura," often called the common migraine, and "migraine with aura," often called a classic or classical migraine. In 1988 the Headache Classification Committee of the International Headache Society (IHS) issued the first "Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain." These diagnostic criteria allowed physicians to diagnosis each patient based on a consistent criteria with consistent language. (Society H. C., 1988) An update was issued in 2004 (Society H. C.-C., 2004) and the first revision was published the following year (Society I. H., 2005) (See table 5 and 6). This section discusses migraine without aura, migraine with aura, associated syndromes to migraine headache, the migraine postdrome and predrome phases, prevention and treatment, and the pathology of migrainous attacks.

Migraine without Aura.

Migraine without aura is often referred to as common migraine or hemicrania simplex. The diagnostic criteria includes at least five attacks lasting 4-72 hours when untreated or unsuccessfully treated, and at least two of the following four characteristics: (a) unilateral location; (b) pulsating quality (throbbing or varying with the heartbeat); (c) moderate or severe intensity; or (d) aggravation by or causing avoidance of routine physical activity (i.e. walking or climbing stairs). During the headache the patient must have at least one of the following: (e) nausea and/or vomiting; and/or (f) photophobia

and/or phonophobia. Migraine without aura must not be attributed to any other disorder such as: head trauma, vascular disorders, non-vascular intracranial disorders, substance abuse or withdrawal, non-cephalic infection, metabolic disorders or disorder of the facial or cranial structures (Society I. H., 2005). Individuals meeting the criteria, but who have had fewer than five attacks may be coded probable migraine without aura. Observing the more stringent guidelines, these individual were not included in this study. New guidelines for two new entities, pure menstrual migraine and menstrual-related migraine, were released in the 2005 edition of the IHS criteria. They were included in the migraine without aura group for the purpose of this study.

Migraine with Aura.

Migraine with aura is also referred to as ophthalmic, hemiparesthetic, hemiplegic, aphasic, classic or classical migraine, complicated migraine and migraine accompagnée. It is described as idiopathic, with reoccurring symptoms localized to the cerebral cortex or brain stem gradually developing over 5- 20 minutes and lasting less than 60 minutes. This is typically followed by headache, nausea and/or photophobia within an hour of aura symptoms. The headache usually lasts 4-72 hours. To diagnose a migraine with aura the patient must exhibit at least two attacks with at least one of the following three criteria, not including motor weakness: (a) fully reversible visual symptoms including positive features (e.g. flickering lights, spots or lines) and/or negative features (i.e. loss of vision); (b) fully reversible visual sensory symptoms including positive features (i.e. pins and needles) and/or negative features (i.e. numbness); or (c) fully reversible dysphasic speech disturbance. The migraineurs must also experience at least two of the following to meet diagnostic criteria for typical aura with migraine headache: (a) homonymous visual

symptoms, and/or unilateral sensory symptoms; (b) at least one aura symptom develops gradually over ≥ five minutes and/or different aura symptoms occur in succession over ≥ five minutes; and (c) each symptom lasts ≥ five minutes and ≤ 60 minutes. Migraine with aura must also not be attributed to any other disorder (Society I. H., 2005).

For the purpose of this study, all individuals meeting migraine with or without aura criteria, including all of the following: typical aura with migraine headache, typical aura with non-migraine headache (aura, but headache does not meet migraine criteria), familial hemiplegic migraine (migraine must occur in first or second degree relative and include motor weakness) or sporadic hemiplegic migraine (motor weakness, but no incidence in first or second degree relative with motor weakness), were included. In addition, basilar-type migraine (migraine with aura clearly originating from the brainstem (e.g. dysarthria [slow, slurred speech], vertigo, tinnitus [ringing in the ears], hypacusia [impairment of hearing], diplopia [double vision], ataxia, decreased level of conscious) and/or both hemispheres simultaneously affected, but no motor weakness), and retinal migraine (repeated attacks of monocular visual disturbance, including scintillations, scotomata or blindness, associated with migraine headache) were included in the migraine group.

The most common form of migraine with aura displays one or more of the following symptoms: visual disturbances, unilateral paresthesias (pins and needles feeling) and/or numbness, unilateral weakness, aphasia or unclassifiable speech difficulty. Visual disturbances are the most common symptoms reported during a migraine headache (Society I. H., 2005). Visual disturbances may be in the form of loss of vision, seeing stars, zigzag lines or sparkles. It often presents as a zigzag figure near a

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point of fixation that spreads left or right leaving a trail in its wake. During typical migraine headache aura symptoms such as sensory, motor or cognitive dysfunction usually disappears after 10-15 minutes (Ardila & Sanchez, 1988). Ardila and Sanchez (1988) described aura symptoms as any of the following : Anomia (forgetting the name of things), difficulty speaking, depersonalization (feeling as if another person), seeing the world as strange, macropsia and micropsia (increase or decrease of apparent object size), simultaneous agnosia (when only the full or partial object is recognized), automatic behavior, inability to understand language, olfactory hallucinations, achromatopsia (disappearance of colors), chromatopsia (modification of object colors), palinopsia (visual perseveration- reports seeing figures or images repeatedly), pelopsia (the object seems to become larger and approach the patient), gustatory hallucinations, alexia (inability to read), acalculia (calculation disturbance), telopsia (objects seem small and far away), transient global amnesia, or hemisomatognosia (unilateral misperception of one's own body).

Associated Syndromes for Migraine Headache

Migraine headache has been associated with fatigue, stress, and other life events in chronic migraine patients. Fatigue is a symptom of depression and migraine, and both are co-morbid with chronic fatigue syndrome. Peres, Zuerman, Young and Silberstein (2002) reported 84.1% of chronic migraine patients in their study suffered from fatigue with 66.7% meeting the CDC criteria for chronic fatigue syndrome (Peres, Zukerman, Young, & Silberstien, 2002). This fatigue may be due to a decrease in quality of sleep (Seidel, et al., 2009) leading to daytime fatigue and decreases in productivity and function. Decreases in quality of sleep as well as altering patterns of sleep may lead to a

vicious cycle of sleep deprivation causing decreases in both cognitive and psychomotor function (Scott, McNaughton, & Polman, 2006).

Life stress is another precursor to migraine headaches (Wacogne, Lacoste, Guillibert, Hugues, & Le Jeunne, 2003; Passchier, 1994). Many patients report puberty or other stressful life events such as birth of a child, getting married, college-related anxieties or a new job as precipitating migraine events (Wacogne et al., 2003). During pregnancy, most individuals report a favorable impact on their migraines (43% of migraineurs with aura and 76 % of migraineurs without aura), while few report more frequent and intense migraines (Granella, et al., 2000). Anxiety, depression and family history of migraine were also associated with migraine headaches, with most attacks beginning at the end of the night (early am) (Wacogne et al., 2003).

Migraine sufferers are characterized by more marked disabilities when coping with pain, especially passive coping (Siniatchkin, Riabus, & Hasenbring, 1999). Two research studies suggest increased headache intensity is associated with higher levels of depression and emotional distress (Magnusson & Becker, 2003; Oedegaard, et al., 2006). Other co-morbid diseases of migraine are hyper- or hypotension, Reynaud's syndrome (associated with vasoconstriction and reflexive vasodilatation of blood vessels to the extremities), mitral valve prolapse, angina and stroke, epilepsy, positional vertigo, some functional gastrointestinal disorders, asthma and allergies (Silberstein & Goadsby, 2002). It is important to determine if an individual has an associated syndrome, or recently experienced a life-changing event prior to his/her migraine attack, so physicians can determine how to help prevent and best treat their migraine attacks.

Migraine Prodromal Phase.

The warning phase of the migraine (that may occur) which is up to 48 hours prior to the main migraine attack is the prodromal phase. The most common signs of discomfort such as dizziness and cervical neck pain are often unnoticed by the migraineurs and accepted as normal (Waelkens, 1985). Migraine represents a genetic component to headache with a lowered threshold of susceptibility to a variety of headache triggers (Loder, 2002; McCrory, 2000). Triggers associated with migraine headache consist of a myriad of factors that can include psychological symptoms (i.e. stress, depression, anxiety), or physical symptoms (fatigue, intellectual effort, physical effort). Migraines may also be related to bodily processes (menstruation, ovulation, sleep patterns), or environmental changes (being overly hot or cold, weather pattern changes). Migraines can be related to ingested substances such as oral contraceptives, nitrates, cheese, chocolate or alcohol, or may be related to skipping meals (Robbins, 1993; Turner, Molgaard, Gardner, Rothrock, & Stang, 1995; Wacogne et al., 2003; Puri, et al., 2006). Triggers for migraine may cause a migraine one time, and on another occasion not trigger a migraine headache (Robbins, 1993).

Triggers for migraine are routine in a college student's activities of daily living. The daily fare for a college student includes varying sleep patterns and stress related to a job, class work, procrastination, and varying importance placed on each class and the work related to that class. A single midterm may cause the average student to stay up all night studying, feel stressed, or skip dinner in lieu of snacks such as chocolate. In the aftermath of the exam, many migraineurs will experience the postdromal phase of migraine and later that evening a migraine headache.

Other triggers in college students may be varied. Many college students use oral contraceptives, which have been found to worsen migraine headaches in many patients (Granella et al., 2000). Migraineurs with a shorter history of migraine are often unaware of what triggers their migraines and therefore suffer needlessly. While these triggers are shown to precipitate migraines in migraineurs, one study reported similar triggers in non-migraineurs prior to headache (Charbriat, Danchot, Michel, Joire, & Henry, 1998). The most common triggers for both migraineurs and non-migraineurs were fatigue, and or sleep, food, drinks, menstruation, heat/cold/weather and infections. A possible explanation for this discrepancy may be due to genetic decreases in threshold levels related to pain (Loder, 2002) resulting in a migraine headache in one individual while another individual may exhibit a common headache.

Migraine Postdromal Phase.

The postdromal phase of the migraine occurs after the main migraine. These symptoms are often used to diagnose migraine in the absence of aura. Patient's rarely spontaneously volunteer information about the postdromal phase of migraine unless specifically asked by their physician. This may occur because the focus of the migraine is on the most painful and unbearable portion, the headache phase. Common symptoms reported in a group of 40 migraineurs that completed a questionnaire on the day after their most recent attack included descriptions such as feeling listless, weary, and unable to summon up energy, everything an effort, wooly headed, not thinking clearly, and confused. The migraineurs reported the symptoms lasted anywhere from 2-27 hours (mean 18). They also complained of reduced physical activities in the postdromal phase that included descriptions of reduced activity in the following areas: walking, slower in

all actions, slow to turn head, unable to read, and impaired fine motor coordination (Blau, 1991). Another study of 827 migraineurs reported an average postdromal phase of 25.2 hours with 88% reporting postdromal periods of $\leq$24 hours (category 18-24 hours) with 68% of their subjects reporting postdromal symptoms. Many migraineurs experience low-grade headaches or a feeling of fatigue and inability to concentrate similar to a hangover from alcohol abuse that occurs in the postdromal phase (Kelman, 2005b). Because not all individuals experience a postdromal phase it is difficult to classify when the migraine ended, therefore most studies determine time since initiation or start of the migraine. The scope of postdromal symptoms suggests involvement of the entire brain, in particular, the frontal lobe and hypothalamic areas (Blau, 1991).

Migraine Treatment.

There are many different solutions in a comprehensive headache treatment plan involving prevention, education, and pharmacotherapy. Educating the patient on techniques of biofeedback, relaxation, life style regulations such as daily routines and regular sleep patterns can decrease the intensity and frequency of each migrainous event. In addition, patients can be educated on when to initiate pharmacotherapy during an attack which can also decrease the intensity and frequency of a migraine headache (Silberstein & Goadsby, 2002).

Migraine is an episodic and progressive disorder in which an individual with a mild condition can progress into having frequent attacks that may change cognitive processes in the brain (Silberstein & Goadsby, 2002). During a migraine attack, there is progression in aura development (if present) and intensity of pain. Patients desire an acute treatment that brings rapid, complete, and well-tolerated pain relief. Most

individuals will utilize acute prevention pharmacotherapy, along with acute treatment if they have attacks more than two to three days a week, have profound disability with each attack, it is a recurring migraine that significantly interferes with activities of daily living despite acute treatment, or if co-morbid disease is present (Silberstein & Goadsby, 2002). The American migraine study reported that 41% of patients used prescription drugs for their migraine headaches (Lipton et al, 2001). The major medication groups utilized to prevent migraine headaches are anti-convulsants, anti-depressants, and anti-hypertensives. Literature suggest that efficacy of some drugs are first noted at four weeks and continues to increase for three months (Silberstein & Goadsby, 2002). During the migraine, hyper excitability (i.e. photophobia, phonophobia) may respond faster than pain to treatment (Linde, Mellberg, & Dahlöf, 2006). Each treatment has a different level of effectiveness for every individual, and often includes side effects that some patients cannot or will not tolerate. Therefore, many individuals will utilize over the counter medications.

Over the counter medications for migraine are available and usually consist of aspirin, caffeine, and acetaminophen. The American migraine study reported that approximately 58% of migraineurs primarily use over the counter therapy (Lipton et al, 2001). The best time for acute therapy is within the first 60 minutes of the onset of headache. This management strategy halts the sequence of the attack into the development of central sensitizations and cutaneous allodynia, and thereby modifies the progression of the attack. This will help to decrease pain intensity (Gallagher, 2004). Strategies used to decrease or combat progressions are to avoid triggers, early

intervention, use of preventative treatment including pharmacotherapy (Gallagher, 2004), and to utilize daily headache diaries to identify triggers (Wilkinson, 1994).

Pathology of Migraine.

The pathology of migraine differs in migraineurs who suffer from aura than those that do not suffer from aura (Society I. H., 2005). Most patients with migraine exclusively suffer from attacks without aura. Many migraineurs who have attacks with aura experience attacks of migraine both with and without aura on varying occasions (Society I. H., 2005)

The older vascular theory of migraine proposed that the aura was secondary to intracranial vasoconstriction and that the headache was an inflammatory reaction around the walls of the dilated cephalic vessels (Graham & Wolff, 1938). This theory supported the pulsing nature of the pain, however there appears to be a wave of "oligemia" (reduced blood flow) which starts in the posterior aspect of the brain and spreads to both the parietal and temporal lobes along the cortical surface, not the vascular distribution pattern (Graham & Wolff, 1938). Therefore, arterial vasospasm alone cannot be responsible for the decreased blood flow (Goadsby & Olsen, 1996).

A subsequent theory is the neurogenic theory (Moskowitz, 1993). This proposed that head pain is centrally generated and involves both serotonergic and adrenergic pain modulating systems (Derman, 1994). Several lines of evidence link serotonin to migraine. These include the drop in serotonin blood levels during migraine, as well as serotonin as an effective treatment and serotonin antagonist as a prevention of migraine headaches (Derman, 1994). Following this theory, it is now widely held that migraine is a

neurovascular disorder with brain involvement with the pain occurring secondary to involvement of the trigeminovascular system (Ravishankar & Demakis, 2007).

Many systems are involved and affected during migraine. The extrapyramidal system is a complex neural network that provides a proper execution of voluntary movements by correctly processing proprioceptive, cognitive, and motor information in the brain (Barbanti & Fabbrini, 2002). There is some evidence that the extrapyramidal system is involved in migraine (Barbanti & Fabbrini, 2002). Migraineurs often recognize an exacerbation of their headaches as they bend over or exert themselves, this is referred to as "central sensitization" (Unger, 2005). The central nervous system becomes more excitable over time and less inhibited, leading to an increased perception of pain (Unger, 2005).

Researchers suggest migraine headaches may produce structural and functional brain dysfunctions (Elkind & Scher, 2005; Swartz & Kern, 2004; Kruit, et al., 2004). Specifically, MRI studies on migraines suggest asymptomatic subcortical and abnormalities in the cerebellar region of the posterior circulation (Swartz & Kern, 2004) as well as deep white matter changes (Swartz & Kern, 2004; Kruit, et al., 2004). Reversible changes in the brain were confirmed via positron emission tomography (PET) and magnetic resonance imaging (MRI) in one case study (Gentile, Rainero, Daniele, Binello, Valfré, & Pinessi, 2009). Leistad et al. (2006) reported that less pronounced and more regional trigeminocervical sensitization seems to be important in migraines. After 60 minutes of cognitive stress, subjects were tested. Results included increased muscle pain (visual analogue scale) that developed in the trapezius and neck regions. However, there were no differences between migraine and controls in electromyographic (EMG)

studies (Leistad, Sand, Westgaard, Nilsen, & Stovner, 2006). With so many systems involved, migraine is difficult to treat, and often requires many trials with different types of medications prior to reaching a therapy, due to the varying drug pathways.

Approximately 36% of individuals who suffer from migraine headaches reported aura as a symptom (Lipton et al., 2001). During migraine with aura there is decreased cerebral blood flow to the clinically affected area and often includes a wider area in the brain (Society I. H., 2005). Research also suggests a decreased blood flow during the pre-headache phase with pain occurring during the subsequent vasodilatation of the same area (Hassinger, Semenchuk, & O'Brian, 1999). Most medications intervene with migraine through one of the following methodologies: (1) vasoconstriction, (2) compounds that inhibit the cortical depression that accompanies headache, or (3) constriction of cranial vessels and arteriovenous anastomoses within the carotid vasculature (Unger, 2005).

Side of pain, handedness, and genetics play a role in migraine pathology. A study of 1,283 migraine patients studied location and triggers for migraine (Kelman, 2005a). Results reported that 67.1% migraineurs reported pain in the eyes, 58% in the temporal region, 55.9% frontal area, 39.8 occipital area, 39.7 neck areas, 17.5% diffusely and 24.1% at the vertex of the head. Hemi cranial pain was present in two-thirds of all migraines (Kelman, 2005a). Migraineurs are commonly left handed (Waldie, Hausmann, Milne, & Poulton, 2002). Migraines are also theoretically genetically linked, with many individuals indicating at least one other family member experiencing migraines (Ziegler, Hur, Bouchard, Hassanein, & Barter, 1998). Pain location, often makes the migraine difficult to diagnose, especially for the migraines that do not follow the typical presentation.

Differential Diagnosis for Migraine Headache

When a patient presents with a headache it is important to determine the type and cause of the headache. Primary and secondary are the two categories for classifying headaches (Millea & Broadie, 2002). Primary headaches include migraine, tension-type, and cluster headaches and have no apparent underlying organic disease process. Secondary headaches are a result of underlying organic disease and are a symptom of a recognized disease process. Primary headache is treated symptomatically, with the goals centralizing on relief and prevention, while secondary headaches primarily treat the underlying disease, but also treat the symptoms (Millea & Broadie, 2002). The IHS criterion separates headache diagnosis into 14 main codes or categories and further separates them into sub categories. Not all categories are discussed because they are related to secondary causes. The following section will present differential diagnosis for migraine headache, headache attributed to rhinosinusitis, tension-type headache, cluster headache, headaches related to substances or their withdrawal, and medication overuse headache.

Headache Attributed to Rhinosinusitis.

Migraineurs frequently report runny nose, congestion, and ocular symptoms, such as reddening or swelling, during migraines. These are cranial autonomic symptoms (Gupta & Bhatia, 2007). Many of these symptoms are also associated with sinusitis. As a result, some physicians have misdiagnosed a migraine headache for a sinus headache. Sinus headache related to acute sinusitis is relatively rare, and must occur in conjunction with fever, diagnostic testing such as MRI, CT imaging, or lab results (Society I. H., 2005) and include purulent discharge (Schreiber et al., 2004; Kelman, 2005a). Schreiber

et al. (2004) examined individuals diagnosed with a sinus headache and found that 88% of sinus headache patients had migraine-type headaches fulfilling IHS criteria. In addition, Kelman (2005) investigated physician diagnosed migraine headaches and reported that 67.1% of patients' pain was located in the eyes, while 55.9% report pain in the frontal region of their head. Both of these locations are also associated with "sinus" headaches (Kelman, 2005a). Therefore, an incorrect diagnosed of sinus headache may be assigned, thus decreasing the prevalence, and delaying treatment of this debilitating disease.

Cluster Headache.

During a physician exam, it is essential to diagnose all types of headaches that the individual is experiencing and list them in the order of importance to the patient (Society I. H., 2005). To fulfill the diagnostic criteria, patients must have had at least five attacks occurring from one every other day to eight per day. These headaches must not be attributable to another disorder (Beck, Sieber, & Trejo, 2005). In addition, headaches must cause severe or very severe unilateral orbital, supraorbital or temporal pain lasting 15 to 180 minutes if untreated. They must be accompanied by at least one of the following: ipsilateral conjunctival injection and lacrimation, ipsilateral nasal congestion or rhinorrhea (flowing nasal discharge), ipsilateral eyelid edema, ipsilateral forehead and facial sweating, ipsilateral miosis and or ptosis, or a sense of restlessness or agitation (Society I. H., 2005). Cluster headaches are episodic or chronic. Episodic cluster headache is two cluster periods lasting seven to 365 days that are separated by pain-free remission periods that last one month or longer (Beck, Sieber, & Trejo, 2005). Chronic attacks occur over more than one year without remission, or with remission lasting less

than one month (Beck, Sieber, & Trejo, 2005). The absence of aura, nausea or vomiting has helped to distinguish migraine from cluster headache (Van Vliet, Eekers, Haan, Ferrari, & Group, 2003), as well as the near daily attacks. The classic feature is restlessness, with one study describing behaviors such as pacing and rocking with their head in their hands in 93% of patients (Bahra, May, & Goadsby, 2002).

Tension-Type Headache.

Tension-type headache typically manifests as pain that radiates from the forehead to the occiput in a band-like fashion. This band-like pain will also move into the neck and shoulders and cause muscular tightness and pain (Millea & Broadie, 2002). Diagnostic criteria through the IHS require the patient to have at least ten headaches fulfilling the following criteria, and less than 180 per year or 15 per month (Society I. H., 2005). Headaches must last from 30 minutes to seven days and may be continuous. The headache must also have two of the following pain characteristics: (1) bilateral location; (2) pressing or tightening (non-pulsating quality); (3) mild to moderate intensity; or (4) not aggravated by routine activity such as walking or climbing stairs. Tension-type headache may not include nausea or vomiting, but may have either photophobia or phonophobia: however, if both are present, it would not meet the diagnostic criteria. Tension-type headaches often occur with pericranial tenderness on manual palpation (Society I. H., 2005). Tension-type headache is separated from typical migraine by features such as unilateral pain, aggravation from activities of daily living, throbbing pain and nausea may not be present (Millea & Broadie, 2002). Tension-type headaches are classified as chronic if they occur at least 15 days per month for more than three months (Society I. H., 2005).

Headaches Associated with Substances or their Withdrawal.

The diagnostic criteria for headaches associated with substances or their withdrawal must include the following: Headache with at least one of the following characteristics (a) bilateral, (b) frontotemporal location, (c) pulsating quality, or (d) they are aggravated by physical activity (Society I. H., 2005). The headache must be associated with the ingestion of a specified substance such as alcohol, food component, or additive known to cause headaches. The headache must develop within 1-12 hours after intake of the substance. The headache must resolve within 72 hours. Headaches associated with substance abuse or their withdrawal includes the following substances: nitrates, monosodium glutamate, alcohol (withdrawal), ergotamine and analgesics (abuse), caffeine (withdrawal) or birth control pills (Society I. H., 2005). In this study, individuals were specifically asked to differentiate between headache related to substance abuse (i.e. alcohol, caffeine) and migraine headache in the migraine questionnaire.

Medication-Overuse Headache.

Well recognized for decades, analgesic abuse related migraine is a vicious cycle of chronic pain and dependence on analgesics, followed by a rebound headache (Boes & Capobianco, 2005). Specific criteria for analgesic overuse headache includes that the headache is present on greater than 15 days of the month, with simple analgesics taken on 15 or more days per month for more than three months (Society I. H., 2005). Regular overuse of one or more acute or symptomatic drug treatment for headache, longer than three months is a requisite amid the symptoms. The headache must have worsened over the period of analgesic overuse and must resolve or revert to its previous pattern within

two months of the discontinuation of analgesics (Society I. H., 2005). Primary headaches are presented in Table 2, secondary headaches are presented in Table 3 below.

Table 2: Primary Headache Classification Criteria

Migraine without Aura
Diagnostic Criteria A. At least 5 attacks fulfilling criteria B-D B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated) C. Headache has at least two of the following characteristics 1. unilateral location 2. pulsating quality 3. moderate or severe pain intensity 4. aggravation by or causing avoidance of routine physical activity D. During headache at least one of the following 1. nausea and/or vomiting 2. photophobia and phonophobia E. Not attributed to another disorder
Typical Migraine with Aura
Diagnostic Criteria A. At least two attacks fulfilling criteria B-D B. Aura consisting of at least one of the following, but no motor weakness 1. Fully reversible visual symptoms including positive features (eg. flickering lights, spots or lines) and/or negative features (ie. loss of vision) 2. Fully reversible sensory symptoms including positive features (eg. Pins and needles) and/or negative features (numbness). 3. Fully reversible dysphasic speech disturbance C. At least two of the following 1. Homonymous visual symptoms and/or unilateral sensory symptoms 2. At least one aura symptom develops gradually over $\geq$ 5 minutes and/or different aura symptoms occur in succession over $\geq$ 5 minutes. 3. Each symptom lasts $\geq$ 5 minutes and $\leq$ 60 minutes. D. Headache fulfilling criteria for migraine without aura begins during the aura or follows aura within 60 minutes E. Not attributed to another disorder

Table 2 Continued

Cluster Headache
Diagnostic Criteria A. At least five attacks fulfilling criteria B-D B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes if untreated. C. Headache is accompanied by at least one of the following symptoms. 1. Ipsilateral conjunctival injection and/or lacrimation 2. Ipsilateral nasal congestion and/or rhinorrhea 3. Ipsilateral eyelid edema 4. Ipsilateral forehead and facial sweating 5. Ipsilateral miosis and/or ptosis 6. A sense of restlessness or agitation D. Attacks have a frequency from one every other day to 8 per day E. Not attributed to another disorder
Primary Exertional Headache
Diagnostic Criteria A. Pulsating headache fulfilling criteria B and C B. Lasting from 5 minutes to 48 hours C. Brought on and occurring only during or after physical exertion D. Not attributed to another disorder
Tension-Type Headache
Diagnostic Criteria A. At least 10 episodes occurring on <1 day per month on average (<12 days per year) and fulfilling criteria B-D* Note that more episodes per month will change it to episodic or chronic. B. Headache lasting from 30 minutes to 7 days. C. Headache has at least two of the following characteristics: 1. Bilateral location 2. Pressing/tightening (non-pulsating quality) 3. Mild or moderate intensity 4. Not aggravated by routine physical activity such as walking or climbing stairs D. Both of the following: 1. No nausea or vomiting (anorexia may occur) 2. No more than one of photophobia or phonophobia E. Not attributed to another disorder. .

Table 3: Secondary Headache Classification Criteria

Headache attributed to a substance abuse or its withdrawal
Diagnostic Criteria A. Headache with at least one of the following characteristics fulfilling C and D 1. Bilateral 2. Frontotemporal location 3. Pulsating quality 4. Aggravated by physical activity B. Ingestion of specified substance such as alcohol, food component or additive C. Headache develops within 1-12 hours after substance intake dependant on substance D. Headache resolves within 72 hours
Medication-Overuse Headache
Diagnostic Criteria A. Headache present on >15 days/month fulfilling criteria C and D B. Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache. C. Headache has developed or markedly worsened during medication overuse. D. Headache resolves or reverts to its previous pattern within 2 months after discontinuation of overused medication.
Headache attributed to Rhinosinusitis
Diagnostic Criteria A. Frontal Headache accompanied by pain in one or more regions of the face, ears, or teeth fulfilling criteria C and D. B. Clinical, nasal, endoscopic, CT and/or MRI imaging and/or laboratory evidence of acute or acute-on-chronic rhinosinusitis. C. Headache and facial pain develops simultaneous with onset or acute exacerbation of rhinosinusitis. D. Headache and/or facial pain resolve within 7 days after remission or successful treatment of acute or acute-on-chronic rhinosinusitis

Epidemiology of Migraine

In order to effectively treat and manage migraine it is important to investigate the prevalence and economic burden of the disease. Recognition of the disability by general practitioners is very important; however, it is still inconsistent due to underreporting by

patients, as well as failure of the physician to attain an accurate description and history of their headaches. The prevalence, incidence, and burden of migraine are discussed in this section.

Prevalence and Demographics of Migraine Headaches.

A study conducted by Lipton et al. (2001) reported the prevalence of migraine headache was estimated at 18% for females and 6% for males in 1989 (Lipto et al., 2001). Lipton et al. (2002) replicated the study in 1999 and found the prevalence rate of migraine headache in the United States remained stable between 1989 and 1999. Results of the 1999 study reported the prevalence of cases increased linearly from aged 12 to 40 years and then declined in both sexes after 40 years of age. Prevalence was highest in subjects between the ages of 30 to 49 years, higher in whites compared to blacks, and was inversely related to household income. Approximately 23% of households contain at least one member who suffers from migraine headaches (Lipton et al, 2002; Lipton et al., 2001). Similar prevalence rates of migraine in Caucasian (15.3%), African-American (14.3%) and other (11.6%) races (Bigal, Kolodner, Lafata, Loetta, & Lioton, 2006). Brazilians reported a one-year and age adjusted prevalence rate of 15.2, with higher incidence in women, individuals with less than 11 years of education, individuals who did not exercise and individuals with poverty level income (Queiroz, et al., 2009). Research shows one-year prevalence is an excellent method to determine current trends in migraine.

In lifetime prevalence studies, many individuals report remission of the disorder or low migraine frequency. For example, a study that examined lifetime prevalence of migraine in the Netherlands found 33% lifetime prevalence and 25% one-year prevalence

in women (Launer, Terwindt, & Ferrari, 1999). In men, the lifetime prevalence was 13.3%, and the one-year prevalence was 7.5% (Launer, Terwindt, & Ferrari, 1999). In a follow-up study done in Denmark, researchers reported that 42% of subjects had experienced remission and 38% had a low frequency of migraine headaches (1-14 headache days per year) (Lynberg, Krogh, Rasmussen, Jørgensen, & Jensen, 2005).

Very few studies have investigated college-aged individuals who suffer from migraine headaches. One research study conducted on male and female NCAA Division I basketball players revealed only 2.9% of the population had migraine headaches that met IHS guidelines (Kinart, Cuppett, & Berg, 2002). Results revealed females reported more frequent migraine headaches that last longer and throb, which are accompanied by phonophobia and photophobia. However, this study had a low response rate (13.2%) with only 25% of schools participating and only included basketball players (Kinart, Cuppett, & Berg, 2002).

Prevalence and Incidence of the Diagnosis of Migraine.

The prevalence of diagnosis of migraine headaches have increased over the past decade, however, approximately 50% of migraine sufferers still remain undiagnosed (Lipton et al, 2001; Bigal, Kolodner, Lafata, Loetta, & Lioton, 2006). The American migraine study reported 38% diagnosis in 1989 increasing to 48% in 1999 (Lipton et al, 2001). This study utilized a validated, self-administered questionnaire distributed via U.S. mail to a sample of 20,000 households in the United States. Questions included were self-diagnosed or physician-diagnosed along with frequency and intensity of their symptoms. In the physician-diagnosed group, subjects were significantly more likely to report symptoms of nausea, vomiting, blurred vision, aura, neurological signs, photophobia, and

phonophobia when compared to the self-diagnosed group. Pulsatile pain occurred with equal frequency in both groups. The physician-diagnosed percentage was higher in females than males, associated with older age individuals, and household income greater than $50,000 per year (Lipton et al, 2001). Prevalence of migraine has a trend to decrease with increasing post high school education (Bigal, Kolodner, Lafata, Loetta, & Lioton, 2006). These studies demonstrated that while physician diagnosis may represent a population that is more severely afflicted, diagnosis is not essential to many migraineurs.

Studies comparing physician diagnosed and self-diagnosed migraineurs demonstrate an inconsistency in diagnosis despite the IHS published criteria (Lipton, Stewart, Celentano, & Reed, 1992). In a study by Lipton et al. (1992) physician-diagnosed migraine headaches were reported in 41% of females and 29% of males. In the self-diagnosed group, 80% indicated some headache related disability. The researchers also reported that most, but not all of physician diagnosed migraine headaches agreed with IHS diagnosis. A study conducted in France presented 49 general practitioners (GP) with a questionnaire aimed at identifying if the patient was a migraine sufferer, and requested a diagnosis. The patient also independently completed a similar questionnaire. Results indicated that the GP's did not recognize 59.7% of the patients as having suffered a migraine headache (recognized by IHS criteria) and only 28% recognized the patients as having management of their migraine (Vuillaume De Diego & Lanteri-Minet, 2004). A recent study found an 82% agreement between clinical interview diagnosis of migraine and diagnosis of migraine from a 4 to 8 week headache diary (Phillip, Lyngber, & Jensen, 2007). These studies show an increasing trend in physician interview to be more sensitive to migraine diagnosis, and more reliance on a headache diary to assist in this process.

Medically recognized migraine diagnosis was described by Rozen et al. (1999) as an incidence rate. The investigators defined medically recognized migraine as individuals who met diagnostic criteria of the IHS guidelines. Cases were classified independent of physician recognition of the disease. Results revealed that the incidence rate of medically recognized migraine increased for all female patients, with a peak incidence rate between 20 to 29 years. Male incidence rates increased slightly overall, with a relative increase from 10 to 19 (89%) years of age (Rozen, Swanson, Stang, McDonnell, & Rocca, 1999). With females reporting more frequently occurring migraines then males, and the proportion of migraine headaches that goes undiagnosed, the burden of migraine impacts society in many areas.

Burden of Migraine.

Migraine is currently ranked by the World Health Organization as number 19 among all diseases worldwide that cause disability (Society I. H., 2005). It is also more common than many other chronic or disabling diseases in the primary care setting and equals the prevalence of asthma and diabetes combined (Unger, 2005). Based on both direct and indirect costs, the burden of migraine is vast. Indirect costs are lost functionality at work, decreased social functioning, decreased patient well being, disability, and loss of productivity at home. Results of the 1999 American migraine study revealed that 91% of individuals who suffered from migraine headaches reported functional impairment with 53% of respondents indicating that their headaches caused severe impairment or required bed rest (Lipton et al, 2001). Approximately 31% missed at least one day of work in the past three months due to their migraine; while 51% reported school or work productivity was reduced by at least 50% during a migraine

episode. The frequency of severe headache was similar for males and females; however, 62% reported one or more severe headache per month, with only 10.8% reporting headaches more than once per week. The most frequently neglected aspect of the migraineurs life was household work with 76% of respondents reporting avoiding household work at least once during the previous three months due to their migraine headache (Lipton et al, 2001). A Dutch study where 1,292 of a large cohort of over 6,000 were given questionnaires on headache found that migraineurs suffered the burden of a median of 12 migraines per year, and 25% had at least two attacks per month (Launer, Terwindt, & Ferrari, 1999).

Kelman (2006) studied the changes of migraine through cross-sectional data in a large cohort. Results suggest that there were no significant changes related to age in duration, frequency, sex, or triggers across a group ranging from 16-80 years. One exception was that migraineurs in the 50+ age group tended to suffer from a less severe migraine (pain), and are less affected by each attack (Kelman, 2006). Frequency of migraine was positively associated with higher levels of disability for emotion, cognition and pain in a primary study outcome utilizing the Health Utilities Index, which is a widely used patient reported questionnaire (Brown, Neumann, Papadopoulos, Ruoff, Diamond, & Menzin, 2008). However, most data is self-reported related to cognition, with individuals reporting feelings of decreased cognition, not specifically tested in those arenas.

With frequent attacks, migraine is directly costly to both the individual and the economy as a whole. On average female migraineurs required 5.6 days of bed rest, while males required 3.8 days of bed rest each year, resulting in a total of 112 million days each

year (Hu, Markson, Lipton, Stewart, & Berger, 1999). Estimated cost to employers hover around $13 billion per year due to missed workdays and impaired work function. Furthermore, direct medical costs were estimated at one billion per year (Hu et al., 1999). Another study that measured direct and indirect cost found individuals who suffered from migraines had statistically higher direct medical costs, higher cost of low work productivity, and higher combined total cost of direct and indirect costs compared to the migraine free group (Edmeads & Mackell, 2002). This gap increased when they compared moderate and severe migraine headaches. Severe migraineurs had significantly higher costs in all categories. On average, they found that migraine workers lost statistically more days (nine vs. six in the comparison group) from work or household activities in the previous six months than non-migraine workers (Edmeads & Mackell, 2002). Another study reported that migraineurs used on average 2.3 more physician office visits than controls, and were more likely to be seen in an emergency room, or admitted to a hospital adding up to an average $697 more in medical care costs during the year compared to those without migraine (Lafata, Moon, Leotta, Kolodner, Poisson, & Lipton, 2004). It is well recognized that lost time due to migraine headaches are a result of short-term (hours-days/ non-permanent) effects, however, no research to date has examined the relationship between cognitive function and migraine headaches.

Neurocognitive Function of Migraine Patients.

Several studies have examined cognitive function and migraine headaches; however, research is inconclusive as to whether migraine headaches lead to cognitive dysfunction over time (Jelicic, van Boxtel, Houx, & Jolles, 2000; Magnusson & Becker, 2003; Gaist, et al., 2005; Launer, Terwindt, & Ferrari, 1999; Waldie, Hausmann, Milne,

& Poulton, 2002). Furthermore, direct comparison is often difficult due to methodological problems such as selection bias (convenience sample or hospital sample) and small sample size (Hooker & Raskin, 1986; Leijdekkers, Goudswaard, Menges, & Oriebeke, 1990; Le Pira, et al., 2004; Le Pira, Zappalà, Giuffrida, Lo Bartola, Morana, & Lanaia, 2000; Haverkamp, Hönscheid, & Müller-Sinik, 2002; Zeitlin & Oddy, 1984). In addition, most studies have utilized individuals in their 30's and 40's and beyond, that presumably have a long history of migraine (Zeitlin & Oddy, 1984; Hooker & Raskin, 1986). As a result, it is difficult to determine long-term (years/permanent) effects of migraine headache on an individual's cognitive function. The following sections will concentrate on migraine headaches associated with and without cognitive impairments and reversible cognitive decline.

Migraine is not Associated with Long- Term Cognitive Decline.

A number of studies have found that migraine headaches are not associated with cognition (Bell, Primeau, Sweet, & Loftland, 1999; Lipton et al, 2002; Hu, Markson, Lipton, Stewart, & Berger, 1999; Schreiber et al., 2004; Kalaydjian, Zandi, Swartz, Eaton, & Lyketsos, 2007). Bell, Primeau and Sweet et al., (1999) compared groups of 20 individuals recruited from a specialty clinic for the treatment of chronic pain. The researchers found that migraine headaches were not associated with cognitive impairment when compared to chronic pain and mild traumatic brain injured (MTBI) patients. This study is difficult to compare with other studies due to the high number of migraines per month the patients reported. The migraine subjects reported they had migraines on average of 13.5 days per month for the last six months and five to six incapacitating migraines per month. Most studies criteria include migraine headaches at a much lower

rate, such as greater than six per year with averages of 34 to 37 migraines per year (Lipton et al, 2002). Therefore, Bell, Primeau and Sweet et al., (1999) average of 13.5 migraines a month would amount to 162 migraines a year which is much higher than the average migraineurs experience.

Matching control and experiment groups in studies can be a daunting task. Twin studies considered the ultimate epidemiological study because of the concordance in the control and experimental group, are rare. A Dutch twin study found a lifetime diagnosis of migraine was not associated with cognitive deficits in middle-aged subjects (Gaist, et al., 2005). In a study of children with migraines and their unaffected sibling, there was no cognitive difference between the control group of sibling pairs and the migraine group of sibling pairs (Haverkamp, Hönscheid, & Müller-Sinik, 2002). Another study of female college students found no significant differences between migraine with aura, migraine without aura and controls on a battery of memory and neuropsychological tests (Burker, Hannay, & Halsey, 1989). Leijdekkers et al. (1990) also found there were no significant differences on test performance between a migraine and control group matched by age, education, and social background. However, all the subjects recruited were from a local migraine group, which may have contributed to a reporting bias. Additional research utilizing 95 elderly volunteers, found no significant differences in cognitive ability in individuals with a long history of migraine (Pearson, Chronicle, Maylor, & Bruce, 2006). Previous research has focused on long-term cognitive function following a migraine; however, very few studies have examined short-term cognitive function during migraine headaches.

Reversible Cognitive Decline.

A reversible cognitive decline was defined as a cognitive decline during the headache interval, which completely subsides during a measured period followed by a period where the individual is headache free. Subjects tested when headache free and 30 hours following recovery from a headache and nocturnal sleep showed a reversible cognitive decline when comparing migraine and cluster headaches (Meyer, Thornby, Crawford, & Rauch, 2000). Results indicated that 86% of subjects showed cognitive decline, however sleep and serotonin antagonists reversed the cognitive impairments. One major problem with the Meyer and colleagues study was the lack of comparison to a control group.

A study presented at the American Association for the Study of Headaches found temporary impairments of immediate and sustained attention and verbal learning were found accompanying headache intervals in a study where 30 migraineurs were interviewed in their clinic or via telephone during the headache interval (Black, Horn, Miller, & Logue, 1997). Another study reported self-administered testing of the Neurobehavioral Evaluation System (NES2) when the migraineurs were both headache-free as well as 30 hours after a headache showed slower response times, but were not measurably impaired 30 hours after a headache and nocturnal sleep (Mulder, Linssen, Passchier, Orlebeke, & De Geus, 1999). Bedside testing administered over the phone, and or self-administered are not the golden standard for encompassing the full gamut of cognitive impairments that occur after a migraine headache.

Similarly, two prescription drug studies utilizing Sumatriptan (injection and nasal spray) found that cognitive impairments were reversible 15 minutes after medication

administration (Farmer, Cady, Bleiberg, & Reeves, 2000; Farmer, et al., 2001). Cognitive function was measured in 15 minute intervals post sumatriptan administration and was completely back to baseline 135 minutes post-dose (Farmer, Cady, Bleiberg, & Reeves, 2000). In both these studies cognitive function (simple reaction time, sustained attention/concentration, working memory, visual-spatial processing) and alertness/fatigue were adversely affected during a migraine headache. However, results of these studies may be skewed due to lack of comparison to a control group and small sample size. Another open label study on the effects of topiramate monotherapy in migraine treatment showed that while the migraine and control group were comparable with no differences at baseline. A side effect of the medication was decreased word fluency. (Romigi, et al., 2008). No research to date has examined short-term cognitive function comparing a migraine and control group to their baseline cognitive function

Migraine is Associated with Long-Term Cognitive Decline.

Migraine studies have reported long-term (years/ permanent) cognitive decline in information processing, reaction time, verbal ability and visual processing (Hooker & Raskin, 1986; Zeitlin & Oddy, 1984; Waldie, Hausmann, Milne, & Poulton, 2002; Wray, Mijovic-Prele, & Kosslyn, 1995). One study found a loss of cognitive habituation in migraine, and an increased processing time (Evers, Bauer, Suhr, Husstedt, & Grotemeyer, 1997). Hooker and Raskin (1986) compared classic (migraine with aura) and common (migraine without aura) migraine headaches. The classic migraine headache group exhibited slower dominant hand motor speed, less dexterity, less efficient learning of new associations between dissimilar symbols, and dysphasic errors compared to the common migraine group. Both migraine groups exhibited poorer free recall of semantic material

and lesser ability to discriminate forms and analyze spatial relationships in the tactile modality. In addition, five subjects reported cognitive difficulties due to their migraine headaches. However, this classic study did not have a control group, and mainly examined differences between aura and no aura migraines.

Research shows information processing declines in migraine sufferers over time (Zeitlin & Oddy, 1984; Wray, Mijovic-Prele, & Kosslyn, 1995)). Zeitlin and Oddy (1984) found that severe migraine sufferers consistently gave poorer performances on a series of memory and information processing tasks. A limitation to this study was a lack of a control group and subjects were limited to a migraine clinic. Another study conducted in New Zealand consisted of 979 subjects individually assessed on a variety of measures on ten different occasions from age three to 26 at certain pre-determined age intervals. Twelve percent of the 979 subjects fulfilled the IHS diagnostic criteria for migraine headaches. Results indicated that migraine patients were significantly impaired on verbal ability, independent of headache history (severity of pain of average migraine headache), when compared with tension-type headache and controls (Waldie, Hausmann, Milne, & Poulton, 2002). Results also revealed that visual processing is also slower in migraine patients (Wray, Mijovic-Prele, & Kosslyn, 1995). Overall, many studies have found neurocognitive deficits in migraineurs, with the main limitation of the studies lacking a control group and only using diagnosed migraine patients.

Researchers suggest migraine headaches may produce structural and functional brain dysfunctions (Elkind & Scher, 2005; Swartz & Kern, 2004; Kruit, et al., 2004). In a study of Dutch adults 30 to 60 years of age, patients with migraines exhibited a higher prevalence of infarct in the cerebellar region of the posterior circulation and deep white

matter (Kruit, et al., 2004). Swartz and Kern (2004) concluded from a meta-analysis of published case-control studies utilizing magnetic resonance imagining that migraine patients are at higher risk of having asymptomatic sub cortical and deep white matter abnormalities. Abnormalities found in the cerebellar region of the posterior circulation may affect long-term cognitive function. Overall, cognitive function is impaired during a migraine. While long-term changes are important, the short-term effects should not be overlooked, due to the impact on the daily lives of migraineurs. Migraines headaches, impacting daily, weekly, or even monthly can effect decisions, actions, and may possible determine long-term outcomes in an individual's life.

Physical Activity and Migraine.

Exercise through the life span is important to the health and well-being of all individuals. Currently, there are inconsistent research results on the relationship between exercise and migraine. It is well known that regular exercise can decrease stress levels. Research has shown stress to be a trigger for migraine (Turner, Molgaard, Gardner, Rothrock, & Stang, 1995). Consequently, exercise has been promoted as a method of migraine management and prevention (Folkins & Sime, 1981). Case report data shows that some individuals use exercise as a successful method of aborting a migraine headache. During the prodromal (aura and pre-migraine symptoms) phase the individual may go for a run to prevent the subsequent headache (Darling, 1991). On the contrary, exertional exercise without a proper warm-up can also be a trigger for migraine headaches. This may occur as a result of a Valsalva maneuver (holding ones breath in an effort to lift heavier weights), or initiating vigorous exercise without warming up and

stretching, which allows the body to adapt to the new energy level (Lambert & Burnet, 1985; Rooke, 1968).

Very few studies have examined the relationship between migraine and exercise. Lockett and Campbell (1991) initiated a six-week cardiovascular exercise program and found decreases in the pain level during their migraine headache. They also found trends toward decreased frequency, intensity, and duration, but felt that with an increased period, significant differences would arise. Another six-week study where subjects exercised at 60% of their max heart rate for 40 minutes (10 minute warm-up, 20 minute exercise, 10 minute rest) three times a week found that subjects reported a significant decrease in intensity and frequency of migraine (Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003). One study reported a reduction in vascular headache activity in four out of five subjects after a six week exercise intervention (Fitterling, Martin, Gramling, Cole, & Milan, 1988). The results of this study suggest maintenance of an exercise program is essential for decreased migraine frequency.

Migraine and Exercise Physiology.

Physiological changes associated with exercise provide a plausible explanation for exercise moderated pain relief (Darling, 1991). The endorphin system is known for its analgesic properties, lower plasma beta-endorphin levels are found in migraineurs (Fettes, Gawel, Kuzniak, & Edmeads, 1985), and serotonin, which is known to inhibit pain perception (Anthony, 1984) has been found to drop during a migraine attack and cause vascular changes (Anthony, 1972). Research on beta-endorphin levels after exercise in migraineurs showed increased levels with regular exercise (Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003). Serotonin, plasma beta-endorphin levels and

endorphins increase during exercise, which alters the vasodilation process and provides a natural preventative, or relief of a migraine headache (Farell, Gates, Maksud, & Morgan, 1982). Perception of pain decreases after a single bout of resistance exercise (Koltyn & Arbogast, 1998; Whiteside, Hansen, & Chaudhuri, 2004). This may also be facilitative during a migraine.

Physical Activity Defined.

Regular physical activity done at a moderate intensity level is proven to result in health benefits (U.S. Department of Health and Human Services, 2008). Healthy People 2010, established in 2000, contains 467 objectives designed to serve as a road map for improving the health of all people in the United States during the first decade of the 21st century. At the midpoint of 2005, a check-up survey completed by Healthy people 2010 found that the country is moving toward the physical activity recommendations of 50% of adults, whereas many of the other goals are not meeting their outcomes (Department of Health and Human Services Centers for Disease Control and Prevention, 2008). In 2007, 50.7 % of adults in Michigan are meeting the physical activity guidelines

The Centers for Disease Control and Prevention (CDC) defined physical activity reccomendations for adults as moderate-intensity for at least 150 minutes per week, or vigorous-intensity for at least 75 or more minutes per week. In addition to cardiovascular activity, participants must perform at least two days a week of muscle strengthening activities that work all major muscle groups (legs, hips, back, abdomen, chest, shoulder, arms). Moderate physical activity can be defined as some increase in breathing or heart rate, or any activity that burns 3.5 to 7 kcal per minute such as walking briskly, mowing the lawn, dancing, and swimming, bicycling on level terrain or gardening. Vigorous

physical activity is a large increase in breathing or heart rate (conversation is difficult or broken), and any activity that burns more than 7 kcal per min. This represents the effort a healthy individual might expend while jogging, mowing the lawn with a non-motorized push mower, participating in high-impact aerobic dancing, swimming continuous laps, bicycling uphill, or carrying more than 25 pounds up a flight a stairs (U.S. Department of Health and Human Services, 2008).

Physical Activity and Neurocognitive Function.

The physiological effects of exercise on the human body are well known. Physical activity causes changes in the cardiovascular, skeletal and respiratory systems to improve the bodies function. Most prior research has focused on the ability of the exercisers to perform motor tasks both during and after exercise, as many exercisers report that exercise training improves psychological well being and mood state (women) (Cramer, Neiman, & Lee, 1991, Folkins & Sime, 1981). The CDC reported from their 2007 National Health Interview Surveys that people with a college degree were three times as likely to report regular leisure time physical activity (43.3%) than those who did not complete high school (14.9%) (CDC's MMWR Weekly, 2009).

Extensive research in the last two decades has shown that exercise can have a strong positive effect on cognitive function (Medina, 2003; McMorris & Keen, 1994; Davey, 1973). Studies that have focused on physical activity and neurocognitive function have mainly focused on an elderly population (Eusop, Sebban, & Piette, 2001) and have reported that physical activity decreases the atrophy in the brain that is association with aging (Schuit, Feskens, Launer, & Kromhout, 2001). Previous research has found that exercisers exhibited improvements in pattern matching and problem solving (Medina,

2003). McMorris and Keen (1994) found that exercise affects reaction time during maximal training in their small sample study (12) where individuals took simple reaction time tests at rest and while cycling at a 70%, and 100% workload. Other studies have investigated how cognition is affected during exertion. One study looked the individual's ability to perform perception of geometric figures while performing hand dynamometer at four levels and found the testing at moderate tension levels to be facilitative (Andreassi, 1965). A 12-minute treadmill test in which discrimination tasks were performed both during and after exercise was found to be facilitative at both samples (McGlynn, Laughlin, & Rowe, 1979). Bicycle pedaling at a constant resistance measured at 15 seconds, 30 seconds, and 2, 5, and 10 minutes with the cognitive task of short-term memory found facilitative effects after short bouts, and impairments after 10 minutes (Davey, 1973). Comprehensive reviews of the effect of exercise on cognitive processes reveal mixed results (Tomporowski & Ellis, 1986). These tests looked at the effect of physical exertion of a variety of tasks from simple arithmetic to reaction time. Most found that exercise bouts had a facilitative effect or no effect on the tests.

Few studies have investigated the relationship of cognition and exercise in young adults. One recently published study with young adults (mean age 21.1) found the cognitive effects of physical activity could be observed using a simple paradigm, and that physical activity has a beneficial effect on the cognitive processes of young adults (Kamijo & Takeda, 2009). Another study found that a lifestyle of physical activity appeared to play a more dominant role in simple reaction time and discrimination reaction time than age. Older men who were active were compared to both active and non-active younger men and it was found that older men that were active were at a

similar level as non-active younger men when looking at reaction time. Spiriduso repudiated the hypothesis that most of the slowing of reaction time was attributable to the Central Nervous System processing in aging rather than response speed and timing (Spirduso, 1975).

Instrument Validity

Headache Impact Test (HIT).

Headache impact test is a test derived from several traditional migraine instruments including the Migraine Quality of Life Questionnaire, the Headache Disability Instrument, the Headache Impact Questionnaire, and the Migraine Disability Assessment. The HIT consists of 53 items to assess the individuals' status of disability related to migraine. The HIT normally requires about five to ten minutes to complete. The HIT is available free online at http://www.headachetest.com or can be taken on paper (Pryse-Phillips, 2002; Vuillaume De Diego & Lanteri-Minet, 2004). The test has multiple levels with each question based on the individual's answer to the preceding question that is appropriate for a person with that level of disability. The instrument has strong correlations with the previously validated traditional migraine tests from 0.51 to 0.87. This test was validated utilizing the item response theory (Cella & Chang, 2000) and compared to the Migraine-Specific Quality of Life Questionnaire, the Headache Disability Instrument, the Migraine Disability Assessment and the Headache Impact Questionnaire. Over 10,000 subject's scores were utilized to validate each test question (Pryse-Phillips, 2002). The HIT normally requires five or fewer questions to allow a reliable estimate of a subject's score. Confidence intervals are set at five to 15 for severe and less severe impact, respectively. The first question is the standard question, and based

on the reply a score is assigned within the computer program. The next question is then selected based upon the level of disability that was indicated in the first question. If the answer is in a consistent response, further questions may or may not be required to achieve the response that fits in the narrow pre-specified confidence limits set. The level of disability is then expressed around an arbitrary mean of 50, which reflects the average disability suffered by members of the headache population. The HIT-6 is a paper version of the HIT and an example is available in Appendix A (Pryse-Phillips, 2002).

Behavior Risk Factor Surveillance System.

The Behavioral Risk Factor Surveillance System (BRFSS) was established in 1984 by the CDC. Collectively it is a state-based system of surveys that collect health risk behavior information, preventive health practices and access health care information related to chronic disease and injury (www.cdc.gov). For the purpose of this study eight standard core questions relating to establishing an individual's physical activity level recommendations were utilized.

Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).

ImPACT version 5.0 is a computer-based program that will be used to assess neurocognitive function and migraine symptoms (Lovell, 2007). The software program is run from either a desktop PC or laptop using Windows NT operating system or higher (Lovell, Collins, Podell, Powell, & Maroon, 2000). The program uses a keyboard and external mouse to allow participants to select responses and navigate through the six test modules. Normative data can be found in Tables 7 and 8.

The ImPACT protocol consists of three categories. The first category includes a demographic information section. The user navigates through a series of instructional

screens where they enter descriptive information about themselves, such as demographics, years in school, presence of any learning disabilities, and neurological disorders.

The second category consists of 22 symptoms. Participants first indicate yes or no that they are experiencing a symptom then quantify the severity using a seven point Likert scale. These concussion symptoms are similar to migraine symptoms that include headache, nausea, vomiting, balance problems, dizziness, fatigue, trouble falling asleep, sleeping more than usual, sleeping less than usual, drowsiness, sensitivity to light, sensitivity to noise, irritability, sadness, nervousness, feeling more emotional, numbness or tingling, feeling slowed down, feeling mentally foggy, difficulty concentrating, difficulty remembering, and visual problems. Participants self-rate their symptoms by clicking on a number between zero (not experiencing) and six (severe).

The third category consists of six neurocognitive test modules. It is important to note that ImPACT has multiple built-in word/design groups. This is important to limit practice effects. A different word/design group will be administered to the participant for each ImPACT test. Module one of the neurocognitive test battery focuses on word discrimination. This section is used to evaluate verbal memory and attentional processes. Subjects are presented with 12 words two times each for 750 milliseconds. Individuals are then tested to recall words from a 24-word list. There are 12 target words and 12 non-target words. Using the mouse, subjects are prompted to select "yes" or "no" depending on whether or not the word was presented in the original list. After a 20 minute delay, subjects are asked again to recall this list of words. Displayed at the end of the battery is a total score of percent correct.

Module two evaluates attention and visual recognition through design memory. Similar to Module one, 12 target designs are presented twice for 750 milliseconds. Following the presentation subjects are asked to recall these designs, choosing from the 12 target and 12 non-target designs presented. Subjects are prompted to click "yes" or "no" depending on whether or not the design was originally presented. After a 20 minute delay, subjects are asked again to recall this list of words. A total score of percent correct is given at the end of the battery.

Module three is designed to measure visual working memory, visual processing speed, and visual memory. This section incorporates a distracter task which is a reaction time test that asks the subject to click the left mouse button if a blue square appears, and the right mouse button if a red circle appears. For the memory test, a random assortment of X's and O's are displayed for 1.5 seconds. Of this random assortment, three X's and O's are illuminated in yellow. The subject is instructed to remember the placement of these illuminated objects. Immediately following the presentation of the three illuminated X's and O's, the subject is asked to complete the distracter task. After the completion of the distracter task, the memory screen reappears and the subject is asked to click on the X's and O's that were originally highlighted. Four trials are completed for this section. Scores for this section include percent correct for identification of the X's and O's and also reaction time scores for the distracter task.

Module four is a symbol-matching task that evaluates processing speed, learning, and memory. A grid with nine common symbols and accompanying numbers is presented to the subject. The subject is presented with a symbol below the grid, and is asked to click the number of the corresponding design. After 27 trials, the symbols are removed

from the grid. The symbols again are presented below the grid, and the subject is asked to recall the correct symbol/number pairing by clicking the appropriate button. Reaction time scores and memory scores are both calculated.

Module five measures choice reaction time and impulse control. Subjects are presented with the words red, green, and blue each written in their respective color. Subjects are instructed to click the mouse when the word correctly matches with the color ink. For this section, a reaction time score and task error score are provided.

The sixth and final module examines working memory and visual motor response speeds. This module is comprised of both a distracter task and memory component. Participants are presented with and asked to remember three letters. Once the letters are removed from the screen, the participant is presented with the distracter task. A 5x5 grid appears on the screen consisting of 25 numbered boxes. The participant is asked to count backwards, clicking on the corresponding numbered box with the mouse. Following the completion of the distractor task, the participant must input the three letters in the exact order they were previously presented. There are five trials for this test module.

ImPACT has been utilized in several studies to determine neurocognitive function (Maroon, Lovell, Norwig, Podell, Powell, & Hartl, 2000; Mihalik, Stump, Collins, Lovell, Field, & Maroon, 2005). A consistent and fluid process will make each test easily endurable for all individuals. ImPACT was utilized because it is an efficient method for measuring neurocognitive function in college-aged students.

Computation of Composite Scores

Verbal Memory Composite Score
Average of these scores:

- Word Memory total percent correct (immediate + delay) / 2
- Symbol Match (hidden symbols)/9*100
- Three letters Total letters correct

Visual Memory Composite Score
Average of these scores:

- X's and 0's Total correct (memory)/12*100
- Design memory-total percent correct (immediate + delay) / 2

Reaction Time Composite Score
Average of these scores:

- X's and 0's average correct RT
- Symbol Match average correct RT/3
- Color Match average correct RT

Processing Speed Composite Score
Average of the following scores:

- X's and 0's-total correct (interference) total/4
- Three letters-average counted correctly*3
- Symbol Match (average correct responses)

Table 4: Approximate Classification Ranges for Index Scores-University Women

	Verbal Memory	Visual Memory	Processing Speed	Reaction Time
Impaired	< 70	< 48	< 23.3	> .70
Borderline	71 - 82	49 – 59	23.4 - 29.7	.69 - .64
Low Average	83 - 86	60 - 69	29.8 - 34.3	.63 - .60
Average	87 - 97	70 - 88	34.4 - 42.1	.59 - .52
High Average	98 - 100	89 – 93	42.2 - 46.3	.51 - .50
Superior	---	94 – 96	46.4 - 49.2	.49 - .48
Very Superior	---	97 – 100	> 49.3	< .47

Data from www.impacttest.com

Table 5: Approximate Classification Ranges for Index Scores- University Men

	Verbal Memory	Visual Memory	Processing Speed	Reaction Time
Impaired	< 71	< 51	< 23.8	> .75
Borderline	72 - 77	52 - 60	23.9 - 28.3	.74 - .67
Low Average	78 - 82	61 - 68	28.4 - 32.4	.66 - .61
Average	83 - 94	69 - 94	32.5 - 42.0	.60 - .52
High Average	95 - 97	95 - 97	42.1 - 46	.0 .51 - .48
Superior	98 - 99	98 - 99	46.1 - 50.0	.47 - .45
Very Superior	100	100	> 50.1	< .44

Data from www.impacttest.com

Summary of the Literature

Migraine headaches are an episodic and progressive disorder that affects 18-25% of females and 6-13% of males (Lipton et al, 2002; Lipton et al, 2001; Launer, Terwindt, & Ferrari, 1999; Lipton, Stewart, Celentano, & Reed, 1992). Migraines are classified as migraine with aura or migraine without aura using the IHS diagnostic criteria. During a migraine attack, progression is seen in aura development (if present) and intensity of pain, with prodromal and postdromal symptoms often leaving the migraineurs performing at decreased capacity for up to a week surrounding a migraine attack. With frequent attacks, migraine is directly costly to both the individual and the economy as a whole. Furthermore, indirect and direct cost relating to migraine headaches are estimated at 13 billion dollars, affecting society in many venues including work productivity, absenteeism and social function (Edmeads & Mackell, 2002).

College students are expected on a daily basis to be ready to perform on pop quizzes, tests or practical skills tests. Often students will study for months for a licensure or certification test which the outcome will determine their future in their profession. From 18-28 years of age the prevalence of migraine increases yearly, and the life of the

college student is full of migraine triggers (irregular sleep patterns, stress, alcohol, etc.), therefore it is important to determine if migraines affect their cognitive function following an attack.

Previous research has focused on long-term cognitive function following a migraine headache and has produced contradictory results. Very few studies have examined short-term cognitive function and recovery patterns following migraine headaches. Little research has examined the effect of physical activity on the recovery pattern of migraine headaches. Some individuals may suffer from exertional migraine, while others ward off a migraine through exercise. The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur migraines.

CHAPTER 3

Methods

The purpose of this study was to examine neurocognitive function and recovery patterns between two groups of college aged students who experience migraine headaches: a group who meet physical activity recommendations and a group who did not meet physical activity recommendations and compare them to a control group who did not experience migraine headaches. This chapter isdivided into six major sections: (a) Experimental Design, (b) Research Participants, (c) Instrumentation, (d) Procedures (e) Data Analysis, and (f) Threats to Internal and External Validity.

Experimental Design

A quasi-experimental design was used to compare baseline neurocognitive scores and migraine symptoms to post-test neurocognitive scores and symptoms. The independent variables were migraine status (migraine [M], non-migraine [NM]), physical activity (meet physical activity recommendations [PA], do not meet physical activity recommendations [NPA]) and testing occasion (baseline [B], within 24 hours [24h], 24-48 hours [48h], and one week [7days]). The dependent variables were the four composite scores of ImPACT. The four subscales of ImPACT are verbal memory composite score, visual memory composite score, reaction time composite score, and processing speed composite score. The ImPACT composite scores are collectively referred to as neurocognitive function.

Research Participants

A total of 122 people volunteered to participate in the study. Twenty-three males and 99 females were baseline tested. One hundred and two individuals completed physical activity data with 74 meeting physical activity recommendations and 28 not meeting the aerobic (but not necessarily weight lifting) physical activity recommendations of the CDC. Of the 122, 71 were migraineurs with 54 of them physician diagnosed and the other 17 met IHS criteria for diagnosis of migraine. Subjects were matched to a control for age, sex and education level. Age was considered a match if the subjects were plus or minus one year. Education level was considered matched if the subjects were in their first or second years of college, third or fourth years of college, or beyond their fourth year of college. Ethnicity was recorded, but not considered for group designations due to the local area not consisting of an ethnically diverse population. Migraine subjects were included if they were (a) physician diagnosed with migraine headaches or (b) self-diagnosed with migraine headaches and meet the IHS criteria. Controls subjects must have had HIT score less than 50 to be included in this study. Physical activity questions were asked, but participants were not told that they were grouped by physical activity level to encourage truthful reporting.

The subjects in this study were a convenience sample of individuals recruited from Health, Physical Education and Recreation classes along with others via word of mouth and advertisement in the Northwind, a weekly student paper for Northern Michigan University (NMU). Other methods of recruiting were via e-mail through NMU professors. A letter was sent to local physicians explaining the study and asking them to

give a flyer with contact information to any patients who were college students (18-28 yrs) they treat who suffer from migraine headaches. In addition, several physicians posted them in their waiting room.

Exclusion criteria were substance abuse, diseases linked to decreased cognitive skills, individuals with cluster or tension-type headache, a history of a learning disability or special education, central nervous system disease, history of head trauma including concussion within the last six months, or color-blindness. Individuals who were pregnant were excluded due to hormonal changes that might have changed their migraine profile. Individuals with learning disabilities and previous special education, including all individuals who have been formally diagnosed with a learning disability or attended special education classes, along with individuals who have self-reported any past speech therapy, learning problems (e.g. reading or math), or have attention deficit hyperactivity disorder (ADHD). Individuals in this group tend to have lower scores on ImPACT that may skew the current data (Iverson, Lovell, Podell, & Collins, 1999).

Originally, data collection was to occur over a one- year time frame: however, this time interval was not adequate and required an additional year. This additional time was necessary due to attrition of subjects (who completed baseline, and did not follow-up after the baseline, or dropped out of the study) and subjects who reported that they suffer from migraines, but did not have a migraine headache during the time interval. To decrease attrition of subjects, frequent reminder e-mails were sent to the subjects.

Subjects had the chance to win numerous prizes for completing all phases of the study including two I-Pod shuffles (approximate value $75.00), and 15 five or ten dollar gift certificates to local area businesses. Chances of winning a prize were greater than one

in six. Once a subject completed all aspects of the study, he/ she picked a slip of paper out of a bowl and find out what they won. All subjects received at least a candy bar type item (gum, Mentos, candy, granola bar) of their choice.

Sample Size Estimate.

Sample size estimates were derived from free software downloaded from the CDC called EPI CALC 2000. Power analysis assumed a .80 power. Based on normative data for university women (Iverson, Lovell, & Collins, 2003) and the reliable change estimates (Iverson, Brooks, Collins, & Lovell, 2006). Power estimates for sample size were derived (see Table 9). Sample size was confirmed utilizing Cohens *d* with an effect size of .80 derived from the formula ES= (M1-M2)/s where M indicates the mean and s indicates the standard deviation (Thomas, Nelson, & Silverman, 2005).

Table 6: Sample Size Estimates

Impact category	Average score, SD	Reliable change estimates	Power estimate at the .80 level. Subjects per group/ total subjects
Verbal memory	87-97, 5	+/- 9 points	6 per group/24 total
Visual memory	70-88, 9	+/- 14 points	6 per group/24 total
Processing speed	34.4-42.1, 3.85	+3/-7 points	(+3) 25 per group/ 100 total (-7) 4 per group/ 16 total
Reaction time	.59-.52, .035	+/- .06 sec	5 per group/ 20 total
Total sample size			25 per group/100 total

Instrumentation

Headache Impact Test (HIT).

HIT is a test derived from several traditional migraine instruments including the Migraine Quality of Life Questionnaire, the Headache Disability Instrument, the Headache Impact Questionnaire, and the Migraine Disability Assessment. The HIT consists of 53 items that assess the individuals' status of disability related to migraine. The HIT takes approximately five to ten minutes to complete. The test has multiple levels with each question based on the individual's answer to the preceding question that is appropriate for a person with that level of disability. The instrument has strong correlations with the previously validated traditional migraine tests from 0.51 to 0.87(Cella & Chang, 2000). This test was validated utilizing the item response theory and compared to the Migraine-Specific Quality of Life Questionnaire, the Headache Disability Instrument, the Migraine Disability Assessment and the Headache Impact Questionnaire. Over 10,000 subject's scores were utilized to validate each test question (Pryse-Phillips, 2002). The HIT is available free online at http://www.headachetest.com/ (Pryse-Phillips, 2002; Vuillaume De Diego & Lanteri-Minet, 2004).

Migraine History Questionnaire.

The migraine history questionnaire (Appendix C) was developed from the IHS classification 2005 criteria. Participants were asked to answer all questions about headaches that were not caused by head injury, pregnancy, hangover or acute illness. The questionnaire includes questions about history of severe headache in the past six months and characteristics of their headache. In addition, it asked participants questions related to aura (if they experienced it) and medications used as treatment for their migraine

headaches. It was pilot tested on a collegiate population to clarify all questions and answers. It was utilized to determine self-reported migraine headaches in the absence of a physician diagnosis. Similar questionnaires were utilized in the American migraine study (Lipton et al., 2001) and a prevalence study in collegiate basketball players (Kinart, Cuppett, & Berg, 2002).

Physical Activity Questionnaire.

The physical activity questionnaire (Appendix D) was an eight question assessment from the Behavioral Risk Factor Surveillance System (BRFSS). The BRFSS is a nationally recognized test that was established in 1984 by the CDC. The BRFSS measures current fitness level related in conjunction with the American College of Sports Medicine (ACSM) and the CDC guidelines (About the BRFSS). If they meet or exceed ACSM/CDC healthy guidelines they were included in the "meet physical activity recommendations" (PA) group. If they do not exercise or do not meet the currently recommended guidelines, they were not included in the "do not meet physical activity recommendations" (NPA) group. PA was defined as 150 minutes of moderate physical activity per week or 75 minutes of vigorous activity per week. If they did not meet this threshold they were considered NPA.

24 Hours Questionnaire.

The intention of the 24 hour questionnaire (Appendix E) was to capture information about the individuals' migraine just after it occurs so it is still fresh in their memory. Questions were asked about the medication they took, time frame, hours of sleep they have had since their migraine, if they experienced an aura with their migraine, location (right or left) and level of the pain during their migraine. They were also asked

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to list anything that they perceived may have been a trigger for their migraine. These were sorted into psychological triggers (i.e. stress), environmental triggers (i.e. hot or cold), food related triggers (i.e. red wine), and others (i.e. ovulation or menstruation). Participants were also asked to shade in the location of their pain on a picture of the skull. Location areas included the front of the head, occipital, crown of the head, temporal, behind the eyes or other.

Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).

ImPACT version 5.0 (ImPACT Applications Inc.) is a computer-based program that was used to assess neurocognitive function and migraine symptoms (Lovell, 2007). The software program was run on the researcher's laptop using Windows Vista (Lovell, Collins, Podell, Powell, & Maroon, 2000). The program uses a keyboard and external mouse to allow participants to select responses and navigate through the six test modules. All students at NMU have a laptop upon admission and they were tested on a similar model laptop.

The ImPACT protocol consists of three categories. The first category includes a demographic information section. The participant was asked to navigate through a series of instructional screens where he/she was asked to enter descriptive information about himself/ herself, such as years in school, presence of any learning disabilities, and neurological disorders.

The second category consists of 22 symptoms that participants rate using a seven point Likert scale. These concussion symptoms are similar to migraine symptoms and include headache, nausea, vomiting, balance problems, dizziness, fatigue, trouble falling asleep, sleeping more than usual, sleeping less than usual, drowsiness, sensitivity to light,

sensitivity to noise, irritability, sadness, nervousness, feeling more emotional, numbness or tingling, feeling slowed down, feeling mentally foggy, difficulty concentrating, difficulty remembering, and visual problems. Participants self-rated their symptoms by clicking on a number between zero (not experiencing) and six (severe).

The third category consists of six neurocognitive test modules. It is important to note that ImPACT had multiple built-in word/design groups. This was important to limit practice effects. A different word/design group was administered to the participant for each ImPACT test. Module one of the neurocognitive test battery focuses on word discrimination. This section was used to evaluate verbal memory and attentional processes. Subjects were presented with 12 words two times each for 750 milliseconds. Individuals were then tested to recall words from a 24-word list. There were 12 target words and 12 non-target words. Using the mouse, subjects were prompted to select "yes" or "no" depending on whether or not the word was presented in the original list. After a 20 minute delay, subjects were asked again to recall this list of words. A total score of percent correct was displayed at the end of the battery.

Module two evaluated attention and visual recognition through design memory. Similar to module one, 12 target designs are presented twice for 750 milliseconds. Following the presentation subjects were asked to recall these designs, choosing from the 12 target and 12 non-target designs presented. Subjects were prompted to click "yes" or "no" depending on whether or not the design was originally presented. After a 20 minute delay, subjects were asked again to recall this list of designs. A total score of percent correct was given at the end of the battery.

Module three was designed to measure visual working memory, visual processing speed, and visual memory. This section incorporates a distractor which is a reaction time test that asks the subject to click the left mouse button if a blue square appears, and the right mouse button if a red circle appears. For the memory test, a random assortment of X's and O's are displayed for one and one-half seconds. Of this random assortment, three X's and O's are illuminated in yellow. The subject was instructed to remember the placement of these illuminated objects. Immediately following the presentation of the three illuminated X's and O's, the subject was asked to complete the distractor task. After the completion of the distractor task, the memory screen reappears and the subject was asked to click on the X's and O's that were originally highlighted. Four trials were completed for this section. Scores for this section include percent correct for identification of the X's and O's and reaction time scores for the distractor task.

Module four was a symbol-matching task that evaluates processing speed, learning, and memory. A grid with nine common symbols and accompanying numbers was presented to the subject. The subject was presented with a symbol below the grid, and was asked to click the number of the corresponding design. After 27 trials, the symbols were removed from the grid. The symbols were presented below the grid, and the subject is asked to recall the correct symbol/number pairing by clicking the appropriate button. Reaction time scores and memory scores were both calculated.

Module five measures choice reaction time and impulse control. Subjects were presented with the words red, green, and blue each written in their respective color. Subjects were instructed to click the mouse when the word correctly matches with the color ink. For this section, a reaction time score and task error score were provided.

The sixth and final module examined working memory and visual motor response speed. This module is comprised of both a distractor task and memory component. Participants were presented with and asked to remember three letters. Once the letters were removed from the screen, the participant was presented with the distractor task. A 5x5 grid appears on the screen consisting of 25 numbered boxes. The participant was asked to count backwards, clicking on the corresponding numbered box with the mouse. Following the completion of the distractor task, the participant must input the three letters in the exact order they were previously presented. There were five trials for this test module.

Reliability and Validity of ImPACT.

Test-retest reliability for ImPACT was assessed over eight days across four administrations, yielding correlation coefficients ranging from 0.66 to 0.85 for the verbal memory index, 0.75 to 0.88 for the processing speed index, and 0.62 to 0.66 for the reaction time index (Lovell, Collins, Fu, Burke, & Podell, 2001). Using reliable change indices, repeated administrations over a 2-week period revealed no practice effects (Iverson G. L., Lovell, Collins, & Norwig, 2002c*)*. In another study, one-week test-retest reliability coefficients were as follows: 0.70 for verbal memory, 0.67 for visual memory, 0.79 for reaction time, and 0.86 for processing speed, with significant test-retest differences for only the processing speed composite scores on with-in subject comparisons (Iverson, Lovell, & Collins, 2005). Concurrent validation of ImPACT revealed correlations with the Symbol-Digit Modalities test (SDMT) which ranged from 0.37 and 0.46 for visual and verbal memory indices, to 0.60 and 0.70 for reaction time and processing speed indices, respectively (Iverson, Lovell, & Collins, Validity of

ImPACT for measuring attention and processing speed following sports-related concussion., 2005). Since the SDMT is believed to measure scanning and tracking aspects of attention, as well as processing speed these coefficients represent good convergent and divergent validity (Spreen & Strauss, 1998). Correlations between ImPACT visual and verbal memory composites with the Brief Visual Spatial Memory Test-Revised total score (r=.50) and the delayed recall score (r=.85) have been established; the processing speed composite was shown to correlate with the Trailmaking Tests A (r= -.49) and B (r= -.60), and the SDMT (r=.68) (Iverson, Franzen, Lovell, & Collins, 2004. Schatz and colleagues documented a combined sensitivity of 81.9% for ImPACT indices and total symptom score, and a specificity of 89.4%; positive likelihood ratio was approximately 8:1 and negative likelihood ratio was 2:1 (Schatz, Pardini, Lovell, Collins, & Podell, 2006).

Procedures

Baseline Evaluation.

After completing informed consent, collegiate students were administered the Migraine History Questionnaire (10 minutes) (Appendix C), the HIT (10 minutes), a Physical Activity Questionnaire (Appendix D) and the ImPACT (approximately 25 minutes) neurocognitive test battery in the researcher's office. The subjects received information about how to reach the researcher after a migraine headache (Appendix B). Subjects were encouraged to treat their migraine as usual throughout the study. This meant that if they normally took over the counter medications, or prescription medications or slept following a migraine, they should continue that pattern with no changes. If subjects experienced a migraine in the past week or were experiencing any

symptoms of an oncoming attack they were not baseline tested. Another time was arranged for these subjects to take the baseline measures. All subjects indicated they were alcohol and drug free for 24 hours prior to all tests. After baseline testing was complete, subjects determined a quiet location for all post-tests. If the student resided in a dorm, the post-tests were administered in a common study room in the students' dorm. If the student resided off campus, the post-tests were administered in place at the students' home or at NMU, whichever location the student was the most comfortable. If the location was the student's home, testing was administered in the living room, kitchen, or a common area that is quiet. The experimenter was not in the room during baseline or post-testing. The HIT score was the impact of headaches variable for the purpose of this study.

Post-tests Evaluation.

After a subject suffered a migraine headache, he/she was administered the ImPACT neurocognitive test battery minus the demographic/descriptive section (approximately 20 minutes) within 24 hours, 48 hours, and 7 days post-migraine. Migraine was determined to initiate from the onset of headache symptoms. Migraine subjects also completed the 24 Hour Questionnaire during the first post-test. All post-tests were administered in a comfortable environment to the subject. The physical activity questionnaire were given at the first post-test except for the final volunteers to capture current physical activity levels. All volunteers that completed the physical activity questionnaire at the baseline testing completed testing within one month of the baseline or were excluded from the physical activity data analysis. This excluded two individuals.

Data Analysis

Analysis of the data included both descriptive statistics and inferential statistical analysis of the ImPACT scores. The ImPACT software yields individual scores as well as composite scores for verbal memory, visual memory, processing speed, and reaction time composite scores. Higher scores on verbal memory, visual memory, and processing speed indicate a better performance. Lower scores on reaction time indicate a faster reaction time, thus, better performance. The migraine questionnaire was utilized to qualify those individuals who have self-diagnosed their migraine, to assure that the IHS criteria are met. All analyses were conducted using the Statistical Package for the Social Sciences version 16.0 (SPSS Inc.).

Hypotheses 1, 2, and 3.

Hypotheses one, two, three, and the related sub-hypotheses were concerned with the effects of testing occasion, migraine status, and physical activity on neurocognitive function post-migraine headache. Descriptive statistics (means and standard deviations) are presented for each of the four ImPACT composite scores for each of the independent variables. A four testing occasion (baseline, up to 24 hrs, 48 hrs, 7days) x two migraine group (M and NM) was utilized . A one-way ANOVA, or MANOVA was utilized to determine the significance of each of these hypotheses. All tests were conducted at the $p \leq .05$ level of significance, and each subsequent post-hoc test were conducted at the $p < .05$ level.

Exploratory Hypotheses.

Hypotheses four and five were concerned with the effects of sex and diagnosis status on pain. Descriptive statistics (means and standard deviations) are presented for

each of the independent variables: migraine status, sex, diagnosis status and testing occasion. An independent t-test with pain as the dependant variable was conducted at the $p \leq .05$ significance level.

Hypothesis six and the related sub-hypotheses were concerned with the effects of physical activity on the impact of headaches. Descriptive statistics (means and standard deviations) are presented for each of the independent variables: migraine status, impact of headaches, and physical activity. A two physical activity (PA and NPA) x two migraine group (M and NM) two-way analysis of variance (ANOVA) test with HIT scores as the dependent variable were conducted at the $p \leq .05$ significance level.

Research Questions.

Research question seven concerned the pain level reported at 24 hours post-migraine for college students who use prescription medication, over-the-counter medications or no medications for their migraine headache. The independent variables are migraine status (migraine only), and medication status (RX, OTC, none) exercise. A one migraine by three medication status (Rx, OTC, none) ANOVA test with pain scores as the dependent variable were conducted at the $p \leq .05$ significance level, and each subsequent post-hoc test were conducted at the $p \leq .05$ level.

Research Question 8 concerns the effect of exercise post-migraine on pain levels 24 hours post-migraine. Descriptive statistics (means and standard deviations) are presented for each of the independent variable migraine status. An independent t-test with pain as the dependant variable was conducted at the $p \leq .05$ significance level, and each subsequent post-hoc tests were conducted at the $p \leq .05$ level.

Research Question nine concerns the effect of sleep on neurocognitive function post-migraine. Descriptive statistics (means and standard deviations) were presented for each of the four ImPACT composite scores for each of the independent variables. A one testing occasion (24 hrs) x four sleep levels (none, a little-4, 4-8, more than 8 hours) analysis of a one-way repeated measures ANOVA was used to determine the significance of this research question. The ANOVA tests were conducted at the $p \leq .05$ level of significance and each subsequent post-hoc test were conducted at the $p < .05$ level.

Threats to Validity and Study Limitations

In a quasi-experiment with no randomization to group, it is especially important to determine all threats to internal and external validity and carefully control for each threat. The next two sections will list all threats to internal and external validity and explain the controls the experimenter took for each threat (Thomas, Nelson, & Silverman, 2005), then limitations of the study will be examined.

Threats to Internal Validity.

Internal validity was defined as the extent to which the results of a study can be attributed to the treatments used in the study. There are nine threats to internal validity. Each threat to internal validity was discussed in the following manner, definition first, then how the study controlled the threat.

History: Events occurring during the experiment that are not part of the treatment.

Control: Participants not present during the summer months were not baseline tested until they returned for the fall semester.

Maturation: Processes within the participants that operate as a result of time passing.

Control: An attempt was made to decrease the time between baseline testing and post-testing through reminder e-mails. Time between baseline and post-testing was matched in the controls. The exercise questionnaire was given at the first post-test. With the testing occurring within one year, maturation should have little effect.

Testing: The effects of one test on subsequent administrations of the same test.

Control: Within ImPACT there are five different versions of the post-test. Internal validity has been tested and retested numerous times (Iverson, Franzen, Lovell, & Collins, 2004).

Instrumentation: changes in instrument calibration, including lack of agreement within and between observers.

Control: ImPACT does not need calibration and all data were collected by one researcher.

Statistical regression: The fact that groups selected on the basis of extreme scores are not as extreme on subsequent testing.

Control: Repeated measures were taken on each individual. Individuals will be volunteers who are included based on a history of migraines. The exercise group was determined as to individuals who meet the CDC requirements of moderate exercise and those who do not meet the requirements. A matched group technique was used with age, sex and education as equivalent variables.

Selection bias: Choosing comparison groups in a nonrandom manner.

Control: Controls were matched on age, sex and education level to control for selection bias. Controls were included if they have an HIT score of less than 50. All subjects were volunteers. No special treatment was given to any one group. No extra credit was given to participants. All prizes were drawn from a hat at the end of data collection from individuals who completed the study.

Experimental mortality: loss of participants from comparison groups for nonrandom reasons.

Control: Over sampling was utilized with baseline testing. Reminder e-mails were be sent to subjects frequently.

Selection-maturation interaction: The passage of time affecting one group but no the other in nonequivalent group designs.

Control: All subjects were recruited from the Marquette area and placed in groups be migraine and physical activity status. Controls were place in groups by physical activity status. Subjects were blind to physical activity as a variable. While questions about their physical activity habits were asked, they were not told that this separated them into a group.

Expectancy: experimenters' or testers' are anticipating that certain participants will perform better.

Control: The tester was not in the room while the subject took all tests. All tests were taken in a comfortable, quite room.

Threats to External Validity.

External Validity is defined as the generalizability of the results of the study. There are four threats to external validity. Each threat to external validity is discussed in the following manner, definition first, then how the study controlled the threat.

Reactive or interactive effects of testing: The pretest may make the participant more aware of or sensitive to the upcoming treatment. As a result, the treatment is not as effective without the pretest.

Control: All subjects control or experiment, received the same questionnaires and ImPACT tests in the same order. ImPACT was repeated four times, and no treatment is given in this study.

Interaction of selection bias and the experimental treatment: When a group is selected on some characteristic, the treatment may only work on groups possessing that characteristic.

Control: All tests took place in a normal testing setting that will duplicate a college testing environment. Tests were completed in a comfortable quiet testing environment.

Reactive effects of experimental arrangements: Treatments that are effective in very constrained situations (laboratories) may not be effective in less constrained settings (more like the real world).

Control: During testing in college universities students have a quite comfortable setting in which to take most if not all tests. These testing environments were duplicated in this study.

Multiple-treatment interference: When participants receive more than one treatment, the effects of previous treatments may influence subsequent ones.

Control: The ImPACT controled for subsequent testing through a series of tests that can be taken as post tests. No treatments were given in this experiment. The migraineur treated the migraine with no medication, over the counter medication, prescription medication or sleep as usual. ImPACT is currently used throughout the world.

Limitations of the Study.

Some of the limitations of this study include the population. The population of the upper peninsula of Michigan was not ethnically diverse, thus making the sample mainly white. Generalizability of the results to the general population were difficult, although results may be generalized to a similar population of college-aged individuals 18-28 years. Sex was not be equal due to the prevalence of migraine in females occurring at a rate of three times that of males. It was likely that more females will volunteer for the study due to this ratio. There are difficulties in objectively quantifying the subjective complaints of a migraine, therefore physician diagnosis may have been incorrect.

CHAPTER 4

Results

The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur a migraine. A pre-test, post-test design where the independent variables were: migraine status, physical activity, testing occasion, sex, exercise, sleep and diagnosis status was utilized. The dependent variables were the four composite scores of ImPACT (verbal memory composite score, visual memory composite score, reaction time composite score, and motor processing speed), level of pain, and impact of headache scores. Analysis of the data included both descriptive statistics and inferential statistical analysis of the ImPACT scores including repeated measures ANOVA, MANOVA, one-way ANOVA, two-way ANOVA and t-tests. All data were analyzed at the alpha $\rho < .05$ level. Mauchly's W test for sphericity was utilized for all analyses. Greenhouse-Geisser corrections were made on any analysis that violated sphericity. The following chapter is divided into three sections: (a) demographic data, (b) hypothesis data, and (c) additional findings.

Demographic Data

A total of 122 people volunteered to participate in the study. Twenty-three males and 99 females were administered all baseline tests. Of the 122 participants, 71 were migraineurs with 54 of them physician diagnosed, while the other 17 met IHS criteria for diagnosis of migraine. Of the 71 migraineurs, 44 incurred a migraine and completed

testing, (one completed half of the testing, and was excluded from analysis). The other 27 did not complete subsequent testing because they did not incur a migraine during the testing period. Fifty-one of the volunteers were controls with 50 of the controls completing all testing. One control quit without reply despite several attempts through e-mail. The participants ethnicities were reported on the physical activity questionnaire. Ethnicities were not varied with 83 reporting their ethnicity as Caucasian, two as Black, or African American, two as Asian, and one as Alaskan/ Native American Indian.

Controls and migraineurs were matched for age, sex and education level. Age was considered a match if the subjects were plus or minus one year. Education level was considered matched if the subjects were in their first or second years of college, third or fourth years of college, or beyond their fourth year of college. Education included all completed years of schooling except kindergarten (ex, college freshmen=12). This left 44 subjects in each group (migraine and non-migraine), 6 of these male, and 38 female. Demographic data by group can be found in Tables 7 and 8.

Table 7: Demographic Data of Migraine and Physical Activity Groups

	Migraine PA Group (M, SD)	Migraine NPA Group (M, SD)	Non-migraine PA Group (M, SD)	Non-migraine NPA Group (M, SD)
N	32	12	33	11
Age (yrs)	22.12 ± 2.49	23.38 ± 2.60	21.02 ± 1.80	22.68 + 3.34
Weight (lbs)	154.25 ± 45.47	159.75 ± 32.75	163.30 ± 30.35	152.27 ± 24.41
Heights (in)	66.13 ± 4.82	66.92 ± 2.50	67.15 ± 2.88	66.04 ± 2.77
Sex: Male	6	0	5	1
Female	26	12	28	10
Handedness:				
Right	31	10	27	9
Left	1	1	4	2
Both	0	1	2	0
Education (yrs)	14.66 ± 4.82	15.17 ± 1.27	14.48 ± 1.62	15.45 ± 2.38
Treatment by Dr. for any headaches:				
Yes	21	8	0	3
No	11	4	33	8
Immediate family have migraines:				
Mom	16	7	8	2
Dad	2	4	3	0
Sibling	12	5	3	0
Grandparent	5	1	0	1
None	0	1	18	6
I don't know	0	0	3	3
HIT scores (range 36-78)	59.25 ± 12.46	65.833 ± 3.18	39.76 ± 3.98	43.18 ± 9.35

Table 8
Scores

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Table 8: Hours of Sleep, Total Symptoms, and ImPACT Neurocognitive Composite Scores for Migraine and Physical Activity Groups

	Migraine PA Group (M, SD)	Migraine NPA Group (M, SD)	Non-migraine PA Group (M, SD)	Non-migraine NPA Group (M, SD)
N	32	12	33	11
Hours of Sleep at 48 hours	7.59 ± 1.33	6.96 ± .865	7.08 ± 1.74	7.32 ± 1.23
Hours of Sleep at 7 days	7.45 ± 1.27	7.58 ± 2.15	7.21 ± 2.04	7.41 ± 1.48
Total symptoms at Baseline	13.00 ± 11.35	16.83 ± 17.34	6.12 ± 6.58	4.91 ± 7.96
Total symptoms at 24 hours	46.69 ± 20.82	50.250± 19.44	5.36 ± 8.92	8.46 ± 19.31
Total Symptoms at 48 hours	18.69 ± 18.10	24.17 ± 13.64	5.03 ± 5.87	5.36 ± 16.51
Total Symptoms at 7 days	6.13 ± 8.01	8.58 ± 12.21	5.12 ± 12.39	2.91 ± 6.61
Verbal Memory Composite Scores at Baseline	87.7 1± 8.00	86.03± 7.67	89.81 ± 7.17	89.37 ± 6.95
Verbal Memory Composite Scores at 24 hours	86.41 ± 9.43	83.65 ± 8.48	90.60 ± 8.41	91.76 ± 6.60
Verbal Memory Composite Scores at 48 hours	85.35 ± 9.08	8.71 ± 8.79	88.34 ± 10.04	87.18 ± 8.16
Verbal Memory Composite Scores at 7 days	89.95± 7.88	87.07 ± 8.56	89.58 ± 11.80	90.18 ± 9.24
Visual Memory Composite Scores at Baseline	73.20 ± 11.30	74.65 + 9.36	72.76 ± 12.44	81.92 ± 6.74
Visual Memory Composite Scores at 24 hours	69.66 ± 13.18	66.84 ± 14.60	76.42 ± 11.95	83.14 ± 7.57

Table 8

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Table 8. Continued

Visual Memory Composite Scores at 48 hours	72.60 ± 10.96	74.65 ± 13.59	74.62 ± 12.15	82.01 ± 10.62
Visual Memory Composite Scores at 7 days	74.16 ± 12.95	73.35 ± 10.04	77.18 ± 13.26	80.60 ± 9.55
Motor Processing Speed Scores at Baseline	37.90 ± 5.37	36.61 ± 7.38	36.88 ± 7.64	40.25 ± 4.99
Motor Processing Speed Scores at 24 hours	35.14 ± 5.86	34.05 ± 6.06	38.04 ± 6.70	41.05 ± 5.03
Motor Processing Speed Scores at 48 hours	37.85 ± 5.44	34.50 ± 8.43	39.49 ± 6.43	41.65 ± 4.11
Motor Processing Speed Scores at 7 days	37.39 ± 8.57	35.66 ± 5.87	40.68 ± 7.21	42.64 ± 6.45
Reaction Time Composite Scores at Baseline	0.60 ± 0.07	0.61± 0.08	0.58 ± 0.06	0.55 ± 0.06
Reaction Time Composite Scores at 24 hours	0.62 ± 0.09	0.62 ± 0.10	0.57 ± 0.06	0.56 ± 0.06
Reaction Time Composite Scores at 48 hours	0.58 ± 0.07	0.61 ± 0.09	0.56 ± 0.07	0.53 ± 0.05
Reaction Time Composite Scores at 7 days	0.57 ± 0.06	0.56 ± 0.09	0.57± 0.08	0.53 ± 0.05

Hypothesis Data

The following hypotheses were tested for the study. All of the hypotheses were tested at the .05 level. Mauchly's W sphericity test was performed on all analyses, and corrected with Greenhouse-Geisser corrections if violated.

Results: Effects of Testing Occasion on Neurocognitive Function among the Migraine Group

H1a. Baseline neurocognitive function scores will be higher than 24 hours post-migraine scores for migrainous college students.

H1b. Neurocognitive function scores at 24 hours will be lower than 48 hours post-migraine scores for migrainous college students.

H1c. Neurocognitive function scores at 48 hours will be lower than 7 days post-migraine scores for migrainous college students.

H1d. Neurocognitive function scores at baseline will exhibit no difference than 7 days post-migraine scores for migrainous college students.

Results: A series of one-way ANOVAs with repeated measures was used to determine if the neurocognitive function scores differed at baseline, 24 hours, 48 hours, and 7 days in the migraine group. Means and standard deviations for each ImPACT score x time are shown in Table 9. Results revealed a main effect for verbal memory composite scores (ρ=.045) (see Table 10). Post-hoc pairwise comparisons with Bonferroni adjustments for multiple comparisons revealed the migraine group scored significantly worse at 24 hours (ρ=.018) and 48 hours (ρ=.011) compared to seven days following a migraine (see Table 11).

A main effect was also found for visual memory composite scores (ρ=.041) (see Table 10). Post-hoc pairwise comparisons with Bonferroni adjustments for multiple

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comparisons revealed the migraine group scored worse at 24 hours (ρ=.052) compared to baseline, and then significantly improved from 24 hours to 48 hours (ρ=.043), and 24 hours to 7 days (ρ=.006) (see Table 12).

A significant main effect was found for reaction time composite scores (ρ=.001). Again using Bonferroni corrections, multiple comparisons revealed significant improvements between 24 and 48 hours (ρ=.024), and baseline to seven days (ρ=.003) (see Table 13) following a migraine. No significant differences were found on motor processing speed (ρ=.109).

Table 9: Means and Standard Deviations for ImPACT Composite Scores for Migraine Group

	Verbal Memory Composite Scores (M,SD)	Visual Memory Composite Scores (M,SD)	Motor Processing Speed Scores (M,SD)	Reaction Time Composite Scores (M,SD)
Baseline	87.25 ± 7.86	73.60 ± 10.72	37.55 ± 5.92	0.60 ± 0.07
24 Hours	85.66 ± 9.17	68.89 ± 13.47	34.84 ± 5.87	0.62 ± 0.09
48 Hours	85.83 ± 8.93	73.13 ± 11.61	36.93 ± 6.46	0.58 ± 0.07
7 days	89.15 ± 8.07	73.94 ± 12.12	36.92 ± 7.90	0.57 ± 0.07

Table 10: One-way ANOVAs for Migraine Group x Time for Neurocognitive Composite Scores

	df	F	P-value	Power
Verbal Memory Comp. Score	3	2.764	0.045*	0.657
Visual Memory Comp. Score	3	2.83	0.041*	0.669
Motor Processing Speed Score	3	2.062	0.109	0.518
Reaction Time Comp. Score	3	9.361	0.000012*	0.996

* Significant at the $p < .05$ level

Table 11: Pairwise Comparisons for Migraine Group Verbal Memory Composite Scores

	Mean Difference	Standard Error	Significance
Baseline to 24 hours	1.591	1.179	0.184
24 hours to 48 hours	0.169	1.50	0.911
48 hours to 7 days	3.334	1.261	0.011*
Baseline to 7 days	1.912	1.305	0.150
24 hours to 7 days	3.503	1.422	0.018*

* Significant at the $\rho < .05$ level

Table 12: Pairwise Comparisons for Migraine Group for Visual Memory Composite Scores

	Mean Difference	Standard Error	Significance
Baseline to 24 hours	4.704	2.354	0.052
24 hours to 48 hours	4.238	2.031	0.043*
48 hours to 7 days	0.805	1.910	0.676
Baseline to 7 days	0.339	2.036	0.869
24 hours to 7 days	5.043	1.734	0.006*

* Significant at the p <.05 level

Table 13: Pairwise Comparisons for Migraine Group for Reaction Time Composite Scores

	Mean Difference	Standard Error	Significance
Baseline to 24 hours	0.020	0.014	0.921
24 hours to 48 hours	0.032	0.010	0.024*
48 hours to 7 days	0.023	0.009	0.067
Baseline to 7 days	0.035	0.009	0.003*
24 hours to 7 days	0.055	0.012	<0.01*

* Significant at the p <.05 level

Results: Effects of Testing Occasion on Neurocognitive Function among the Non-Migraine Group

H1e. Neurocognitive function scores at baseline will exhibit no difference than 24 hours, 48 hours or seven days post-baseline scores for non-migrainous college students.

Result: A series of one-way ANOVAs with repeated measures was used to determine if the neurocognitive function scores differed at each time in the non-migraine group. Post-hoc pairwise comparisons with Bonferroni corrections were completed to determine if there were any significant differences by time. Means and standard deviations for each composite score x time are shown in Table 14. Results revealed a main effect for motor processing speed (ρ=.011) (see Table 15). Pairwise comparisons revealed a learning effect with the non-migraine group performing significantly better from baseline to 7 days (ρ=.047) (see Table 16). There were no significant differences found for verbal memory composite scores (ρ=.180), visual memory composite scores (ρ=.304, or reaction time composite scores (ρ=.179).

Table 14: Means and Standard Deviations for ImPACT Composite Scores for the Non-migraine Group

	Verbal Memory Composite Scores (M,SD)	Visual Memory Composite Scores (M,SD)	Processing Speed Scores (M,SD)	Reaction Time Composite Scores (M,SD)
Baseline	89.70 ± 7.04	75.05 ± 11.91	37.72 ± 7.17	0.57 ± 0.06
24 Hours	90.89 ± 7.94	78.10 ± 11.33	38.79 ± 6.40	0.57 ± 0.06
48 Hours	88.05 ± 9.53	76.47 ± 12.11	40.04 ± 5.97	0.56 ± 0.07
7 days	89.73 ± 11.11	78.03 ± 12.42	41.17 ± 7.00	0.56 ± 0.07

Table 15: One-way ANOVAs for Non-migraine Group x Time for Neurocognitive Composite Scores

	df	F	P-value	Power
Verbal Memory Comp. Score	3	1.655	0.180	0.426
Visual Memory Comp. Score	3	1.149	0.332	0.304
Motor Processing Speed Score	3	3.829	0.011*	0.810
Reaction Time Comp. Score	3	1.661	0.179	0.427

* Significant at the $p < .05$ level

Table 16: Pairwise Comparisons for Non-migraine Group for Motor Processing Speed Composite Scores

	Mean Difference	Standard Error	Significance
Baseline to 24 hours	1.067	1.140	1.00
24 hours to 48 hours	1.239	1.047	1.00
48 hours to 7 days	1.141	0.739	0.779
Baseline to 7 days	3.447	1.237	0.047*
24 hours to 7 days	2.380	1.078	0.195

* Significant at the $p < .05$ level

Results: Effects of Migraine Status on Neurocognitive Function

H2a. The migraineurs and non-migraineurs will exhibit no difference in neurocognitive function at baseline.

H2b. The migraineurs will exhibit lower neurocognitive function scores than the non-migraineurs at 24 hours post-migraine.

H2c. The migraineurs will exhibit lower neurocognitive function scores than non-migraineurs at 48 hours post-migraine.

H2d. The migraineurs will exhibit lower neurocognitive function scores than the non-migraineurs at 7 days post-migraine.

Results: A repeated measures MANOVA for group x time was used to determine differences between the migraine and non-migraine groups. Means and standard deviations for both groups are presented in Tables 9 (migraine) and 14 (non-migraine).

A significant interaction was found for group x time for visual memory composite scores (ρ=.036), motor processing speed composite scores (ρ=.044), and reaction time composite scores (ρ=.002) (see Table 17, Figures 1-4). There were no significant

differences for verbal memory composite scores for the interaction between group x time (ρ=.100). To further examine the relationships occurring at each time, Univariate ANOVAs were performed.

Post-hoc univariate ANOVAs for baseline composite scores revealed a significant difference for reaction time composite scores with migraineurs exhibiting a slower reaction time (ρ=.045) compared to the non-migraine group. Verbal memory composite scores (ρ=.128), visual memory composite scores (ρ=.549) and motor processing speed composite scores (ρ=.899) were not significantly different for the migraine and non-migraine groups at baseline (see Table 18).

Univariate ANOVAs for neurocognitive composite scores at 24 hours revealed that migraineurs had a significantly slower reaction time (ρ=.002), decreased verbal memory (ρ=.005), decreased visual memory (ρ=.001) and decreased motor processing speed (ρ= .003) after a migraine headache when compared to non-migraine controls at 24 hours (see Table 19).

Univariate ANOVAs for neurocognitive composite scores at 48 hours indicated a significantly decreased motor processing speed (ρ=.022) as well as a continuance of a slower reaction time (ρ=.028) after a migraine when compared to non-migraine controls. Verbal memory (ρ=.263) and visual memory (ρ=.109) composite scores were not significantly different at 48 hours between groups (see Table 20).

Univariate ANOVAs for ImPACT composite scores at seven days indicated that the migraine group performed significantly worse in motor processing speed compared to the non-migraine group (ρ=.009), while verbal memory (ρ=.785), visual memory

(ρ=.121), and reaction time (ρ=.883) were not significantly different between the migraine and non-migraine controls (see Table 21).

Table 17: Repeated Measures MANOVAs for Group x Time for Neurocognitive Composite Scores

	df	F	P-value	Power
Verbal Memory Comp. Score	3	2.103	0.100	0.534
Visual Memory Comp. Score	3	2.898	0.036*	0.687
Motor Processing Speed Score	3	2.741	0.044*	0.660
Reaction Time Comp. Score	3	5.116	0.002*	0.919

* Significant at the ρ <.05 level

Table 18: Univariate ANOVA for Group Differences at Baseline for Neurocognitive Composite Scores

	df	F	P-value
Verbal Memory Comp. Score	1	2.364	0.128
Visual Memory Comp. Score	1	0.361	0.549
Motor Processing Speed Score	1	0.707	0.899
Reaction Time Comp. Score	1	4.128	0.045*

* Significant at the ρ <.05 level

Table 19: Univariate ANOVA for Group Differences at 24 hours for Neurocognitive Composite Scores

	df	F	P-value
Verbal Memory Comp. Score	1	8.176	0.005*
Visual Memory Comp. Score	1	12.052	0.001*
Motor Processing Speed Score	1	9.093	0.003*
Reaction Time Comp. Score	1	10.034	0.002*

* Significant at the $\rho < .05$ level

Table 20: Univariate ANOVA for Group Differences at 48 hours for Neurocognitive Composite Scores

	df	F	P-value
Verbal Memory Comp. Score	1	1.271	0.263
Visual Memory Comp. Score	1	1.742	0.109
Motor Processing Speed Score	1	5.456	0.022*
Reaction Time Comp. Score	1	4.982	0.028*

* Significant at the $\rho < .05$ level

Table 21: Univariate ANOVA for Group Differences at 7 days for Neurocognitive Composite Scores

	df	F	P-value
Verbal Memory Comp. Score	1	0.075	0.785
Visual Memory Comp. Score	1	2.450	0.121
Motor Processing Speed Score	1	7.142	0.009*
Reaction Time Comp. Score	1	0.022	0.883

* Significant at the $\rho < .05$ level

Figure 1. Means of Group x Time for Verbal Memory Composite Scores

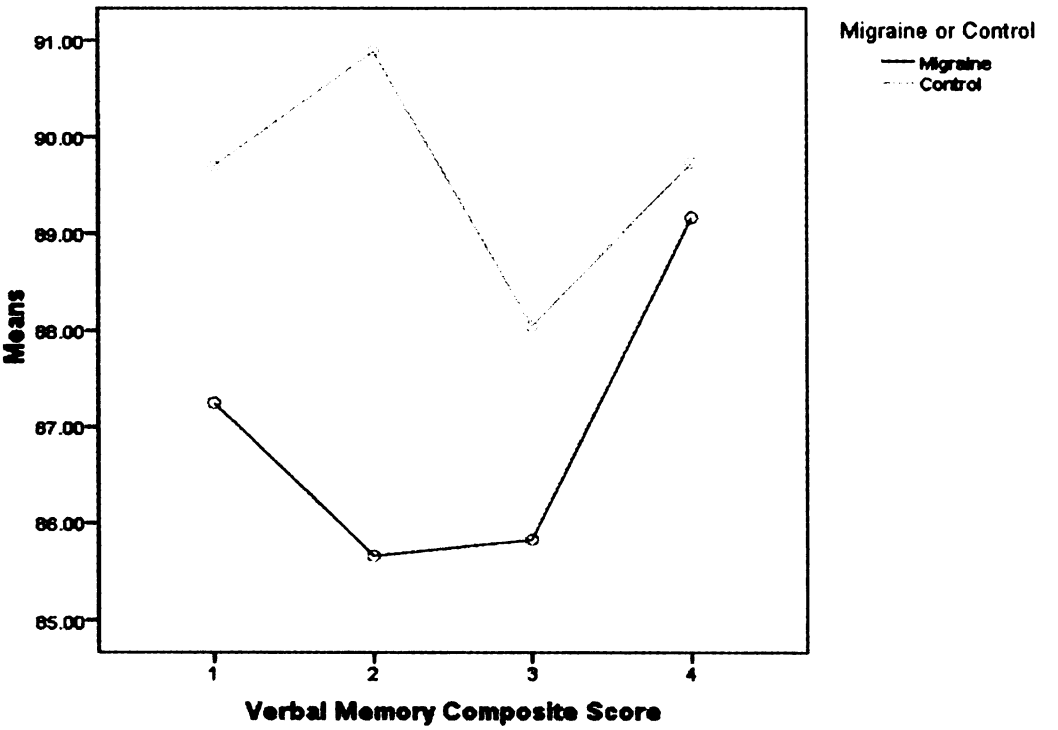

Figure 2. Means for Group x Time for Visual Memory Composite Scores

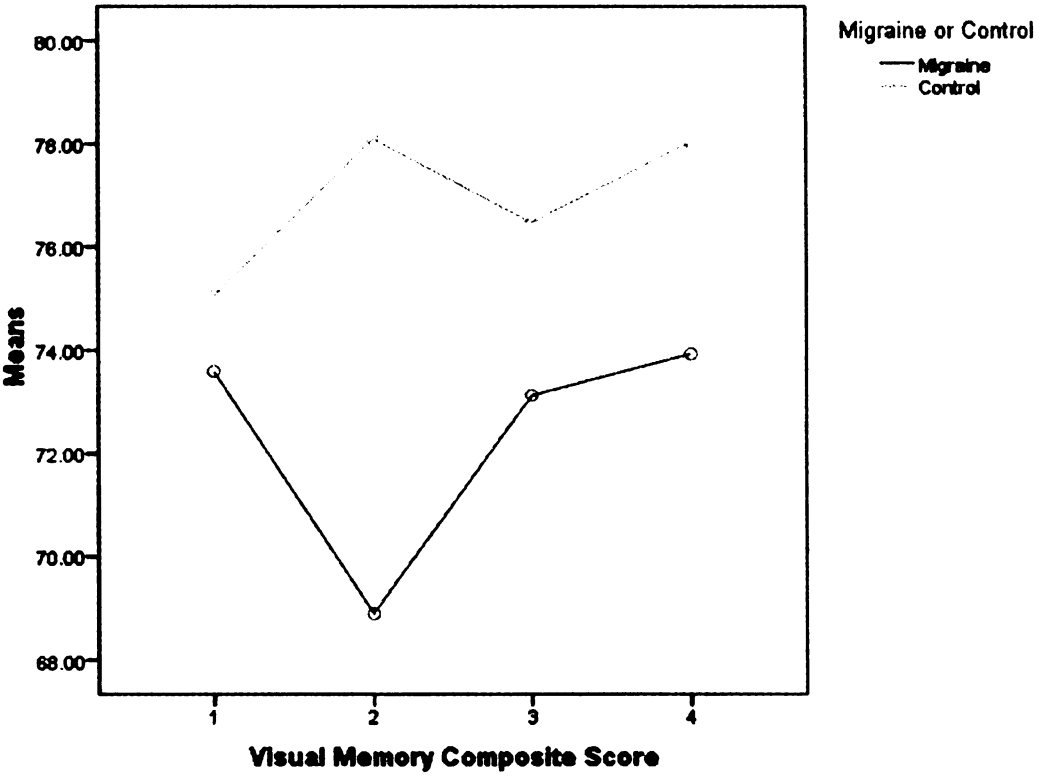

Figure 3: Means for Group x Time for Motor Processing Speed Composite Scores

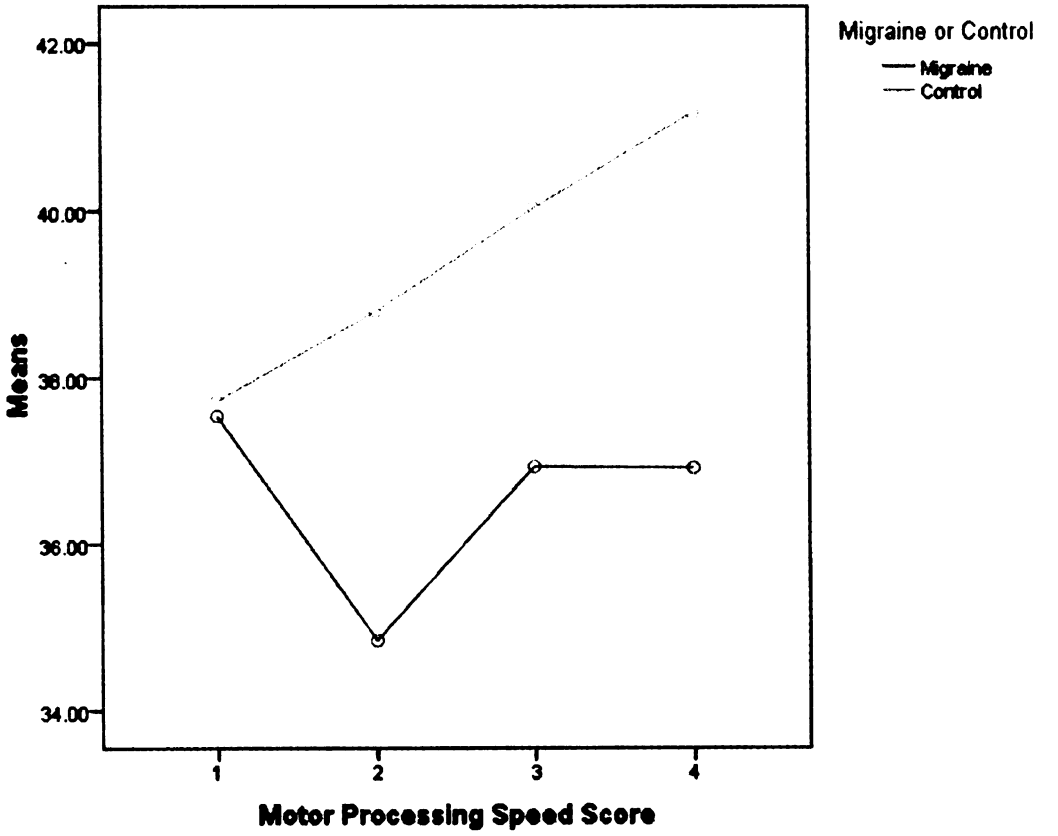

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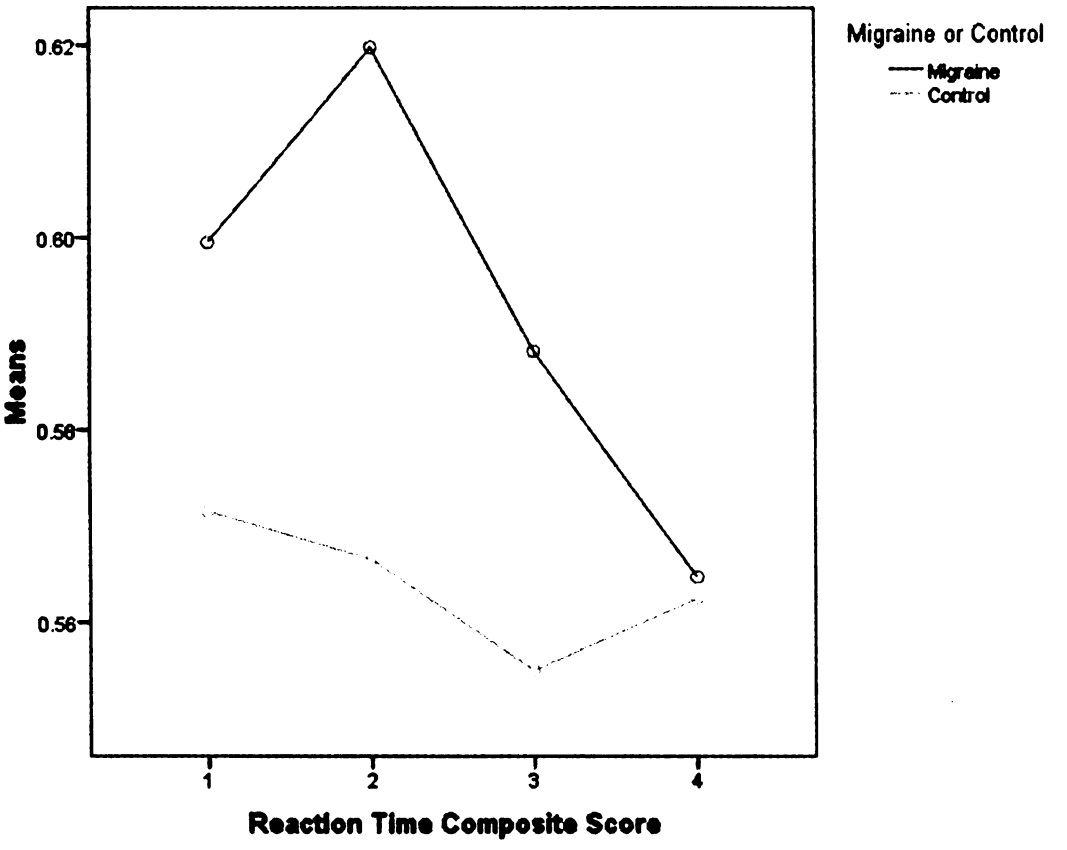
Figure 4: Means for Group x Time for Reaction Time Composite Scores.



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Results: Effects of Physical Activity by Testing Occasion on Neurocognitive Function

H3a. Physically active migraineurs will exhibit higher neurocognitive function scores than non-physically active migraineurs at 24 hours.

H3b. Physically active migraineurs will exhibit higher neurocognitive function scores than non-physically active migraineurs at 48 hours.

H3c. Physically active migraineurs will exhibit no difference on neurocognitive function scores than non-physically active migraineurs at 7 days.

H3d. Physically active non-migraineurs will exhibit no difference in neurocognitive function scores than non-physically active non-migraineurs at any testing occasion.

Results: Due to the change in testing protocol in the administration of the BRFSS, the number of subjects completing the same protocol decreased to 42. This left 31 individuals who were considered PA and 11 who were considered NPA. Repeated measures ANOVAs revealed no significant main effects between physically active and non-physically active migraineurs for verbal memory composite scores (ρ =.325), visual memory composite scores (ρ=.545), motor processing speed composite scores (ρ=.716) and reaction time composite scores (ρ =.314) (see Table 22).

Repeated measures ANOVAs found no significant main effects between physically active and non-physically active non-migraine controls for verbal memory composite scores (ρ =.869), visual memory composite scores (ρ=.627), motor processing speed composite scores (.933) and reaction time composite scores (ρ = .232) (see Table 23).

Table 22: Repeated Measures ANOVA for Neurocognitive Function Composite Scores for Migraine x PA Status x Time

	df	F	P-value	Power
Verbal Memory Comp. Score	3	1.139	0.325	0.224
Visual Memory Comp. Score	3	0.612	0.545	0.149
Motor Processing Speed Score	3	0.336	0.716	0.102
Reaction Time Comp. Score	3	1.177	0.314	0.251

* Significant at the $\rho < .05$ level

Table 23: Repeated Measures ANOVA for Non-Migraine x PA Status x Time for Neurocognitive Function Scores

	df	F	P-value	Power
Verbal Memory Comp. Score	3	0.239	0.869	0.094
Visual Memory Comp. Score	3	0.583	0.627	0.168
Motor Processing Speed Score	3	0.144	0.933	0.076
Reaction Time Comp. Score	3	1.44	0.232	0.376

* Significant at the $\rho < .05$ level

Exploratory Hypotheses

The purpose of the exploratory hypotheses was to examine the relationships between additional variables collected throughout the study. The independent variables were:

1. migraine status — migraine (M) and non-migraine (NM])
2. sex — female and male
3. diagnosis status — physician diagnosed (PD) and self-diagnosed (SD)
4. testing occasion — 24 hours only
5. physical activity — met physical activity recommendations (PA)
   did not meet physical activity recommendations (NPA).

The dependent variables were level of pain and impact of headache scores. The Headache Impact Test (HIT) score was referred to as impact of headache scores.

H4. Female migraineurs will rate their pain higher than male migraineurs at 24 hours post-migraine.

Result: Six males and 38 females completed the 24 hour questionnaire reporting their pain level 24 hours after a migraine. A t-test revealed females (6.167 ± 2.228) significantly rated their pain higher than males (7.592 ± 1.283) after a migraine ($\rho=.028$) (Table 24).

H5. Physician diagnosed migraineurs will rate their pain higher than self-diagnosed migraineurs at 24 hours post-migraine.

Result: Thirty-three migraineurs had obtained a diagnosis of migraine from their physician, while 11 had not sought physician diagnosis, but met IHS 2005 diagnostic

criteria. A t-test revealed there were no significant differences between the physician diagnosed (7.58 ± 1.50) and self-diagnosed (6.86 ± 1.42) groups (ρ=.175) (see Table 24).

Table 24: T-test for Pain level at 24 hours x Sex or Diagnosis Status

	df	F-value	P-value
Males vs Females	42	1.474	0.028*
Physician Diagnosed vs Self-diagnosed	42	0.227	0.175

* Significant at the ρ <.05 level

H6a. Physically active individuals will score lower than non-physically active individuals on their impact of headache score.

H6b. Physically active migraineurs will score lower than non-physically active migraineurs on their impact of headache scores.

H6c. Physically active non-migraineurs will score lower than non-physically active non-migraineurs on their impact of headache scores.

Result: A two-way ANOVA was used to determine the impact of migraine group and physically activity on HIT scores. Means and standard deviations were reported in Table 25. Physically active individuals rated their headache impact scores significantly lower than non-physically active individuals (ρ= .020). Lower HIT scores in physically active migraineurs (ρ=.080) and physically active controls (ρ=.094) compared to non-physically active migraineurs and controls approached significance (see Table 26).

Table 25: Means and Standard Deviations for Migraine Group and PA Status for HIT Scores

	Migraine PA Group (M, SD)	Migraine NPA Group (M, SD)	Non-migraine PA Group (M, SD)	Non-migraine NPA Group (M, SD)	All PA (M, SD)	All NPA (M, SD)
N	32	12	33	11	65	23
HIT scores (range 36-78)	59.25 ± 12.46	65.83 ± 3.16	39.76 ± 3.98	43.18 ± 9.35	49.35 ± 13.41	55.00 ± 13.36

Table 26: Two-way ANOVA for Migraine Group x PA Status

	df	F-value	P-value	Power
All	1	5.660	0.020*	0.652
Migraine	1	3.226	0.080	0.419
Non-migraine	1	2.945	0.094	0.389

* Significant at the $\rho < .05$ level

Results: Exploratory Research Questions

The purpose of the exploratory research questions was to examine the relationship between additional variables previously not researched in the literature. The independent variables were migraine status (migraine only), exercise (yes and no), and sleep (none, a little to 4 hours, 4-8 hours, more than 8 hours). The dependent variables were pain, and the four composite scores of ImPACT.

RQ 1. Was there a difference in pain reported at 24 hours post-migraine for college students who use prescription medications, over-the-counter medications, or no medications for their migraine headaches?

Result: A one-way ANOVA found no significant difference between migraine groups (ρ=.205) (Table 27).

Table 27: Means and Standard Deviations for Migraine Group x Type of Medication

	OTC (M, SD)	RX (M, SD)	None (M, SD)	OTC and RX (M, SD)
N	27	7	7	3
Migraine	7.39 $\pm$ 1.52	7.71 $\pm$ 1.70	6.57 $\pm$ 1.13	8.67 $\pm$ .58

RQ 2. Was there a difference in pain reported at 24 hours post-migraine for college students who did or did not exercise during the 24 hours immediately following onset of a migraine headache?

Result: Thirty-seven individuals did not exercise (7.50 $\pm$ 1.34) 24 hours prior to their migraine, and seven did exercise (6.86 $\pm$ 2.19) prior to their migraine. A t-test found no significant differences between individuals who exercised and did not exercise in the 24 hours prior to their migraine (ρ=.303).

RQ 3. Was there a difference in neurocognitive function at 24 hours post-migraine for college students who did or did not sleep during hours immediately following onset of a migraine headache?

Result: Seven individuals had not slept since onset of their migraine, seven had slept a little to four hours, 18 had slept 4-8 hours and 12 had slept more than 8 hours. Means and standard deviations by neurocognitive composite scores are listed in Table 28. A one-way ANOVA found no significant main effects between hours of sleep since migraine for verbal memory composite scores (ρ =.446), visual memory composite scores

(ρ=.421), motor processing speed composite scores (ρ=.955) and reaction time composite scores (ρ= .913) at 24 hours (see Table 29).

Table 28: Means and Standard Deviations for Neurocognitive Function and Hours of Sleep since Migraine

	None	A little to 4 hours	4-8 Hours	More than 8 hours
N	7	7	18	12
Verbal Memory Comp. Score	80.58 ± 7.61	87.50 ± 6.57	86.86 ± 9.65	85.75 ± 10.42
Visual Memory Comp. Score	62.95 ± 15.26	70.24 ± 6.25	72.22 ±10.66	66.58 ± 18.37
Motor Processing Speed Score	34.45 ± 2.93	34.71 ± 6.57	35.40 + 3.96	35.40 ± 3.96
Reaction Time Comp. Score0	0.63 ± 0.07	0.60 ± 0.11	0.63 ± 0.12	0.61 ± 0.06

Table 29: ANOVA for Hours of Sleep since Migraine for Neurocognitive Function

	df	F	P-value
Verbal Memory Comp. Score	3	0.907	0.446
Visual Memory Comp. Score	3	0.960	0.421
Motor Processing Speed Score	3	0.049	0.985
Reaction Time Comp. Score	3	0.175	0.913

* Significant at the ρ <.05 level

CHAPTER 5

Discussion

The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur a migraine. Migraine and non-migraine groups were matched for age, sex and education level. A pre-test, post-test design where the independent variables were: migraine status, physical activity, testing occasion, sex, exercise, sleep and diagnosis status was utilized. The dependent variables were the four composite scores of ImPACT, level of pain, and impact of headache scores. The following section is divided into four sections: (a) discussion of results, (b) conclusions, (c) limitations and (d) recommendations for future research.

Discussion of Results

Effect of Time on Neurocognitive Function Scores

It was first hypothesized that there would be an effect of testing occasion on neurocognitive function. For migraineurs, it was hypothesized that 24 hours post-migraine neurocognitive function would be significantly lower than baseline scores. Then at 48 hours, neurocognitive function would be significantly better than 24 hours and continue to get better by seven day. It was hypothesized that seven days scores would be similar to baseline scores in migraineurs. The non-migraine controls were expected to have similar scores at each time. Each of the four composite scores will be discussed separately with differences noted between migraineurs and non-migraine controls.

The migraine group exhibited significant neurocognitive impairments on verbal memory composite scores. Specifically, verbal memory was impaired 24 hours and 48 hours after incurring a migraine compared to seven days post-migraine. Verbal memory composite score is comprised of the average percentage correct of three tasks: a symbol number match task, word recognition, and a letter memory task with an accompanying distractor task (Iverson, Lovell, & Collins, 2003). As expected the non-migraine group's verbal memory composite scores consistently stayed in the average range compared to normative data with no significant differences noted across time.

Collegiate students who suffered from migraine headaches exhibited verbal memory impairments up to 48 hours following their migraine. Other researchers have reported that migraineurs were found to suffer from temporary impairments in verbal learning after suffering from a migraine headache (Black et al. 1997). However, Black et al. conducted a qualitative study by interviewing 30 migraineurs in their clinic or on the telephone to determine their cognitive deficits. Although, these findings were similar to this study, Black and colleagues used qualitative methods and did not compare their results to controls.

A Dutch life course study found that individuals who suffered from migraine headaches had decreased verbal performance at 26 years of age (individuals were tested from 3-26 yrs at specific intervals) compared to controls aged 3 to 13 years. These verbal memory deficits were not present beyond 15 years. The researchers suggest that verbal memory deficits in migraineurs was unlikely to have resulted from cumulative attacks and may be related to developmental factors (Waldie, Hausmann, Milne, & Poulton,

2002). Other studies have also found no differences at baseline between migraineurs and controls in verbal memory (Bell, Primeau, Sweet, & Loftland, 1999).

These studies are consistent with this study that found baseline verbal memory scores were similar in migraineurs and non-migraineurs, thus, illustrating no verbal memory impairments in college students in their early twenties.

In contrast to this study, Zeitlin and Oddy (1984) found baseline decreases in forced choice word scores for migraineurs when compared to controls. However, there were differences in methodology as Zeitlin and Oddy utilized a small sample of poorly matched subjects, used older subjects (mean age 36 with at least a 10 year history) than tested in this study, and only migraineurs who were considered severely affected by their migraine.

The migraine group exhibited significant neurocognitive impairments on visual memory scores. Specifically, visual memory was impaired at 24 hours, compared with baseline, 48 hours, and seven days. Visual memory composite scores are comprised of the average percent correct of two separate tasks: a recognition memory task that requires the abstract discrimination of a number of line art drawings, and a memory task that requires the identification of a series of highlighted Xs and Os after a distractor task (Iverson, Lovell, & Collins, 2003).

The only research found that measured visual memory following migraine headache were two drug studies utilizing sumatriptan. A drug study with sumatriptan injection during a migraine found similar cognitive declines in all areas, specifically visual memory (matching to sample) (Farmer, Cady, Bleiberg, & Reeves, 2000). Farmer and colleagues found that visual memory scores returned to normal 15 minutes after

injection. While our results were not that specific to medication and did not include the migraine interval, further testing during the headache interval may show increased cognitive deficits at that time. A follow-up study also found cognitive declines in visual memory (matching to sample) (Farmer, et al., 2001). Similar to the last study their cognitive decline resolved quickly after sumatriptan (nasal spray). In contrast to this, Leijdekkers and colleagues (1990) did not find significant differences between controls and migraineurs in pattern memory tests (task similar to ImPACT's visual memory task) two days symptom free after incurring a migraine.

The non-migraine group's motor processing speed composite scores consistently stayed in the average range compared to a normative group with incremental improvements in scores that resulted in the seven days scores being significantly higher scores than baseline scores. These differences between trials were found in other ImPACT tests with insignificant improvements made between trials (Iverson, Lovell, & Collins, 2003). This is most likely due to testing effects and familiarity with the program, although no other studies have found testing effects relating to ImPACT. Therefore, it may have been related to the population utilized.

The migraine group did not exhibit significant differences over time in motor processing speed. The motor processing speed composite score represents the Xs and Os total correct (interference task) and a three letter recall that are completed as distractor tasks for the memory paradigms as well as average correct for symbol match (Schatz, Pardini, Lovell, Collins, & Podell, 2006). This takes into account individuals who may slow down their speed to increase their accuracy (Zeitlin & Oddy, 1984).

To date, no studies have been conducted that specifically examined the relationship of motor processing speed after a migraine headache. However, the Trail-Making test A and Trail-Making test B have been validated to be significantly correlated with motor processing speed (Iverson, Franzen, Lovell, & Collins, 2004). Zeitlin and Oddy (1984) found significant differences between migraineurs and controls in the Trailmaking B test when migraine free, with migraineurs significantly slower. Another study utilized finger tapping for motor speed testing and found no significant differences between migraineurs and controls when migraine free (Leijdekkers, Goudswaard, Menges, & Oriebeke, 1990). Reliable change estimates for ImPACT indices indicate that a decline of three points or an improvement of 7 points is considered within an 80% confidence interval for motor processing speed (Iverson, Lovell, & Collins, 2003). This study found a decrease of 2.7 points at 24 hours and then improvements of 2.1 points at 48 hours. While the results were not statistically significant, further examination of motor processing speed is warrented following migraine headache.

The migraine group in this investigation exhibited significant neurocognitive impairments on reaction time composite scores. Specifically, reaction time was impaired at 24 hours compared to 48 hours and seven days. Reaction time composite scores consist of the speed of the reaction (in milliseconds) when a correct score is given for several tests. This includes a choice reaction test, symbol match test, and a go/no go test (Iverson, Lovell, & Collins, 2003) (see page 61 for computations). In the non-migraine group reaction time scores were consistently in the average range compared to normative scores with no significant differences noted by time.

Collegiate students who incurred a migraine had decreased reaction time 24 hours following their migraine. In a study that utilized the Headache Care Center Automated Neuropsychological Assessment Metrics (HCC-ANAM) test during migraine and 15, 30 and 45 minutes after taking sumatriptan found a significant drop in cognitive performance during the migraine. Specifically, simple reaction time, continuous performance test (recall tasks requiring focus, concentration and attention), and math (simple arithmetic) skills were significantly lower 15 minutes after a migraine compared to their baseline scores. However, these impairments were not found at 30 or 45 minutes after a migraine. Similarly to ImPACT, HCC ANAM is a computerized neurocognitive test battery used to measure cognitive deficits. A possible reason for lack of cognitive deficits at 30 or 45 minutes post-migraine may have been due to a learning effect. Furthermore, the HCC ANAM study did not measure cognitive function after 45 minutes. The current study found a decreased reaction time 24 hours post-migraine, which may affect collegiate students' daily lives and performance on tests and term paper.

Overall, these cognitive declines in average college students may result in reduced test grades dependent on the level of individual cognitive decline experienced during and after migraine. Individuals who have a decreased reaction time may be more likely to react slower while driving, potentially resulting in an injury they typically would have been able to avoid. Verbal and visual memory deficits may result in difficulty concentrating when writing a paper or studying for exams. Family, friends, and professors may not understand why the migraineur is still experiencing difficulty processing and remembering one to two days after the migraine headache itself is gone,

leading to frustration and self-doubt. Therefore, cognitive declines following migraine headache affect daily living in various situations.

Effect of Migraine Status on Neurocognitive Function Scores

It was also hypothesized that migraineurs would score significantly less than controls at 24 hours, 48 hours, and seven days for neurocognitive function with baseline testing hypothesized to be equal between the groups. Migraine status had an effect on neurocognitive function of collegiate students. Overall, migraineurs were significantly different than controls for visual and verbal memory, motor processing speed and reaction time scores. Specifically, at 24 hours migraineurs neurocognitive function was decreased in verbal memory, visual memory and motor processing speed and had a slower reaction time when compared to non-migraine controls. At 48 hours motor processing speed remained lower, as well as a continuance of a slower reaction time when migraineurs were compared to non-migraine controls. At seven days, motor processing speed remained lower while verbal memory, visual memory and reaction time were not significantly different between migraineurs and non-migraine controls.

At baseline, the only neurocognitive decreases found were reaction time, with migraineurs exhibiting a slower reaction time than non-migraineurs. One study found slower choice reaction time in migraineurs when headache free (Zeitlin & Oddy, 1984). In a dominant finger tapping test (10 s) individuals with classic migraine exhibited slower pure motor speeds than controls (Hooker & Raskin, 1986). Therefore, there may be reaction time deficits in individuals who suffer from migraine headaches.

Collegiate students were still impaired on motor processing speed 7 days after incurring a migraine compared to controls. Researchers have reported that processing

speed has been found to decline in migraineurs (Evers, Bauer, Suhr, Husstedt, & Grotemeyer, 1997; Wray, Mijovic-Prele, & Kosslyn, 1995). This study provides preliminary data that demonstrate motor processing speed takes the longest to recover following a migraine headache. A possible explanation may be due to structural or functional brain dysfunctions (Swartz & Kern, 2004; Kruit, et al., 2004) that have not yet been detected in a younger population.

Overall, when compared to controls, migraineurs significantly declined after a migraine headache on neurocognitive function tests. These comparisons may provide some insight on how a non-migraine brain functions compared to a migraine brain after a migraine attack. Motor processing delays can change the ability of an individual to execute and modify a plan of action (Gaudino, Geisler, & Squires, 1995). This could affect the individual in physical events, or in academia where new concepts introduced the days after a migraine may not be conceptualized, which can further delay processing when the student is asked to recall or explain the information for a written exam.

Effect of Physical Activity Status on Neurocognitive Function Scores

Finally, it was hypothesized that physically active migraineurs would exhibit higher neurocognitive function scores than non-physically active migraineurs at 24 and 48 hours post migraine. This hypothesis was consequently formed from the relationship between migraines and exercise. Stress is a trigger for migraines (Turner, Molgaard, Gardner, Rothrock, & Stang, 1995). Exercise, a form of migraine management, is known to decrease stress levels (Folkins & Sime, 1981). After a cardiovascular exercise program intervention migraineurs reported decreased frequency, intensity and duration of migraine headaches (Lockett & Campbell, 1991). Therefore, it was expected that regular physical

activity would assist the migraineur in recovering from cognitive declines. It was also hypothesized that neurocognitive function would remain the same in non-migraineurs regardless of their physical activity status. Physical activity was determined by number of minutes per week of moderate and vigorous activity the individual reported. Individuals were considered physically active if they reported exercising more than 150 minutes of moderate activity or 75 minutes of vigorous activity per week. This study found there were no significant differences between physically active and non-physically active migraineurs. In addition, there were no significant differences in non-migraine controls with different physical activity status.

This study had a large majority of collegiate students who were physically active compared to sedentary students. As a result, this may have contributed to the lack of significant differences found in this study. Other research studies that have found an exercise program improves migraine outcomes did not use a collegiate population (Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003; Fitterling, Martin, Gramling, Cole, & Milan, 1988; Lockett & Campbell, 1991). Lockett and Campbell (1991) initiated a six-week cardiovascular exercise program and found decreases in pain level during migraine headache as well as trends toward decreased frequency, intensity, and duration. Similarly, another six-week study where subjects exercised at 60% of their max heart rate for 40 minutes (10 minute warm-up, 20 minute exercise, 10 minute rest) three times a week found that subjects reported a significant decrease in intensity and frequency of migraine (Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003). While, Fitterling and colleagues (1988) reported a reduction in vascular headache activity in four out of five subjects after a six-week exercise intervention. The results of these studies suggest maintenance of an

exercise program is essential for decreased migraine frequency; however, these studies did not examine cognitive function. Furthermore, it is not clear if collegiate students in this study were more aerobically fit compared to other studies. College students in the current study has multiple avenues available to them for physical activity including numerous sports clubs, classes, an onsite recreation facility, as well as a local community that embraces outdoor recreation. They also were more likely to walk to bike to class than a general population would walk or bike to work. With previous research finding physical activity improves migraine outcome, further research is warranted to examine this relationship. In addition, future research should continue to research the collegiate population as well as delve into a general population where larger variety of fitness levels may be found.

Additional Hypotheses and Research Questions

It was hypothesized that females would rate their pain higher than males 24 hours post migraine. Females significantly reported higher levels of pain at 24 hours for their last migraine than males. Female prevalence of migraine is estimated at 18% and males 6% (Lipton et al., 2001; Lipton et al., 2002). College aged females reported more frequent migraines that last longer, and throb more (Kinart, Cuppett, & Berg, 2002). In contrast, an epidemiological study of a nationwide sample found similar frequency of severe headaches between males and females (Lipton et al., 2001).

With approximately 50% of migraineurs seeking diagnosis (Lipton et al., 2001; Bigal, Kolodner, Lafata, Loetta, & Lioton, 2006), and age of the first attack about 18 years, most members of our demographic were expected to have a shorter migraine history. It was hypothesized that physician diagnosed migraineurs would rate their pain

higher than self-diagnosed migraineurs at 24 hours post-migraine. No significant differences were found between groups. Other researchers have found that physician diagnosed individuals more frequently report symptoms (nausea, vomiting, blurred vision, aura, neurological signs, photophobia, phonophobia) of migraine; however, they reported equal levels of pulsitile pain in both physician and self-diagnosed groups (Lipton et al, 2001). A possible explanation for differences between this study and Liptons study may be due to the ability of over the counter medications to effectively treat the individual's migraine. A higher number of migraineurs reported (75%) physician diagnosis compared to the general populations 50% physician diagnosed.

It was hypothesized that physically active individuals would score lower on their impact of headache scores in both migraineurs and non-migraine controls. Headache Impact test (HIT) scores (range 36-78) increased with the amount of reported disability that headaches have on their daily activities, with the highest HIT scores indicating severe daily disruptions. Significant differences were found with physically active individuals rating their daily impact of headaches lower than those who were not physically active. When separated into migraine and non-migraine, physically active individuals consistently scored lower than non-physically active individuals. Previous research has linked moderate exercise to improvements in psychological well being and mood states in women (Cramer, Neiman, & Lee, 1991), and suggested trends toward improvements in frequency, intensity and duration of migraines through a cardiovascular exercise program (Lockett & Campbell, 1991). Others indicate exercise as a method of migraine abortion (Darling, 1991). Regular exercise increases beta-endorphin levels

(Köseoglu, Akboyraz, Soyuer, & Ersoy, 2003), which may cause migraineurs to rate their daily impact of their headaches lower with its natural analgesic properties.

It was hypothesized that the type of medication (OTC, RX, None, OTC and RX) would have an impact on pain levels of migraineurs at 24 hours. Migraineurs were specifically asked to contact the investigator after the onset of a migraine to facilitate a meeting within 24 hours of their migraine. Migraineurs were allowed to sleep, take medication, and any other means necessary to rid themselves of the migraine. Most migraineurs were not still suffering from the migraine during testing, but many still had lingering headaches and other side effects. There were no significant differences found in type of medication. Lipton et al. (2001) found that 41% of the population utilizes prescription medications and 58% utilizes OTC. With most of our population (with 75% seeking physician diagnosis compared to 50% in the general population) utilizing OTC medications (68%), and only 10 (22%) utilizing prescriptions, it is assumed that the OTC was adequate in providing pain relief. Furthermore, OTC medication is easier to access and cheaper for college students who may be struggling with finances due to high cost of tuition.

It was hypothesized that exercise in the 24 hours preceding testing (prior to their migraine) would decrease college students' perception of pain during their migraine. No significant differences were found for individuals who exercise prior to their migraine compared to those who did not exercise. Previous research has found that exercise decreases perception of pain after a single bout (Koltyn & Arbogast, 1998; Whiteside, Hansen, & Chaudhuri, 2004), however, this did not occur in our sample. Although, most of our sample had not exercised (84%) prior to their migraine, it is difficult to compare

our results to other researchers. The finding that a large majority of collegiate subjects in this study did not exercise prior to their migraine may be related to the timing of their migraine. Specifically, the question asked if the individual exercised 30 min or more in the past 24 hours. With individuals testing anywhere from just after their migraine headache up to 24 hours after the onset of their migraine, the exercise bout may have been prior to or after their migraine. Numerous researchers have reported that migraineurs reported reduced physical activity following a migraine headache including activities of daily living (Blau, 1991). Feelings of fatigue or "hangover" in the postdrome phase (Blau, 1991) and prodromal phase fatigue (Charbriat, Danchot, Michel, Joire, & Henry, 1998) are common which may have contributed to their inactivity.

It was hypothesized that the number of hours of sleep after the onset of their migraine headache would affect neurocognitive function scores. There were no significant differences found between the number of hours of sleep for 24 hours neurocognitive function scores after migraine. Most cognitive function studies have been completed during the headache phase (Farmer, Cady, Bleiberg, & Reeves, 2000; Farmer, et al., 2001), therefore the individuals had not had an opportunity to sleep. Collegiate students with the lowest mean (composite verbal and visual memory scores) scores were those who had no sleep prior to testing. The postdrome phase of migraine lasts an average of 25.2 hours and affects the entire brain, particularly the frontal lobes and hypothalamic areas (Blau, 1991). Approximately 41% of our population had 4-8 hours of sleep prior to neurocognitive testing with only 16% experiencing no sleep at all. Common methods of treating a migraine include sleep (Bigal, Kolodner, Lafata, Loetta, & Lioton, 2006), but amount of sleep does not appear to be associated with their level of cognition.

Limitations

This study had several limitations that need to be addressed. First, the population of the upper peninsula of Michigan is not ethnically diverse, thus, making the sample mainly Caucasian. Second, males were under-represented in the sample due to the prevalence of migraines in females occurring at a rate of three times that of males. Our population was similar to prevalence in the general population with males representing 6% of the population of migraineurs. Third, the numbers of physically active and non-physically active individuals were not equal, with much smaller numbers of non-physically active individuals, although in the migraine and non-migraine groups the percentage per group was similar. Fourth, in the 24 hour questionnaire, the question regarding exercise did not specify whether the exercise took place prior to or after the migraine, just if they had exercised in the past 24 hours. With very few of our migraineurs stating they had exercised in the past 24 hours further research is necessary to examine this relationship. Fifth, power was compromised for some analyses. Sixth, Treatment for headache was not standardized. Seventh, there were a higher number of physician diagnosed migraineurs in this sample compared to the general population. Seventh, all history data was subjectively reported by the individuals. Eighth, there are difficulties in objectively quantifying the subjective complaints of migraine.

Conclusions

Overall, migraineur's neurocognitive function is affected in the postdromal phase of migraine, with this cognitive decline reversible within a few days of the headache. This short interval of decline can affect individuals in their daily activities and may lead to deleterious effects if the "wrong" situation (such as a normally avoidable vehicle

accident) presents in the recovery phase. Individuals need to understand their limitations during this period, adjust their schedules according to their own personal deficits, and educate others who may impact their daily lives. The purpose of this study was to investigate the effects of physical activity on neurocognitive function and recovery patterns in collegiate students who incur a migraine headache compared to collegiate students who do not incur a migraine. The following was a list of conclusions deduced from this study.

A. Migraine significantly decreases neurocognitive function scores in verbal memory, visual memory, and reaction time within 24 hours after a migraine headache compared to baseline testing.
B. Migraine significantly decreases neurocognitive function scores in verbal memory after 48 hours. Reaction time, and visual memory significantly improved compared to 24 hours after a migraine headache.
C. Compared to non-migraine controls migraineurs scored significantly slower on reaction time neurocognitive function scores at baseline.
D. Compared to non-migraine controls migraineurs scored significantly lower on neurocognitive function scores for reaction time, verbal memory, visual memory and motor processing speed at 24 hours.
E. Compared to non-migraine controls migraineurs scored significantly lower on neurocognitive function scores for motor processing speed and reaction time at 48 hours.
F. Compared to non-migraine controls migraineurs scored significantly lower on neurocognitive function scores for motor processing scores at 7 days.

G. Physical activity level had no impact on neurocognitive function scores.

H. Females rate their pain higher than males after a migraine.

I. Physician diagnosed migraineurs rate their pain similar to their non-physician diagnosed counterparts.

J. Physically active individuals rate their HIT scores lower than those who are non-physically active.

K. Type of medication and exercise after a migraine does not appear to have an effect on level of pain during a migraine headache.

L. The number of hours of sleep after a migraine does not appear to affect their neurocognitive function scores.

Recommendations for Future Research

While this study focused on the neurocognitive function scores of college-aged individuals, further research is warranted to determine the amount of cognitive deficits the general population may incur after a migraine, and ways to minimize the postdromal effects. The following recommendations were suggested for future research in this area.

A. Testing a general population may allow conclusions to be more generalized.

B. Testing a general population may show differences between certain prescription medications and over the counter treatments on neurocognitive function scores.

C. Exercise related testing such as proprioception, balance, reaction time, and strength should be conducted on individuals who have just incurred a migraine.

D. Test a wider range of physical activity levels (i.e., low aerobic fitness compared to high aerobic fitness) and include strength training to determine if neurocognitive function is affected.

E. Determine if aura affects the level of disability found in neurocognitive function scores.

F. Test individual's cognitive function online (ImPACT version recently available) to allow individuals to test both during headache phase, within 4 hours headache free, and again after a full night's sleep to determine if there is a significant difference by time, and to make it more convenient to the subjects.

G. Determine self-efficacy for tasks prior to and post-migraine to determine if differences exist.

APPENDIXES A-E

APPENDIX A

HEADACHE IMPACT TEST SIX- PAPER VERSION

HEADACHE IMPACT TEST

HIT-6™

(VERSION 1.1)

HEADACHE IMPACT TEST™

This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches.

To complete, please circle one answer for each question.

1 When you have headaches, how often is the pain severe?

Never | Rarely | Sometimes | Very Often | Always

2 How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?

Never | Rarely | Sometimes | Very Often | Always

3 When you have a headache, how often do you wish you could lie down?

Never | Rarely | Sometimes | Very Often | Always

4 In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?

Never | Rarely | Sometimes | Very Often | Always

5 In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?

Never | Rarely | Sometimes | Very Often | Always

6 In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Never | Rarely | Sometimes | Very Often | Always

COLUMN 1	+	COLUMN 2	+	COLUMN 3	+	COLUMN 4	+	COLUMN 5
(6 points each)		(8 points each)		(10 points each)		(11 points each)		(13 points each)

To score, add points for answers in each column.

Please share your HIT-6 results with your doctor.

Total Score ____

Higher scores indicate greater impact on your life.

Score range is 36-78.

HEADACHE IMPACT TEST™

What Does Your Score Mean?

If You Scored 60 or More

Your headaches are having a very severe impact on your life. You may be experiencing disabling pain and other symptoms that are more severe than those of other headache sufferers. Don't let your headaches stop you from enjoying the important things in your life, like family, work, school or social activities.

Make an appointment today to discuss your HIT-6 results and your headaches with your doctor.

If You Scored 56 – 59

Your headaches are having a substantial impact on your life. As a result you may be experiencing severe pain and other symptoms, causing you to miss some time from family, work, school, or social activities.

Make an appointment today to discuss your HIT-6 results and your headaches with your doctor.

If You Scored 50 – 55

Your headaches seem to be having some impact on your life. Your headaches should not make you miss time from family, work, school, or social activities.

Make sure you discuss your HIT-6 results and your headaches at your next appointment with your doctor.

If You Scored 49 or Less

Your headaches seem to be having little to no impact on your life at this time. We encourage you to take HIT-6 monthly to continue to track how your headaches affect your life.

If Your Score on HIT-6 is 50 or Higher

You should share the results with your doctor. Headaches that are disrupting your life could be migraine.

Take HIT-6 with you when you visit your doctor because research shows that when doctors understand exactly how badly headaches affect the lives of their patients, they are much more likely to provide a successful treatment program, which may include medication.

HIT is also available on the Internet at www.headachetest.com.

The Internet version allows you to print out a personal report of your results as well as a special detailed version for your doctor.

Don't forget to take HIT-6 again or try the Internet version to continue to monitor your progress.

About HIT

The Headache Impact Test (HIT) is a tool used to measure the impact headaches have on your ability to function on the job, at school, at home and in social situations. Your score shows you the effect that headaches have on normal daily life and your ability to function. HIT was developed by an international team of headache experts from neurology and primary care medicine in collaboration with the psychometricians who developed the SF-36® health assessment tool.

HIT is not intended to offer medical advice regarding medical diagnosis or treatment. You should talk to your healthcare provider for advice specific to your situation.

APPENDIX B

INFORMED CONSENT

THE EFFECTS OF MIGRAINE HEADACHE AND PHYSICAL ACTIVITY ON COGNITIVE FUNCTION MEASURED BY IMPACT

INFORMED CONSENT

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Dr. Cynthia Prosen
Dean of Graduate Studies
Northern Michigan University
cprosen@nmu.edu
(906) 227-2300

Your voluntary participation is requested in the research study in which the purpose is to examine the effects of migraine headache on an individual's neurocognitive function; specifically: memory, concentration, processing speed, and reaction time. The research study will use the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) computer program as an assessment tool. In this study, ImPACT will be used to test your short and long-term memory, concentration level, processing speed, and reaction time following migraine.

You are being asked to voluntarily participate in this research study. Your voluntary participation will consist of one initial 60-minute orientation and testing session at which you will complete a migraine history questionnaire, the headache impact test (HIT) online at http://www.headachetest.com (10 minutes), a physical activity questionnaire (5 minutes), and a baseline impact test.

If you are in the migraine group, **following your next migraine headache, you are to call Maggy Moore at (517)-331-1444 or (906) 227-2228** to complete a series of three ImPACT tests over the next week. Each of these testing sessions will take approximately 30 minutes. Each subsequent testing session will take place in a common area (such as a dorm common room) agreed on by the participant and examiner. The first test will take place within 24 hours of onset of your migraine. The second test will take place 24-48 hours after onset of your migraine, and include a 24-hour questionnaire, and physical activity questionnaire, and the third test will take place one week following onset of your migraine.

If you are in the control group, the testing session tests will be the same intervals

as the migraine group. These test sessions will be set up at your convenience over a one-week period sometime following your baseline testing and will take place on campus at NMU in room 2011 of the PEIF building. Maggy Moore will be the only person to contact you for testing.

You are free to take any medication prescribed to you by a physician for your migraine or other disorders as well as any over the counter medications that you would normally take for treatment of a migraine headache or other disorders.

There are no foreseeable risks associated with this test, but the benefits that come from your participation will help further advancements in understanding the short-term neurocognitive effects of migraine headache. Test results will be provided at your request at the last session. The HIT test result will be printed for you and will be available to take home after the initial testing session. You will not be compensated for the study; however, you will be entered into a drawing for two I-pod shuffles or several five to ten dollar gift cards to local businesses at the completion of your participation. Chances of winning a prize are greater than 1/7.

NMU students who volunteer for this study should not expect extra course credit nor will their grade be adversely affected if he/she drops out of the study. Furthermore, the NMU instructor is not involved in any part of the research except recruitment and referral.

Participation in this study is voluntary. You must be 18 years or older to participate in this study. Your identity and information recorded during the study will remain confidential. Confidentiality will be protected by; (a) results will be presented in aggregate form in any presentations and publications; and (b) all data will be stored in a computer that has a password necessary to see confidential data. Your privacy will be protected to the maximum extent allowable by law. MSU Institutional Board will have access to all research records for auditing purposes. You may also discontinue participation at any time without penalty. Your participation in this research study will not involve any additional costs to you or your health care insurer.

Any questions concerning participation in this study should be directed to Maggy Moore at (517) 331-1444 or (906) 227-2228 or Tracey Covassin at (517) 353-2010. If you have any questions or concerns about your role and rights as a research participant, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State Human Research Protection Program, at 517-355-2180, Fax 517-432-4503, or e-mail irb@msu.edu or regular mail at 202 Olds Hall, MSU, East Lansing, MI 48824. Or you may contact Dr. Cynthia Prosen, Dean of Graduate Studies of Northern Michigan University (906)-227-2300 cprosen@nmu.edu.

Your signature below indicates your voluntary agreement to participate in this research study.

_____ _____

Print Name (Last, First) Date

_____ _____

Signature Date

APPENDIX C

MIGRAINE HISTORY QUESTIONAIRRE

The Effects of Migraine on Short-Term Cognitive Function Measured by ImPACT

MIGRAINE HISTORY QUESTIONAIRRE

Please answer the following questions about any moderate to severe headaches you have experienced **in the last 6 months**, remembering to not consider symptoms you experienced **related to substance abuse.**

1. Are you subject to moderate to severe headaches? ☐ Yes ☐ No

2. Have you ever received a diagnosis of migraine headache from a physician?
☐ Yes ☐ No

3. Have you had at least one moderate to severe headache in the past 6 months?
☐ Yes ☐ No

4. Have you had a moderate to severe headache in the last 3 months?
☐ Yes ☐ No

5. When you have a moderate to severe headache, is it only on one side of your head?
☐ Yes ☐ No ☐ NA

6. When you have a moderate to severe headache, does the pain throb or pulsate?
☐ Yes ☐ No ☐ NA

7. When you have a moderate to severe headache, do you have nausea or vomit?
☐ Yes ☐ No ☐ NA

8. When you have a moderate to severe headache, does activity make it worse?
☐ Yes ☐ No ☐ NA

9. When you have a moderate to severe headache, does light bother you?
☐ Yes ☐ No ☐ NA

10. When you have a moderate to severe headache, does sound bother you?
☐ Yes ☐ No ☐ NA

11. When you have a moderate to severe headache, does it last for 4-72 hours when you do not take medication?
☐ Yes ☐ No ☐ NA/ I don't know

12. How many moderate to severe headaches have you had in your lifetime?
☐ 1-2 ☐ 3-4 ☐ 5-10 ☐ 10+

13. Do any members of your immediate family suffer from migraine headaches?
☐ Yes ☐ No ☐ NA/ I don't know
If yes, who?
☐Mom ☐Dad ☐Sibling ☐Grandparents ☐ Other _____

14. Do you have any symptoms prior to the moderate to severe headache to let you know that it is coming, that last about 5 minutes to one hour? ☐ Yes ☐ No

If no please stop questionairre here,
Thank you for your participation

A. If yes which of the following best describes these symptoms? You may check more than one symptom.

- ☐ Difficulty in speaking
- ☐ Visual disturbances (flashing lights, zig-zag lines, loss of vision)
- ☐ Anomia (forgetting the name of things)
- ☐ Depersonalization (feeling as if another person)
- ☐ Dizzyness / Lightheadedness
- ☐ Seeing the world as strange
- ☐ Macropsia (apparent increase in object size)
- ☐ Micropsia (apparent decrease in object size)
- ☐ Simultaneous agnosia (only the object or part of the object being looked at is recognized)
- ☐ Motor Weakness
- ☐ Numbness or tingling in face, or extremities
- ☐ Inability to understand language (difficulty/inability with reading)
- ☐ Olfactory Hallucinations (smelling something that is not there)
- ☐ Photophobia (light bothers you) or phonophobia (sound bothers you)
- ☐ Other, Please describe

_____
_____
_____

B. How many of these moderate to severe headaches have you experienced in the past 6 months? _____

C. How many headaches of this nature have you had in the past 3 months?
_____

D. Can you estimate how many headaches of this nature you have had in your lifetime?
☐ 1-2 ☐ 3-4 ☐ 5-10 ☐ 10+

14. Read the criteria listed below, and think about the number of headaches that were moderate to severe that you have had in the last month?

A. Headache attack lasts 4-72 hours (untreated or unsuccessfully treated with medication)

B. The headache had at least two of the following characteristics:
   1. It was only on one side of the head
   2. Pulsed or throbbed
   3. It was moderate to severe in intensity
   4. The pain was aggravated by walking stairs or similar routine activities

C. The headache attack was accompanied by at least one of the following:
   1. Nausea or vomiting
   2. Photophobia (light bothers you) and phonophobia (sound bothers you)

Please tell us the number of headaches in the last month with the above criteria

_____

15. On a scale of 1-10 with 1 being no pain, 5 moderate pain, and 10 severe pain, what would you rate your moderate to severe headache that met the above criteria listed in Question 14?

1 2 3 4 5 6 7 8 9 10
no pain moderate pain severe pain

APPENDIX D

PHYSICAL ACTIVITY QUESTIONNAIRE

Subject # _____

PHYSICAL ACTIVITY QUESTIONAIRRE

BRFSS (www.cdc.gov)

Please answer the following questions related to your physical activity levels. All answers are confidential and will only be made available by the number assigned to you to the investigators involved directly in this study.

1. Name _____

2. Height _____

3. Weight _____

4. How would you characterize your racial group?
☐ White ☐ Black, African-American ☐ Native Hawaiian, Pacific Islander
☐ Asian ☐ Alaskan Native, American Indian ☐ Hispanic

5. During the past month, other than your regular job, did you participate in any physical activities or exercise such as running, calisthenics, golf, gardening, or walking exercise?

☐ Yes
☐ No
☐ I don't know

6. When you are at work, which of the following best describes what you do? Would you say:
☐ Mostly sitting or standing
☐ Mostly walking
☐ Mostly heavy labor or physically demanding work
☐ I don't know

7. We are interested in two types of physical activity: vigorous and moderate. Vigorous activities cause large increases in breathing or heart rate, while moderate activites cause small increases in breathing or heart rate. Now thinking about the moderate physical activities you do in a usual week, do you do moderate activities for at least 10 minutes at a time, such as brisk walking, bicycling, vacuuming, gardening, or anything else that causes small increases in breathing or heart rate?
☐ Yes
☐ No
☐ I don't know

8. How many days per week do you do these moderate activities for at least 10 minutes at a time?
_____ Days of the week

☐I do not do any moderate physical activity for at least 10 minutes at a time

9. On days when you do moderate activities for at least 10 minutes at a time, how much total time per day do you spend doing these activities?
____ Hours ____ Minutes

☐ I don't know

10. Now thinking of vigorous physical activities you do in a usual week, do you do vigorous activities for at least 10 minutes at a time, such as running, aerobics, heavy yard work, or anything else that causes large increases in breathing or heart rate?

☐ Yes
☐ No
☐ I don't know

11. How many days per week do you do these vigorous activities for at least 10 minutes at a time?
_____ Days of the week

☐I do not do any vigorous physical activity for at least 10 minutes at a time

12. On days when you do vigorous activities for at least 10 minutes at a time, how much total time per day do you spend doing these activities?
____ Hours ____ Minutes

☐ I don't know

APPENDIX E

24 HOUR QUESTIONNAIRE

24 HOUR QUESTIONAIRRE

Participant Number ____

Please answer the following questions as honestly and completely as you can about the last 24 hours.

1. How long has it been since the first signs of your migraine headache occurred?
☐ 0-6 hours ☐ 6-12 hours
☐12-18 hours ☐ 18-24 hours

2. What type of medication did you take to treat your migraine headache?
☐ Over the counter available medication (i.e., Advil migraine, Tylenol, etc.)
☐ Prescription medication for migraine (i.e., Maxalt, etc.)
☐ I did not take any medication for my migraine.

3. How many hours of sleep have you had since the first signs of your migraine occurred?
☐ None ☐ A little to 4 hours
☐ 4-8 hours ☐ More than 8 hours

4. Did you exercise for 30 minutes or more at a moderate-to-vigorous intensity in the last 24 hours?
☐ Yes ☐ No

5. Did you experience an aura (visual or sensory disturbance such as tingling, flashing lights, sparkles) with the most recent migraine?
☐ Yes ☐ No

If Yes, Describe the aura and how long the symptom/s lasted.

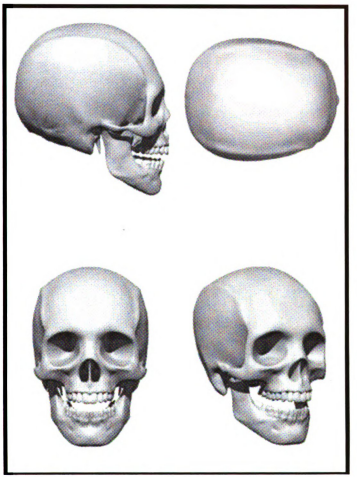
6. On a scale of 1-10 with 1 being no pain, 5 moderate pain, and 10 severe pain, what would you rate your most recent migraine?

1 2 3 4 5 6 7 8 9 10
no pain moderate pain severe pain

7. Regarding location of pain, where was your pain during your most recent migraine located?

☐ Right Side ☐ Left Side ☐ Both

Please circle/shade the location/s of pain



8. Thinking back over the last 24-48 hours, can you pick out one or two factors that may have triggered your migraine? Please describe them below.

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