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Influences of Sleep Disturbances and Mild Traumatic Brain Injury on Gait Performance among College Student-Athletes

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INFLUENCES OF SLEEP DISTURBANCES AND MILD TRAUMATIC BRAIN INJURY ON GAIT PERFORMANCE AMONG COLLEGE STUDENT-ATHLETES

by

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Abstract

INFLUENCES OF SLEEP DISTURBANCES AND MILD TRAUMATIC BRAIN INJURY ON GAIT PERFORMANCE AMONG COLLEGE STUDENT-ATHLETES

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Sleep disturbances from stress are common among college students. In addition, student-athletes in contact sports (e.g., football and soccer) are at a higher risk of receiving a mild traumatic brain injury(mTBI). Stress-related sleep disturbances and mTBI may provoke cognitive and brain changes associated with gait abnormalities. Therefore, the purpose of this study was to examine the association between stress, sleep disturbances, mTBI, and gait performance among college student-athletes. Twelve college student-athletes from men's and women's soccer teams who indicated a history of mTBI (experimental group) and twenty-eight college students without a history of mTBI (control group) were recruited and asked to perform gait analysis with an in-shoe pressure measurement system during and after the midterm exam. Cadence, step time, stride time, stance time, and swing time were measured. Meanwhile, 14-days consecutive wrist actigraphy

data and survey data from two sets of questionnaires were collected to assess their stress, sleep, and fatigue.

The mTBI group had significantly less step time (0.55±0.04 vs. 0.58±0.06 s, p=.011) and stance time (0.65±0.02 vs. 0.70±0.05 s, p=.013) compared to the control group during the exam week. The control group had significantly greater step time and stance time during the midterm exam than after the midterm exam. However, no significant differences in other gait parameters were observed for the mTBI group during and after the midterm exam.

The stress level was positively associated with sleep disturbances, poor daytime functioning, and poor activity correlation. Moreover, stress during midterm exam week increased the activity MESOR in both the control group and the TBI group. However, the effect of stress on the TBI group sleep parameters was higher than the control group.

The outcome of this study was able to facilitate a faster and more accurate diagnosis of concussion with the understanding of mTBI-related lower body gait changes. Moreover, it was an innovative approach to decouple the long-term effect of sleep disturbances on gait changes among TBI athletes.

Chapter 1

Introduction and General Information

Traumatic brain injury (TBI):

Traumatic brain injury (TBI), a head injury that occurs due to trauma, is one of the major health concerns among athletes. The classifications for TBI include mild, moderate, and severe. The American Congress of Rehabilitation Medicine (ACRM) defines that mild TBI is an acute brain injury due to the transfer of mechanical energy from external physical forces to the head resulting in a Glasgow Coma Scale score of 13-15 (Kay et al., 1993). According to a report from the Centers for Disease Control and Prevention (CDC) in 2016, it is estimated that approximately 824 per 100,000 population experience TBI during their lifetime. Among the TBI population, approximately 87% need to visit emergency departments, 11% are hospitalized and 2% die. What's more, it is estimated that the prevalence of sport-related TBI in the US is 1.6 to 3.8 million, annually (Langlois et al., 2006). Moreover, CDC estimates that there are 1.6 to 3.8 million sports-related TBI occurring annually in the US (Langlois et al., 2006), which accounts for 5-9% of all sports-related injuries (Gessel et al., 2007; J. W. Powell & Barber-Foss, 1999). Therefore, it is one of the main concerns among student and collegiate athletes. Based on the division of the National Collegiate Athletic Association (NCAA), from 1988 to 2004, an average of 14.5 game injuries per 1,000 occurred (Hootman, Dick, & Agel, 2007). Since usually college sports are competitive and there is no proper TBI training and protection, collegiate athletes likely receive more TBI than other athletes (Kerr et al., 2014). Most of the TBI in the US occurs in football, wrestling, girls' and boys' soccer, and girls' basketball. The rates of TBI during games are consistently higher than the rates sustained during pre-season (Gessel et al., 2007; Lincoln et al., 2011; Powell & Barber-Foss, 1999; Schulz et al., 2004). It is noticeable that the number of TBI occurrences is probably underestimated because some athletes don't know or refuse to report or to seek medical care in experiencing TBI (Faul, Wald, Xu, & Coronado, 2010). Moreover, it is suggested that head injuries in 15 to 24-year-old people may lead to long-term neuropsychiatric conditions that disrupt their ability to live independently from parental support, resulting in a loss of self-esteem, social isolation, and a considerable burden for their families (Fleminger & Ponsford, 2005).

One of the symptoms of TBI is sleep disturbance which includes insomnia, hypersomnia, or delayed-sleep phase shift (Ouellet, Beaulieu-Bonneau, & Morin, 2015; Singh, Morse, Tkachenko, & Kothare, 2016). Moreover, due to the effect of stress on sleep pattern, sleep disturbances been demonstrated in many college students, particularly during exam time (Lund et al., 2010).

TBI may affect student athletes' quality of life physically and/or psychologically if the symptoms are not properly diagnosed and treated. It is also suggested that people with TBI have lower stability during walking and slower gait speed, which is followed by significantly greater mediolateral motion (Chou et al., 2004). TBI may impact visual input and people with TBI may tend to sway more in both the anteroposterior and mediolateral directions (Ingersoll & Armstrong, 1992; Lehmann et al., 1990; Newton, 1995). Besides, persons with TBI may have difficulty in using their vestibular system and therefore they may show postural sway during quiet standing. They may also show some problems with processing sensory information (Geurts et al., 1996).

The purpose of the study was to identify the effect of mTBI and sleep disturbances on lower body gait changes. It was hypothesized that mTBI subjects compared to the control group will show different gait parameters. Moreover, sleep disturbances related to exam time in college students will cause gait changes. In fact, the first goal of this study was to find out the effect of mTBI on gait changes of UT Tyler student-athletes. The second goal was to find out the effect of sleep disturbances which is, in turn, one of the consequences of mTBI on gait patterns on UT Tyler non-athletic college students without prior mTBI history.

Chapter 2

Literature Review

Mild traumatic brain injury (mTBI)

The definition of TBI is trauma to the head that leads to an injury (Radford et al., 2018). Some factors determine the severity of TBI from mild to severe, such as the duration of coma or post-traumatic amnesia (PTA), Glasgow coma scale (GCS) scores, and the type of functional impairments that happens after injury ("Prognosis of a TBI," 2017). For example, GCS score of 13-15 refers to mild traumatic brain injury (mTBI) (Bruns & Hauser, 2003; Kay et al., 1993; Rimel, Giordani, Barth, Boll, & Jane, 1981), which is very common and accounts for almost 80% of traumatic brain injuries (Naalt, 2001; Vos et al., 2002).

Annually, almost 3.8 million people in the United States are at risk for mTBI (Bacal, 2020). Usually, mTBI occurs with rapid acceleration and deceleration, car accidents, recreational activities, or a foreign object penetrating the brain (Maas, Stocchetti, & Bullock, 2008). Among those causes, sport-related mTBI is common, especially in collegiate athletes, and it’s increasing every year (Bacal, 2020). It is estimated that annually, approximately 300,000 sport-related mTBI occurs in the US (Foley et al., 2014; Gessel et al., 2007; Howell et al., 2014; Prevention, 1997; Sosin et al., 1996). Moreover, mTBI rates are higher in sports permitting body contact such as football, soccer, hockey, and lacrosse than in low/non-contact sports such as volleyball and swimming (Gessel et al., 2012).

Although the highest rate of mTBI is observed in football and boys' lacrosse, there is a possibility of mTBI occurring in all other sports. The rates for girls' sports are similar or higher than that in boys' sports (Lincoln et al., 2011).

Several studies have demonstrated that individuals with mTBI may be more likely to have a poor quality of life (Berger et al., 1999; Polinder et al., 2015; Simpson & Tate, 2007) since mTBI can cause motor, cognitive, behavioral, and emotional dysfunction (Thurman et al., 1999). Also, there are some impairments followed by mTBI including changes in the function of the brain manifesting as fatigue, confusion, memory loss, seizure, coma, and focal sensory or motor neurologic deficit (Bruns & Hauser, 2003; Tams & Kischka, 2009). Moreover, there is some evidence suggesting that one of the recovery functions of TBI is sleep disturbance (Ouellet et al., 2015; Singh et al., 2016).

Sleep disturbance

Sleep plays a vital role in our physical and mental health. Having a good sleep duration has been found to result in decreasing risks of morbidity and mortality (Chaput & Dutil, 2016; Chennaoui et al., 2015). There are different patterns of sleep influenced by cultural, psychological, behavioral, pathophysiological, and environmental situations (Cappuccio et al., 2010). Many consequences have been caused by poor sleep quality and less sleep duration such as anxiety, and some medications (Lund et al., 2010; Noland et al., 2009). It is also suggested that poor sleep can lead to worse functional outcomes such as poor mental health (e.g., anxiety and depression) (Alvaro et al., 2013), and decreased physical health (Gallicchio & Kalesan, 2009). Moreover, sleep disturbance is prevalent after mTBI, and the injury recovery time is increased by 3- to 4-fold in the sleep-disturbed individuals as compared to the good sleepers (Bramley et al., 2017). Sleep problems not only could influence athletes' perception of the injury but also negatively impact their cognition and school performance (Kostyun, 2015). It is also shown that sleep disturbance promoted cognitive brain disorders leading to unsafe gaits characterized by an increase in stride-to-stride variability of stride time (Celle et al., 2014). In other words, some studies demonstrate sleep efficiency can change gait patterns and poor sleep may result in lower gait speed (Dam et al., 2008; Goldman et al., 2007; Roberts, & Duong, 2008). More importantly, sleep disturbance related to mTBI may create depressive symptoms that increase gait variability (Brandler et al., 2012). These studies have shown that gait parameters are indicative of sleep quality, whereas athletes with mTBI history and other stressors may have sleep disturbance that promotes gait changes. Besides, it has been found that stress is the most important predisposing, precipitating, and perpetuating factor that increases the risk of poor sleep quality (Chung & Cheung, 2008).

A few studies have shown that college students are highly likely to show sleep patterns change because of their erratic schedules and stressors, and easy access to over-the-counter (OTC), and recreational drugs (Medeiros, Mendes, Lima, & Araujo, 2001; Oginska & Pokorski, 2006; Tsai & Li, 2004). Poor sleep quality and/or quantity is considered a predictive sign and symptom of many illnesses (Lund et al., 2010) such as changes in metabolic function (Knutson et al., 2007; Spiegel et al., 2004), immune system (Miller & Cappuccio, 2007) and some biomechanics and body movement such as gait abnormalities (Agmon et al., 2016). Poor sleep has been linked to poorer cognitive outcomes, with a decrease in neuropsychological functions such as attention, memory, and executive functioning and cognitive (Bernstein et al., 2018; Leng et al., 2017; Scullin & Bliwise, 2015).

Gait parameters

Gait studies have shown that spatiotemporal measurements and gait speed are the most common factors to predict gait ability, changes in activities, limitation in movement, and functional impairment (Hausdorff et al., 2001; Onder et al., 2005). Some researchers have found out that mTBI can cause a change in gait pattern (Martini et al., 2011). Participants who experienced mTBI showed slower walking velocity, shorter stride lengths, increased whole-body COM sway magnitude, and a conservative gait pattern after injury (Chou et al., 2004; Martini et al., 2011; T. M. Parker et al., 2006). One of the major complications of mTBI is gait abnormalities such as a tendency to fall (Medley et al., 2006; Pervez et al., 2018), reduced aerobic fitness (Bateman et al., 2001), and limited community access (Powell et al., 2002). McFadyen et al. (2003) suggested that stride length decreased to compensate for decreasing postural control and stability following TBI. Additionally, reduced gait speed may be primarily a result of reduced cadence (McFadyen et al., 2003). It is also suggested that decreased cadence, shorter stride length, and increased knee flexion occur as a result of mTBI (Basford et al., 2003; Chou et al., 2004; Williams et al., 2009). It has been shown that slow walking speed and shorter stride length followed by TBI is due to COM anteroposterior displacement and immediate velocity (Basford et al., 2003). Since both the distance between the whole body's COM and the supporting foot and the COM's horizontal (Anterioposterior) velocity is critical to maintaining balance in people with mTBI, they may show sagittal plane movement during gait. What's more, increased COM mediolateral excursion and peak velocity during gait in persons with TBI can cause balance problems in the frontal plane (Kaya et al., 1998; Krebs et al., 1998). Although much research has been done regarding the complication of TBI in terms of neuropsychologic impairments, there are not enough data about the impact of TBI on gait (Cantin et al., 2007) and biomechanical abnormalities that occur followed by TBI (Williams et al., 2009).

Hypothesis and Specific Aims

It was hypothesized that stressors such as midterm exams can result in sleep and gait abnormalities in college student-athletes with a history of mTBI when compared to a control group. College-student athletes with a history of mTBI were assigned to an experimental group whereas college students without a history of mTBI were assigned to a healthy control group. The hypothesis was tested and accomplished the objective of this study by pursuing the following specific aims:

Aim 1: Determine the effects of mTBI on gait abnormalities in college student-athletes.

Expected outcome**:** It is expected that college athletes who experienced mTBI will show gait abnormalities, compared with the healthy control group. Also, the mTBI group will have lower gait parameters including cadence, stride length, stance time, step time, and higher pressure under the feet and COM sway magnitude compared to the healthy control group.

Aim 2: Determine the effect of sleep disturbances caused by midterm exam stress and gait patterns on college student-athletes with mTBI.

Expected outcome: It was expected that stress enhanced sleep disturbances and gait patterns among college student-athletes. Moreover, that gait parameters including cadence, stride length, stance time, step time decreased under the feet and COM sway magnitude increased during exam week compared to the week after the midterm exam for the experimental group. It was expected that total sleep time was less during exam week compare to the week after midterm for the experimental group.

Chapter 3

Materials and Methods

Study overview

The goal of the study was to identify the effect of mTBI and also sleep disturbances on lower body gait changes. It was hypothesized that subjects with mTBI have different gait parameters than the control group. Moreover, college students during exam time have sleep disturbances which itself can cause gait changes. In fact, the first goal of this study was to determine the effect of mTBI on gait changes of UT Tyler student-athletes and the second goal was to determine the effect of sleep disturbances which is, in turn, one of the consequences of mTBI on gait patterns on UT Tyler non-athletic college students without prior mTBI history.

This study took place in the Biomechanics Laboratory at the University of Texas at Tyler (UT Tyler). Two groups of participants (with and without mTBI) walked for 10 minutes while wearing FSCAN sensors in their shoes once during their midterm exam and the week after the midterm exam. Their sleep qualities and quantities were also measured during those periods.

Subjects

Twelve NCAA Division II men's and women's soccer players who indicated a history of concussion were recruited as the experimental group. The reason for choosing subjects from men and women soccer teams was the high risk of TBI in soccer (Gessel et al., 2007). Besides, twenty-eight college non-athletic students from UT Tyler were recruited from the university community through flyers and emails to the university population as a control group.

The sample size (N=40) was determined from a power analysis. Based on a study by Parker (2006), the Cohen's d effect size of stride time was calculated as 0.7 (For stride time in control group: mean= 1.384s, standard deviation= 0.079; and for mTBI group: mean=1.326, standard deviation=0.086). Using G*Power software with α error probability of 0.05 and power (1-β error probability) of 0.8, the estimated sample size is 11 for each group. With an attrition rate of 10%, the sample size for each group should be at least 12. There were 12 participants in the TBI group and 28 participants in the control group.

Individuals 18 or above years of age were eligible for the study. The experimental group consisted of healthy self-reported college student-athletes with a history of TBI within the past five years. The control group included non-athletic college students without prior TBI history. There were no exclusion criteria for gender or specific race and ethnicity in participants. However, individuals with a history of cardiovascular, metabolic, orthopedic, or neurological disease (excluding TBI), and depression were excluded. Individuals were also excluded if they had recent sleep apnea, which gave false-negative results for wrist actigraphy data, and individuals who were on sleep aids and medications for mood disorder were also be excluded. All the conditions were self-reported.

Subjects were recruited and assigned into the experimental group (mTBI group) from the Athletics Department at UT Tyler on a first-come, convenience basis. First, the director of the UT Tyler Athletics Department was contacted to obtain permission before approaching the team coaches to recruit student-athletes from various teams for this study. After obtaining agreement from the team coaches, the researcher attended the team meetings to recruit the potential study participants based on verbal announcements and explaining the study. Non-athletic college students without prior TBI were assigned to the control group. They were also convenient based recruited among students in the UT Tyler health and kinesiology department through flyers and emails to the university population. After explaining the study, each prospective volunteer had to complete the informed consent before participating in the study. All participants received a comprehensive explanation of the proposed study, its benefits, inherent risks, and expected commitments concerning time. Following the explanation of the study, all participants were allowed to ask any questions.

Instrumentation

Both experimental and control groups walked normally for 10 minutes on an indoor flat surface three times. They also wore a miniature wristwatch for 14 days to complete the sleep study (Figure 1).

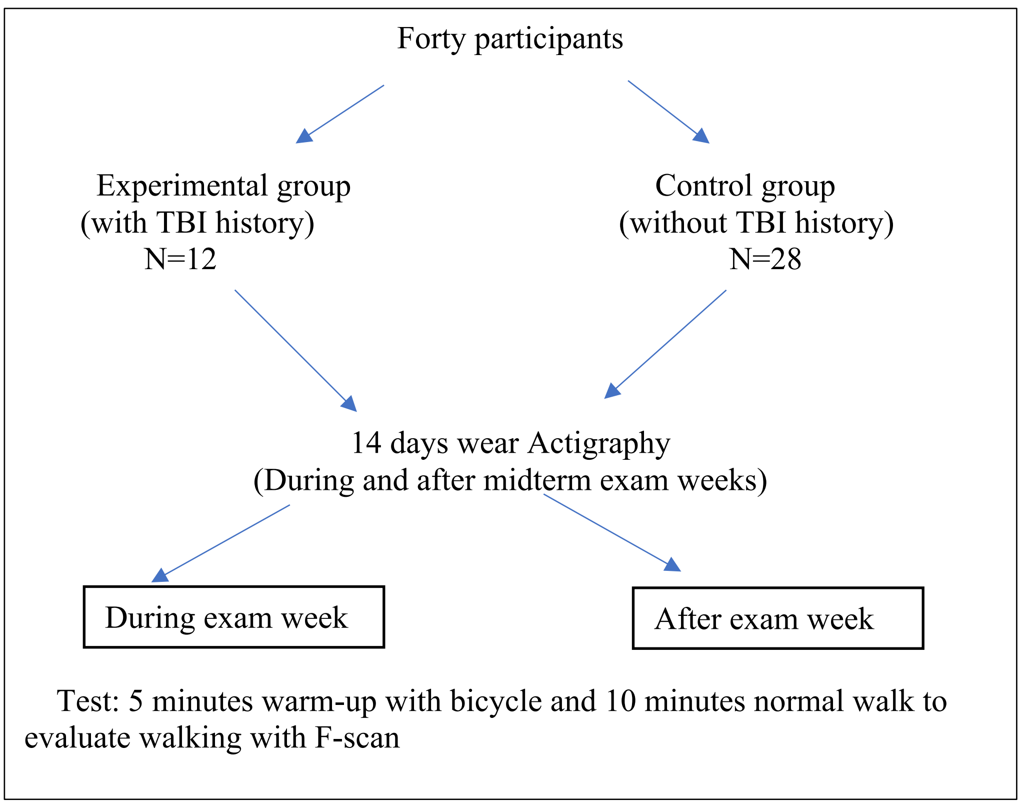

Figure1. The overall procedure of the study

Participants were asked to perform gait analysis with an in-shoe sensor Tekscan (F-Scan, South Boston, MA 02127) during and after the midterm exam. Besides, the pressure distribution of plantar foot during gait could be measure by F-scan. The thickness of each in-show sensor was 0.15 mm and different sizes could be used according to the subject's shoe size. A sensor was placed in each shoe. The sensor was positioned to ensure that the tab exits the shoe on the lateral side of the ankle. Two thick strips of double-sided tape were added to the toe and heel area to secure the sensors in footwear. The subjects were asked to insert their foot into the shoe directly on top of the sensor. Then the ankle bands were wrapped around the subjects. Then the sensor connectors were inserted into the cuff units and both sides of the sensor connector clips are locked in place. The cuff units were attached to the ankle bands by their Velcro backing. The waist belt was attached to the hub. Then cuff cables were connected to the Hub's CH1 and CH2 cable ports and the other ends of the cables to the cuff units. The wireless router was turned on by plugging it into the computer and then turning on the hub.

Before starting the test, the static calibration of the in-shoe sensors was carried out to convert the raw digital output of the in-shoe sensor to actual pressure units. Then the in-show sensor was put in the subject's shoe and the F-scan was attached to their body (Figure 2) and the subjects were asked to walk normally on a flat indoor lab surface along a straight line of approximately 20' in the Biomechanics Lab at UT Tyler. Each gait evaluation from a single visit of the subject required three repeating walks (n =3). The whole process took approximately 15 minutes.

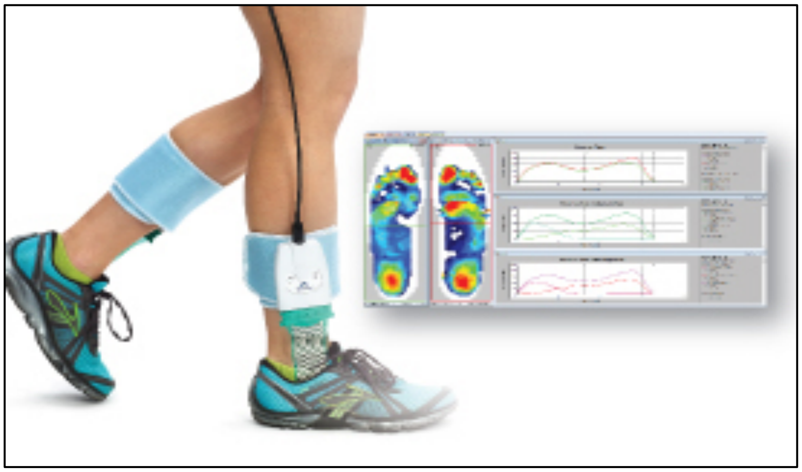

Figure 2. Tekscan (F-scan) and foot pressure distribution during walking

Gait analysis includes cadence, step time, stride time, stance time, and swing time (Figure 3). Step time is defined as the time between heel strike of one leg and heel strike of the contralateral leg. Stride time is the time between heel strike of one leg and heel strike of the same leg. Gait cycle is the time between successive foot contacts of the same limbs which is a repetitive pattern involving steps and strides (Loudon, 2008). Thus, one gait cycle begins when the reference foot contacts the ground and ends with subsequent floor contact of the same foot. Cadence is the rate at which a person walks, expressed in steps per minute.

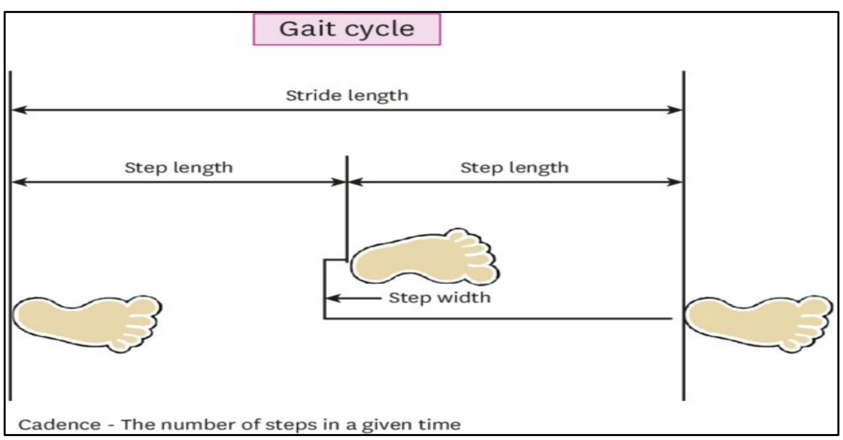

Figure 3. Gait parameters (step length, stride length, and gait cycle) in a person during walking, adapted from (Kim et al., 2018).

Meanwhile, the participants in both control and experimental groups were asked to be equipped with a WP100 device (AMI, Ambulatory Monitoring Inc, New York, USA) (Figure 4) on the non-dominant hand during sleep for 14 days starting from midterm exam weeks until the week after midterm exams. The device also contained an oxygen-saturation sensor and peripheral arterial tonometer (Dvir et al., 2002). The actigraphy had a piezoelectric sensor that continuously recorded movements (e.g., accelerations, linear displacements) at selectable intervals between 5 seconds and 1 hour. Subjects received the device the day of the monitoring with hard copies of instrumental instructions and emergency contact and returned the device in HPC 2165 (Biomechanics Lab) prior to gait study.

Figure 4. Actigraphy sleep watch on the non-dominant hand

Next, the total sleep time (TST), wake after sleep onset (WASO), and circadian activity rhythm (CAR) including Amplitude, MESOR, and Acrophase were collected. Total Sleep Time (TST) refers to the number of hours spent sleeping. Moreover, Wake After Sleep Onset (WASO) is the total amount of time spent awake after going to sleep. Circadian Activity Rhythm (CAR) is the rhythm of sleep and wakefulness reflected in one's rest-activity pattern. Circadian rhythms are the physiological and behavioral changes that occur across 24 hours, regulated by the central circadian pacemaker (Potter et al., 2016). In the circadian rhythm curve, the parameters are Acrophase (AKA phase, time of peak activity), Amplitude (peak-to-bottom difference), and MESOR (mean) of the fitted curve (Figure 5).

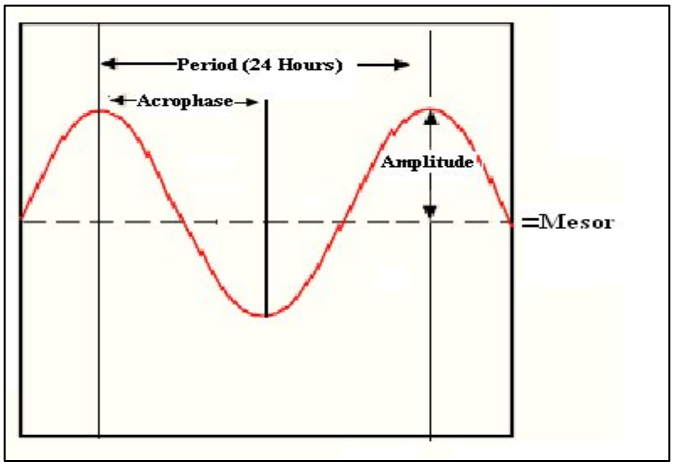

Figure 5. Circadian activity rhythm (MESOR, Amplitude, and Acrophase), adapted from (Stripling, 2008)

The subjects were asked to remove the device during the shower or other activities potentially involved in soaking the device in water. Moreover, they were asked to fill in two sets of self-evaluation questionnaires prior to the gait study to assess their stress, general sleep disturbance scale, and fatigue during and after midterm exam week. They filled out personal information and the following questionnaires: (1) Sleep diary along with Lee Fatigue Scale (2) Daily basis sleep before bedtime and after waking up, for 14 days, and (3) the Perceived Stress Scale and General Sleep Disturbance Scale prior to gait study (Appendix A). Each questionnaire took approximately 5 minutes or less to finish. All of the instruments had sound psychometric properties.

Data Analysis

The gait data including cadence, step time, stride, stance time, pressure under the feet, and COM sway parameters were collected using the software associated with the wireless in-shoe sensor (F-scan), twice on the same subject. The first set of data were collected during the midterm exam week and the second set of data were collected during the week after the midterm exams. Meanwhile, sleep data (sleep quantity and quality) from the miniature wristwatch-like devices (actigraphy) took place under subjects' normal routines for 2 weeks. Sleep data were analyzed by using the automatic sleep-scoring program (Action 4 software). All the electronic data were transferred from the miniature wristwatch-like devices to a password-protected computer in the biomechanics lab at the UT Tyler Department of Health and Kinesiology for subsequent analysis. Statistical analyses were performed using SPSS (Version 24, IBM, Armonk, New York). An alpha level of 0.05 was used to indicate statistical significance for all statistical analyses.

To verify the hypothesis that there were differences in each variable across two-time points (i.e., pre and post) and between TBI group and control group, a mix-design ANOVA (group*time) was used. The primary purpose of mixed ANOVA for this study was to understand if there was an interaction between two independent factors (i.e., time and TBI) on the dependent variables (i.e., gait parameters or sleep parameters). Both the main effects for the two factors and the interaction between them were investigated. If a significant interaction effect was detected, we examined and reported how the treatment conditions differ over time. When either of the main effects was statistically significant, we ran a post hoc test (e.g., Tukey's HSD test) for multiple comparisons to identify where the differences occurred. If the assumption of sphericity for the mixed-design ANOVA was violated, Greenhouse-Geisser corrections were used; if the assumption of normal distribution was not satisfied, a nonparametric test such as Friedman ANOVA was employed.

In the first purpose of the study, which was determining the effects of mTBI on gait abnormalities in college student-athletes, the dependent variables were gait parameters such as stance time, swing time, step time, cadence, and gait cycle. The mixed ANOVA was used to test the hypothesis, that was college athletes who experienced mTBI showed gait abnormalities, compared with the healthy control group. In fact, it was expected that the mTBI group had lower gait parameters including cadence, stride length, stance time, step time, and higher pressure under the feet and COM sway magnitude compared to the healthy control group.

Furthermore, in the second purpose of the study, which was determining the effect of stress such as midterm exams on sleep disturbances among college student-athletes with mTBI, the dependent variables were total sleep time, wake after sleep onset, and circadian activity rhythm including amplitude, MESOR, and acrophase. The mixed ANOVA was used to test the hypothesis, that was college athletes who experienced mTBI and exam week showed sleep abnormalities, compared with the healthy control group. In fact, it was expected that TST, WASO were lower and Circadian Activity rhythm were changed during the exam week compare to the week after the exam in both groups and specially in the TBI group. Demographic measures were evaluated using independent Student's t-tests to compare the differences between the mTBI group and control group (Table 1). The next chapter shoes the results from this study design.

Chapter 4

Results

Overview

The mTBI group had a significantly less stance time (0.65±0.02 vs. 0.70±0.05 s, *p*=.013) and less step time (0.55±0.04 vs. 0.58±0.06 s, *p*=.011) compared with the control group. Significantly greater step time was observed during the midterm exam than after the midterm exam (*p*=0.017). Moreover, there was no significant changes in other gait parameters (cadence, gait cycle, and swing time) during and after the exam week. Additionally, during the exam, the activity MESOR (*p*= 0.038) in both the control group and the TBI group were increased.

Demographics

Forty subjects participated in the study, having an average age of 19.6±1.3 years for the mTBI group and 22.6±3.2 years in the control group, including 9 females (75%) and 3 males (25%) in the mTBI group and 11 males (39.3%) and 17 females (60.7%) in the control group. No significant differences in age, height, and weight were observed between the two groups (Table 1).

Moreover, based on the self-reported survey, mTBI group participants experienced more sleep problems in the past month compared to the control group (0.03). However, other results of the survey showed that there was no significant difference between stress and sleep patterns (sleep quality and quantity) between the TBI and control groups. (Table 1).

Table 1. Mean and Standard deviation (SD) of demographic results

	TBI (n = 12)	Control (n = 28)	P-value

Age (years)	19.6±1.3	22.6±3.	0.05
Gender	Female = 9 (75%) Male = 3 (25%)	Female=17 (60.7%) Male=11 (39.3%)	0.01 0.08
Times after brain injury	1 year ago (4) 2 years ago (2) 4 years ago (1) 5 years ago (5)		
Hours of sleep needed to feel refreshed per 24 hours (minutes)	490±63.1	472±86.6	0.89
Percentage experienced sleep problem in the past month	33.3% (4 out of 12)	21.4% (6 out of 28**)**	**0.03**
Current health status	Good (2) Very good (1) Excellent (9)	Fair (2) Good (4) Very good (13) Excellent (9)	
Ethnicity	White (7) Black (2)	White (13) Black (4)	

	Hispanic (2) Asian (1)	Hispanic (5) Asian (5) Native American (1)	
Sleep quality/quantity	During the exam (2.7±1.31)	During the exam (2.7±1.03)	0.89
	Week after the exam (1.9±0.7)	Week after exam (1.9±0.81)	0.95
Total perceived stress	Exam week (15.6±6.2)	Exam week (15.3±6.7)	0.82
	Week after the exam (15.01±6.1)	Week after exam (13.8±7.3)	0.35

Gait Parameters

In terms of gait parameters, there was a significant difference across the time points (during and the week after the midterm exam) in step time (p=0.017, Tables 2 and 3) and there were significant differences between groups in step time (p=0.011) and stance time (p=0.013) (Tables 2 and 3).

In fact, step time and stance time during the midterm exam was significantly higher in both the TBI and the control group. Besides, the TBI group showed lower step time and stance time compared to the control group (Table 2 and Figures 7, 8). Moreover, there was no significant changes in other gait parameters (cadence, gait cycle, and swing time) during and after the exam week (Table 3, Figures 6,7, 9, and 10).

Table 2. Descriptive statistics (mean ± standard deviation) of gait parameters during the exam week and week after the exam.

		TBI	Control
Cadence (steps/minute)	Exam week	52.0 ± 4.2	49.6 ± 4.3
	Week after exam	52.9 ± 4.4	50.9 ± 3.3
Stance time (minute)	Exam week	0.65 ± 0.02	0.70 ± 0.05
	Week after exam	0.53 ± 0.01	0.68 ± 0.04
Step time (minute)	Exam week	0.55 ± 0.04	0.58 ± 0.06
	Week after exam	0.53 ± 0.02	0.57 ± 0.04
Gait cycle (minute)	Exam week	1.1 ± 0.1	1.2 ± 0.11
	Week after exam	1.1 ± 0.09	1.1 ± 0.7
Swing time (minute)	Exam week	0.5 ± 0.06	0.49 ± 0.07
	Week after exam	0.46 ± 0.05	0.50 ± 0.05

Table 3. Summary statistics from a mixed-design analysis of variance (ANOVA) with repeated measures of gait parameters in which F-statistic (*F*), p-value (*P*), and partial eta squared (η^2) were included.

	Within-subjects (Time)			Between-subject (Group)			Interaction (Time x Group)		
	F	*P*	η^2	*F*	*P*	η^2	*F*	*P*	η^2
Cadence	2.980	0.092	0.073	3.156	0.084	0.077	0.023	0.880	0.001
Stance time	3.161	0.083	0.077	6.716	**0.013**	0.150	0.373	0.545	0.010

Step time	6.223	**0.017**	0.141	7.197	**0.011**	0.159	0.912	0.346	0.023
Gait cycle	4.029	0.052	0.096	3.022	0.090	0.074	0.032	0.858	0.001
Swing time	2.087	0.157	0.052	0.578	0.452	0.015	1.248	0.271	0.032

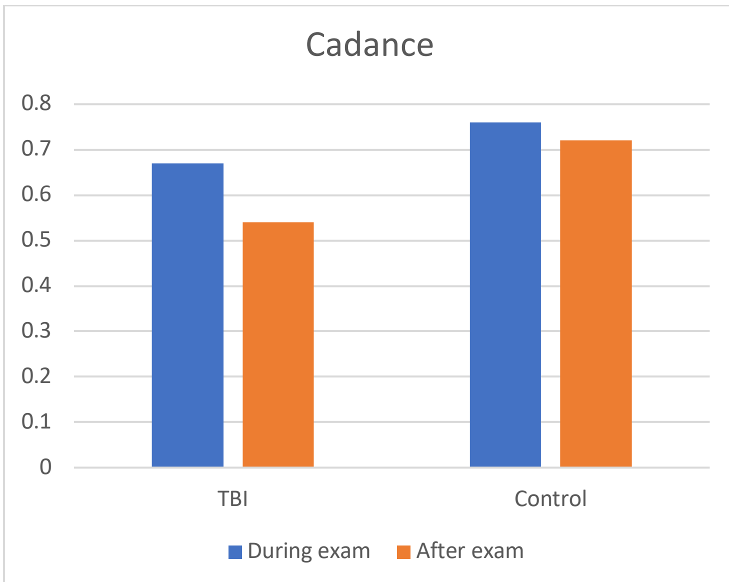

Figure 6. Comparison of cadence (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

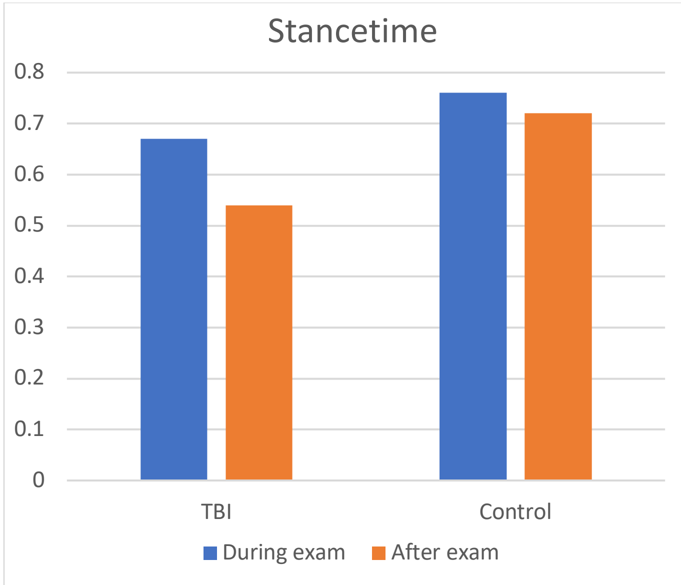

Figure 7. Comparison of stance time (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week. The TBI group had a significantly shorter stance time compared to the control group.

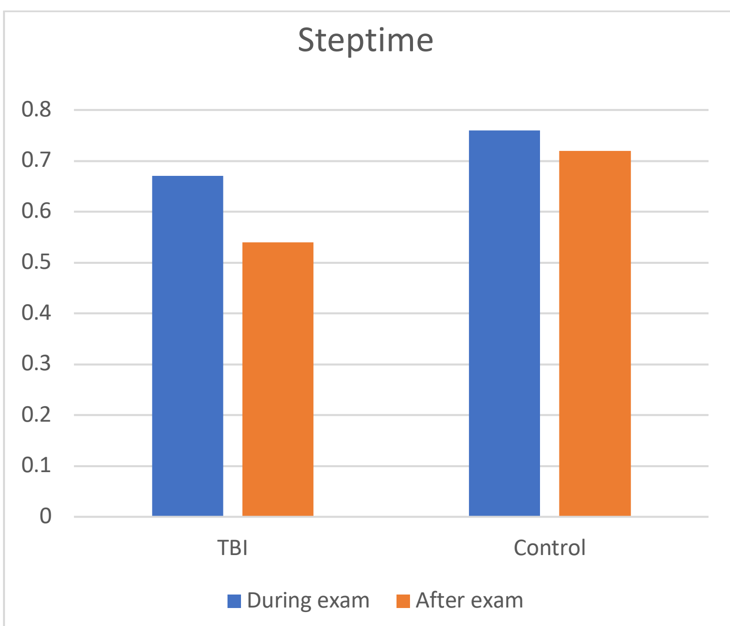

Figure 8. Comparison of step time (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week. The TBI group had a significantly

shorter step time compared to the control group. Besides, during the exam, step time in both the control group and the TBI group were significantly higher than the week after the exam.

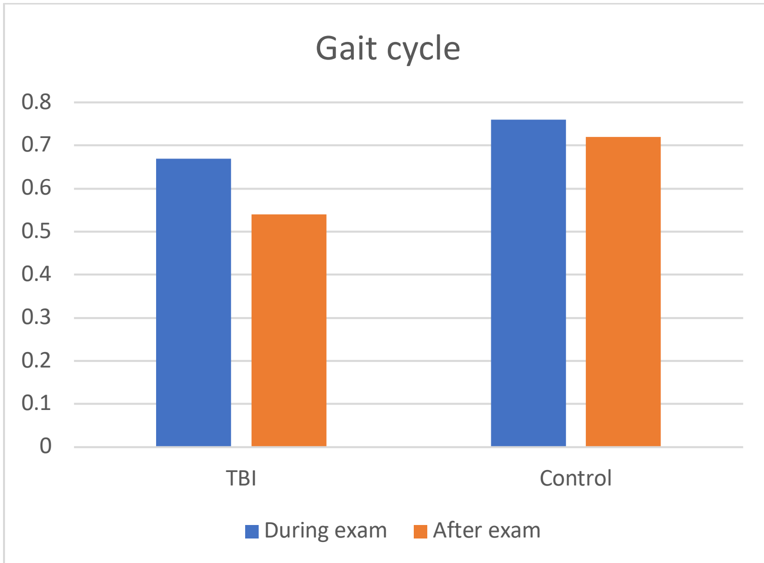

Figure 9. Comparison of gait cycle (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

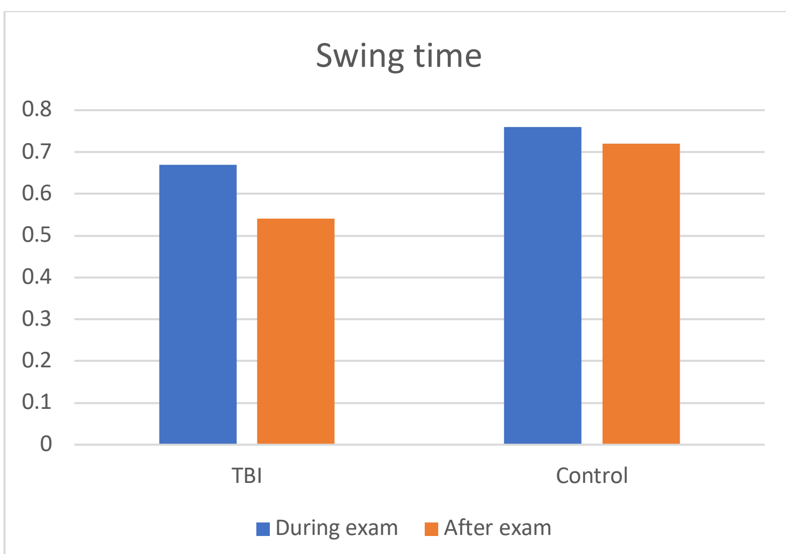

Figure 10. Comparison of swing time (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

Sleep Parameters

The stress level was positively associated with sleep disturbances, poor daytime functioning, and poor activity correlation. Therefore, there was a significant difference across the time points (p=0.038, Tables 4 and 5) in the level of MESOR. It was shown that MESOR in the TBI group is higher than the control group (Figure13). However, this difference is not significant (p>0.05) (Table 4). Other sleep parameters (TST, WASO, Acrophase and Amplitude) did not change significantly during and after the exam week in any of the mTBI and control groups (Table 3 and Figures 11, 12, 14, and 15).

Besides, there were no significant differences between groups in any of the sleep parameters (TST, WASO, MESOR, Amplitude, and Acrophase). It has been shown that there was no significant interaction between time and group.

Table 4. Descriptive statistics (mean ± standard deviation) of sleep parameters during the exam week and week after the exam.

		TBI	Control
TST (minute)	Exam week	402.0 ± 31.1	418.6 ± 47.4
	Week after exam	417.1± 46.9	430.3 ± 48.3
WASO	Exam week	66.8 ± 22.9	66.2 ± 31.5
	Week after exam	70.6 ± 28.9	71.1 ± 31.1

MESOR	Exam week	153.2 ± 9.2	138.0 ± 17.4
	Week after exam	142.9 ±10.9	137.2 ± 15.2
ACROPHASE	Exam week	1573.1±102.6	1596.2 ± 168.8
	Week after exam	1574.7 ± 75.6	1585.9 ± 135.4
AMPLITUDE	Exam week	98.8 ± 30.1	100.7± 14.3
	Week after exam	101.0 ± 18.7	100.8± 17.3

Table 5. Summary statistics from a mixed-design analysis of variance (ANOVA) with repeated measures of sleep parameters (Total Sleep Time (TST), Wake After Sleep Onset (WASO), MESOR, Acrophase, and Amplitude) in which F-statistic (*F*), p-value (*P*), and partial eta squared (η^2) were included.

	Within-subjects (Time)			Between-subject (Group)			Interaction (Time x Group)		
	F	*P*	η^2	*F*	*P*	η^2	*F*	*P*	η^2
TST	2.872	0.098	0.069	1.203	0.280	0.30	0.043	0.837	0.001
WASO	2.274	0.140	0.55	0.000	0.995	0.000	0.028	0.868	0.001
MESOR	4.604	**0.038**	0.106	3.101	0.086	0.074	3.219	0.081	0.076
Acrophase	0.071	0.792	0.002	0.148	0.702	0.004	0.132	0.719	0.03
Amplitude	0.092	0.764	0.002	0.027	0.870	0.001	0.074	0.786	0.002

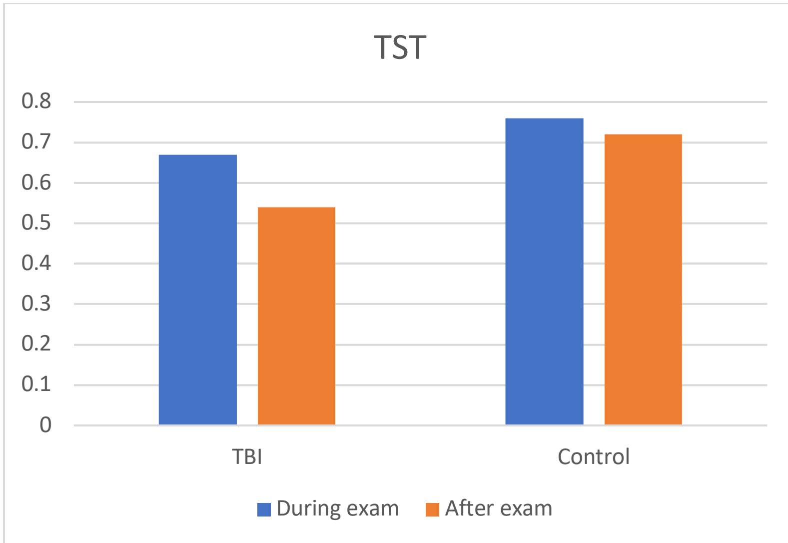

Figure 11. Comparison of Total Sleep Time (TST) (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

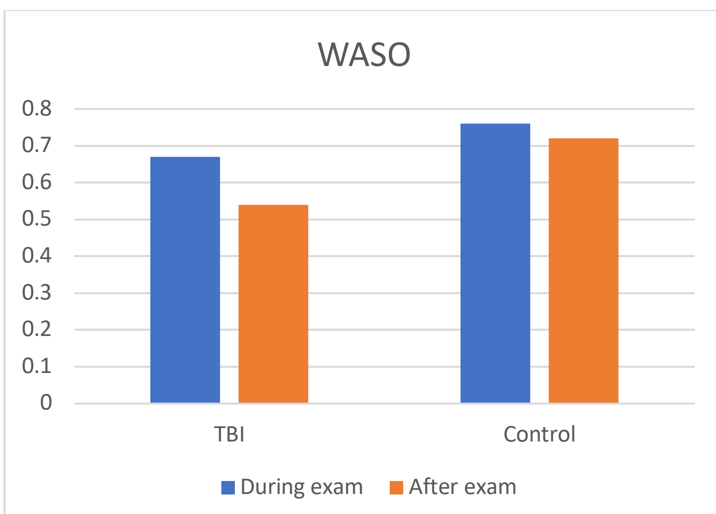

Figure 12. Comparison of Wake After Sleep Onset (WASO) (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

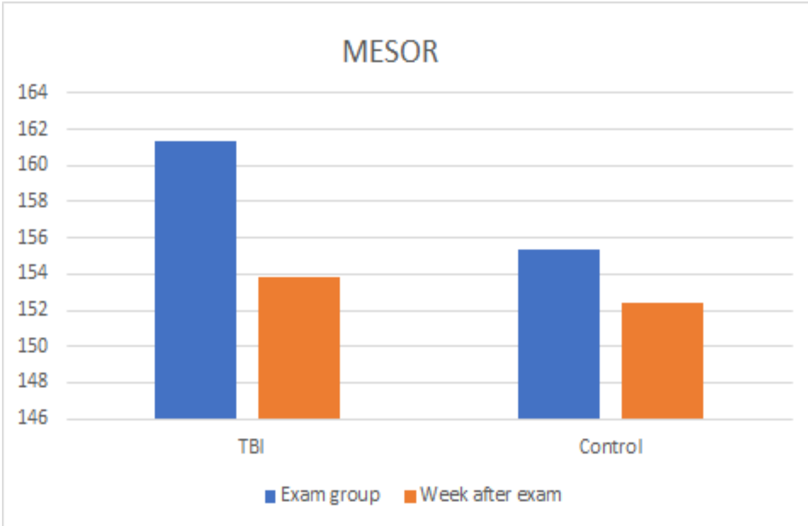

Figure 13. Comparison of MESOR (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week. During the exam week. The activity MESOR in both the TBI and the control group were increases.

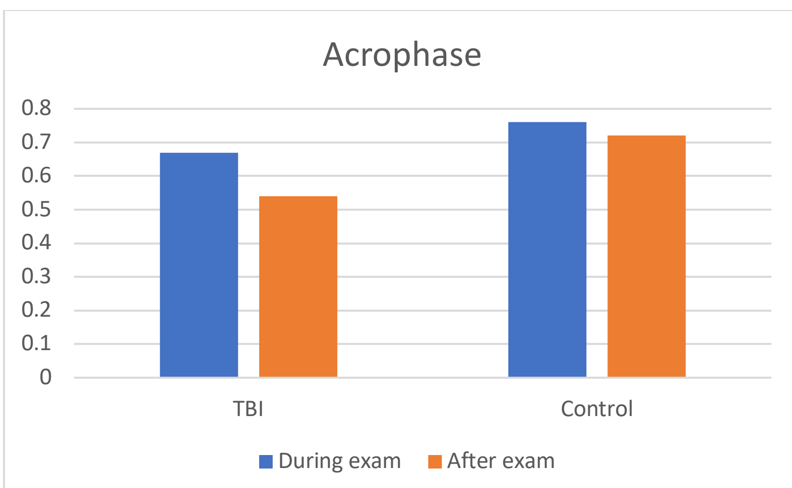

Figure 14. Comparison of Acrophase (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

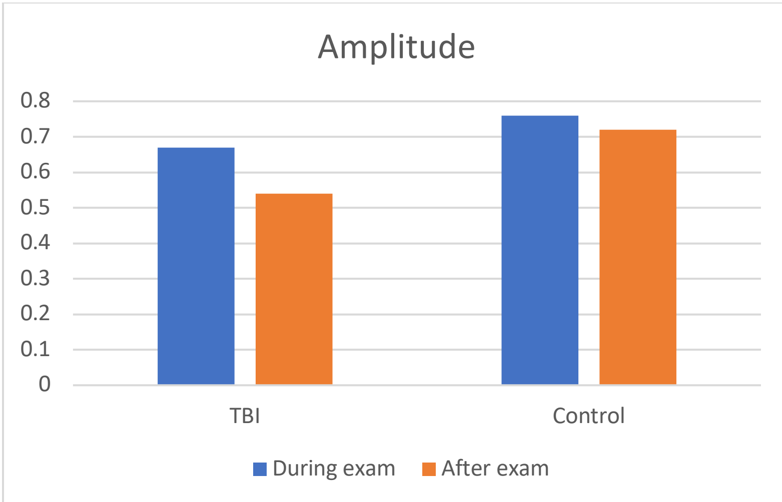

Figure 15. Comparison of Amplitude (Mean ± Standard Deviation) between the TBI group (N=12) and the control group (N=28) during and after the exam week.

The next chapter will discuss the study results in light of the scientific literatures.

Chapter 5

Discussion and Conclusions

Outcome discussion

The main findings of this study were stress during exam week resulted in sleep disturbances in both the mTBI and the control groups. Moreover, stress may cause gait abnormalities in the control group, but not in the mTBI group. Another interesting finding was the mTBI group, compared to the control group, showed shorter step time and stance time (Table 2). The findings support our hypothesis and agree with those of previous researchers who examined the effect of TBI on gait parameters (Chou et al., 2004; Martini et al., 2011; Parker et al., 2008). The explanation is that TBI results in changes of stiffness in the lower extremity, including increases in hip stiffness and decreases in the knee and leg stiffness. Therefore, the change in lower extremity stiffness leads to larger dual-task costs in turning speed and stride time, suggesting a TBI-associated gait change.

On the other hand, based on the questionaries we found that compared to the control group, the mTBI group experienced more sleep problems and needed more hours to sleep in order to get refreshed (Table 1). As Pillar et al. and Mahmood et al. in their studies showed, compared to severe TBI, mild TBI (mTBI) more commonly associated with sleep disturbances (Mahmood et al., 2004; Pillar et al., 2003).

Furthermore, sleep disturbances followed by TBI have been shown to create depressive symptoms that change gait variability (Dam et al., 2008; Goldman et al., 2007; Roberts& Duong, 2008). In fact, these studies have shown that gait parameters are indicative of sleep quality, whereas athletes with mTBI history and other stresses may have sleep disturbance that promotes gait changes. In addition to TBI, stress is one of the most important predisposing, precipitating, and perpetuating factors that can change sleep quality (Chung & Cheung, 2008). In fact, both stress and TBI are stressors that can change sleep parameters and their interaction will increase sleep disturbances (Chung & Cheung, 2008).

Moreover, in our study we showed that step time in all of the participants increased with the existence of stress during the exam week. This result has already approved by previous studies that have shown stress and anxiety can change the gait parameters due to reduce in muscle strength and impaired motor deficiencies (Feldman et al., 2019; Mirelman et al., 2014; Wynaden et al., 2016).

Following the results, the students with mTBI history demonstrated higher MESOR which is 24-hour rhythm-adjusted mean activity movements, during and after the midterm exam, compared to the control group. However, the mTBI group experienced higher MESOR during the exam week and due to the existence of stress compared to the week after the exam. While not statistically significant, MESOR were increased during the exam week in control group. Previous studies have also shown that sleep disturbances following TBI will change the timing and rhythm of sleep. These changes result in alterations in biological sleep-wake schedule and 24-hour rhythm (Weitzman et al., 1981; Thorpy et al., 2012). One explanation is that TBI and stress can alter the rhythm of melatonin secretion and body temperature that leads to circadian change (Smits et al., 2000).

However, it should be noted that some studies suggested TBI does not have any role in circadian dysrhythmia (Ayalon et al., 2007; Steele et al., 2005). While our results demonstrated regardless of MESOR, stress and TBI were not significantly changed other sleep parameters (TST, WASO, Amplitude, and Acrophase) (Table 5 and figures 11, 12, 14, and 15).

Limitations of the study

One limitation of this study was small sample size that likely left this study statistically underpowered and limited the validity of these findings. Future studies should utilize larger samples that might also permit comparisons of males and females or older and younger participants. One should also consider types of measures/ assessment performed for the TBI patients, and length of time between brain injury and evaluation in TBI group.

There are, of course, several other limitations to this study. For example, we did not consider other symptoms associated with TBI associated with the location of the injury or the type of the injury. As a matter of fact, it is unclear whether the nature of injuries may play a role in the development of gait changes and sleep disturbances or not. Furthermore, it should have been considered that the way TBI was treated could change the symptoms and side effects of the injury.

Furthermore, in terms of the effect of stress on gait and sleep, all students' group were included and didn't adequately investigate the psychologic and/or physiologic factors which in turn can change gait and sleep parameters. It should be noted that, of course, some neuropsychiatric disorders such as depression may alter gait, and sleep parameters, and sleep could deteriorate during exam week. Besides, some vascular diseases (such as hypertension, diabetes, or coronary artery disease) may concurrently change sleep and gaits parameters.

Finally, further studies need to examine whether TBI and stress affect sleep and gait parameters.

Future direction

The results of this study have enormous potential benefits to the scientific and sports community and ultimately serve as a translational platform for primary prevention initiatives and early gait-promoting intervention for those who may be at risk for poor gait and health outcomes. Understanding the effects of TBI-related lower body gait changes will facilitate a faster and more accurate diagnosis of concussion. The most significant change in lower body gait happens within 15 - 30 seconds after receiving a TBI (depending on the severity). Most of the current concussion protocols measure the effects of TBI after few minutes at best.

The season-long gait data of student-athletes will enable the development of a gait database, which will be the first of its kind in the field.

An innovative approach of this study was decoupling the long-term effect of sleep disturbances on gait changes among TBI athletes. Sleep disturbances may be induced by physical, mental, or environmental factors. Understanding the role of TBI on sleep disturbances will promote a better treatment strategy toward the rehabilitation process. In fact, with the current preliminary TBI gait database, we can further inform the rehabilitation process and promote the health and safety of collegiate athletes within East Texas and nationally. Theoretically, our gait database will allow athletes to receive better treatment and decrease long-term TBI adverse effects.

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Appendix A

Questionnaire 1

Demographic Data form

1. Your ethnic group: ------ White, ------ Black/ African American, ------ Hispanic, ------ Asian, ------ Native American, ------ others, please specify -------------------------------.

2. Your age: ----------

3. Your Gender ------ Male, ------ Female

4. Your current health status is --------- poor, ---------- fair, --------- good, ---------- very good, --------- excellent.

5. How many hours of sleep per 24 hours do you need to feel refreshed? ------------------

6. Have you experienced sleep problems in the past month? --------- NO, -------- Yes. If yes, please describe.

Questionnaire 2

How often in the PAST WEEK did you:

	Never							Everyday
1. have difficulty getting to sleep	0	1	2	3	4	5	6	7
2. wake up during your sleep period	0	1	2	3	4	5	6	7
3. wake up too early at the end of a sleep period	0	1	2	3	4	5	6	7
4. feel rested upon awakening at the end of a sleep period	0	1	2	3	4	5	6	7
5. sleep poorly	0	1	2	3	4	5	6	7
6. feel sleepy during the day	0	1	2	3	4	5	6	7
7. struggle to stay awake during the day	0	1	2	3	4	5	6	7
8. feel irritable during the day	0	1	2	3	4	5	6	7
9. feel tired or fatigued during the day	0	1	2	3	4	5	6	7
10. feel satisfied with the quality of your sleep	0	1	2	3	4	5	6	7
11. feel alert and energetic during the day	0	1	2	3	4	5	6	7
12. get too much sleep	0	1	2	3	4	5	6	7
13. get too little sleep	0	1	2	3	4	5	6	7
14. take a nap at a scheduled time	0	1	2	3	4	5	6	7
15. fall asleep at a unscheduled time	0	1	2	3	4	5	6	7
16. drink an alcoholic beverage to help you get to sleep	0	1	2	3	4	5	6	7
17. use tobacco to help you get to sleep	0	1	2	3	4	5	6	7
18. use a herb to help you get to sleep	0	1	2	3	4	5	6	7
19. use an over-the-counter sleeping pill to help you get to sleep	0	1	2	3	4	5	6	7

20. use a prescription sleeping pill to help you get to sleep	0	1	2	3	4	5	6	7
21. use aspirin or other pain reliever to help you get to sleep	0	1	2	3	4	5	6	7

The questions below ask about your feelings, thought and activities during the LAST WEEK. Please check one box for each question.

In the last week, how often have you…	Never	Almost never	Some-times	Fairly often	Very often
1. Been upset because of something that happened unexpectedly?	☐	☐	☐	☐	☐
2. Felt that you were unable to control the important things in your life?	☐	☐	☐	☐	☐
3. Felt nervous and “stressed”?	☐	☐	☐	☐	☐
4. Felt confident about your ability to handle your personal problems?	☐	☐	☐	☐	☐
5. Felt that things were going your way?	☐	☐	☐	☐	☐
6. Found that you could not cope with all the things that you had to do?	☐	☐	☐	☐	☐
7. Been able to control irritations in your life?	☐	☐	☐	☐	☐
8. Felt that you were on top of things?	☐	☐	☐	☐	☐
9. Been angered because of things that happened that were outside of your control?	☐	☐	☐	☐	☐
10. Felt difficulties were pilling up so high that you could not overcome them?	☐	☐	☐	☐	☐

Sleep Disturbance scale

Using the 7-point scale below pick what best represents how you are feeling and note the corresponding number on the chart below**.**

Degree of Sleepiness	**Scale rating**
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not fully alert	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; loosing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7

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Office of Research and Technology Transfer

Institutional Review Board

July 26, 2018

Dear Dr. Chou

Your request to conduct the study*: Effect of Mild Traumatic Brain Injuries and Sleep Disturbance on Gaits of Collegiate and Professional Athletes,* IRB #Sum 2018-166 has been approved by The University of Texas at Tyler Institutional Review Board under expedited review. This approval includes the written informed consents that are attached to this letter, and your assurance of participant knowledge of the following prior to study participation: this is a research study; participation is completely voluntary with no obligations to continue participating, and with no adverse consequences for nonparticipation; and assurance of confidentiality of their data.

In addition, please ensure that any research assistants are knowledgeable about research ethics and confidentiality, and any co-investigators have completed human protection training within the past three years, and have forwarded their certificates to the IRB office (G. Duke).

Please review the UT Tyler IRB Principal Investigator Responsibilities, and acknowledge your understanding of these responsibilities and the following through return of this email to the IRB Chair within one week after receipt of this approval letter:

The Progress Report form must be completed for projects extending past one year. Your protocol will automatically expire on the one year anniversary of this letter if a Progress Report is not submitted, per HHS Regulations **prior** to that date

- This approval is for one year, as of the date of the approval letter
-

(45 CFR 46.108(b) and 109(e): http://www.hhs.gov/ohrp/policy/contrev0107.html

- Prompt reporting to the UT Tyler IRB of any proposed changes to this research activity

- **Prompt reporting to the UT Tyler IRB and academic department administration will be done of any unanticipated problems involving risks to subjects or others**

- Suspension or termination of approval may be done if there is evidence of any serious or continuing noncompliance with Federal Regulations or any aberrations in original proposal.
- Any change in proposal procedures must be promptly reported to the IRB prior to implementing any changes except when necessary to eliminate apparent immediate hazards to the subject.
- Approval with waiver

Best of luck in your research, and do not hesitate to contact me if you need any further assistance.

Sincerely,

Gloria Duke, PhD, RN
Chair, UT Tyler IRB