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FACTORS INFLUENCING PERIPHERAL SKIN TEMPERATURE CIRCADIAN RHYTHM IN YOUNG ADULT MALES

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Hannah Tranel, Student

Dr. Jody Clasey, Major Professor

Dr. Heather Erwin, Director of Graduate Studies

FACTORS INFLUENCING PERIPHERAL SKIN TEMPERATURE CIRCADIAN RHYTHM IN YOUNG ADULT MALES

THESIS

A thesis submitted in partial fulfillment of the
Requirements for the degree of Master of Science in the
College of Education
at the University of Kentucky

By

Hannah Tranel

Lexington. Kentucky

Director: Dr. Jody Clasey, Professor of Department of Kinesiology and Health Promotion

Lexington, Kentucky

2014

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ABSTRACT OF THESIS

FACTORS INFLUENCING PERIPHERAL SKIN TEMPERATURE CIRCADIAN RHYTHM IN YOUNG ADULT MALES

Periodic cues, including scheduled exercise, social interactions, sleep habits, and feeding time, have been shown to alter the circadian system. A disruption in circadian rhythms has been shown to have negative effects on health. Frequent skin temperature measures have been shown to be a valid method of assessing circadian rhythm parameters. The purpose of this study was to determine group mean differences in temperature amplitude, stability and lag measures among groups of young men of varying (optimal, fair and poor) adiposities. The strength of the association among the temperatures parameters and measures of body composition, physical fitness and activity, nutritional intake, lipid concentrations, and sleep were also examined. Findings indicated that men with poor adiposity had significantly lower mean amplitude and stability than the optimal or fair groups; with no significant differences in lag among the groups. Factors including physical fitness, physical activity and late night eating contributed to the variance in amplitude; physical activity, time spent in moderate to vigorous activity, late night snacking, and fat mass to stability; and sleep hours and lipid ratios to lag. These findings contribute to the identification of targeted intervention strategies that may improve the circadian synchrony and health of young men.

KEYWORDS: Circadian Rhythm, Metabolic Syndrome, Body Fat, Physical Activity, Physical Fitness,

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May 30, 2014

FACTORS INFLUENCING PERIPHERAL SKIN TEMPERATURE CIRCADIAN RHYTHM IN YOUNG ADULT MALES

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May 30, 2014

I dedicate this project to my Professor Dr. Clasey for always believing in me and helping me to accomplish all my goals. I also want to dedicate this project to my parents Daryl and Mickey and my six siblings who have given me so much love and support throughout the years. They have all helped me become the person I am today.

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Mechanism of Circadian Rhythm

The entrainment of the SCN to light/dark cycles occurs through rods, cones, and retinal ganglion cells (ipRGC) in the retina receiving direct photic input from the environment and sending that signal to the SCN via the retinohypothalamic tract (11). The SCN is able to convey these environmental cues to the peripheral clocks throughout the body through neuronal, humoral, physical (temperature), and behavioral signaling pathways to synchronize peripheral clocks to provide optimal physiology (61). Circadian clocks found in the SCN and peripheral cells function using translational and transcriptional feedback loops that fluctuate with a 24-hour time rhythm.

The feedback loop is made up of a positive loop of transcriptional factors CLOCK and BMAL1 that when activated form heterodimers which initiate the transcription of Period 1 (PER1), Period 2 (PER2), Cryptochrome 1 (CRY1), and Cryptochrome 2 (CRY2) genes. These PER1, 2 and CRY1, 2 genes make up the negative feedback loop to inhibit the actions of CLOCK and BMAL1, thus causing the fluctuations that generate a 24 hour cycle. The degradation of CRY and PER proteins allows the feedback loop to begin again with the transcription of CLOCK and BMAL genes (11, 18,131). A short feedback loop involving REV-ERBalpha and RORalpha nuclear receptors can also affect transcription of BMAL1. After activation, REV-ERBalpha translocates into the nucleus to inhibit transcription of BMAL1; whereas, RORalpha acts as a positive effector on BMAL1 and enhances its expression. At night, there is a disappearance of REV-ERBalpha thus leaving no inhibition and RORalpha signals allow BMAL1 expression to resurface (11).

While the SCN can produce self-sustained rhythms the peripheral clocks may lose rhythm with the loss of input from the SCN. However, in contract to the SCN, the peripheral clocks may regain or reset their rhythm based on behavioral or physiological inputs such as feeding/fasting, sleep/wake and rest/activity (31). Therefore, varying responses to different inputs can cause circadian disruption by: a) reduced amplitude of single oscillators (eg. Weak zeitgeber signal) b) phase shifts that uncouple clocks and reset single oscillators c) a poorly synchronized central pacemaker (86). Many behavior and physiological factors such as feeding, sleep, physical exercise, physical fitness, body composition, metabolic syndrome factors, alcohol consumption and smoking habits can all affect circadian rhythm and its output.

The Effects of Feeding Times on Circadian Rhythms

The effect of food consumption on circadian rhythm was observed in SCN-ablated mice by providing unlimited access to food or providing food only at set times and observing the differences. They found a loss of circadian rhythm when these SCN-ablated mice were allowed unlimited access to food. However, when food was only available at set times the circadian rhythm was restored even though the SCN was not functioning. This indicates that the timing of food intake is crucial to the oscillations of peripheral clock genes and that food consumption can have an effect on the peripheral oscillators even in the absence of SCN input (113). Another study found shifting feeding schedules resulted in changes in circadian gene expression in liver, kidney, pancreas, and heart but not in the SCN. Thus, the feeding schedule has no effect on the SCN but irregular feeding times can cause uncoupling of the peripheral clocks from the SCN. These peripheral clocks that respond to food signals are known as Food Entrainable Oscillators (FEOs) (56). Collectively, information from previous studies demonstrates the ability of food intake to signal changes in peripheral clock gene expression yet; it is not essential to sustain the clock rhythm due to the control by the SCN.

When the SCN and the peripheral clocks are synchronized the rhythm is strongest, however the influence of feeding time has the ability to uncouple these two clocks, allowing peripheral clocks to establish their own rhythm separate from the SCN rhythm. The timing of feeding can result in cues that bypass the SCN signals to peripheral oscillators and cause changes in temperature rhythms through HSF1 or other metabolically sensitive pathways (106). In humans, FEOs activate secretion of ghrelin in response to a scheduled or habitual mealtime. After entrainment of feeding time, ghrelin secretion acts as an input signal to prepare the body for eating through stimulation of appetite or by entraining central clock rhythms to the new set time (141). Therefore, synchronizing signals are sent to the peripheral oscillators from the SCN but these signals can be overridden by feeding times.

Many peripheral oscillators respond to input from SCN as well as changes in metabolic status. These oscillators can regulate transcription/translation of genes influencing metabolic pathways. SCN-controlled metabolic factors such as glucose, adenosine triphosphate/ adenosine monophosphate (ATP/AMP), glucocorticoids, and catecholamines are also dependent on food intake resulting in various signals acting upon peripheral oscillators (31). Changes in metabolism can affect the ratio of ATP/AMP levels, which in turn triggers AMPK to phosphorylate and degrade CRY and PER. The degradation of CRY and PER causes a disruption of the peripheral clock rhythms through CLOCK and BMAL1 (117). Changes in metabolic status also affects NAD+ levels that can lead to changes in circadian rhythms. Signals are sent to AMPK, which travel through a secondary pathway consisting of NAMPT cofactor. Activation of NAMPT increases synthesis of NAD+ and activates SIRT1. SIRT1 and AMPK establish a positive feedback loop back in the liver (35).

SIRT1 can also directly inhibit the binding of BMAL1:CLOCK genes leading to a decreased expression of PER2 (10). During fasting, the SIRT1 pathways increase liver activity and stimulate the process of gluconeogenesis. One study found low levels of SIRT1 in mice eating during their inactive periods and higher levels of SIRT1 in mice eating during their active periods (31). Previous research has shown mice without SIRT1 have increased fat infiltration in the liver compared to those with a functioning SIRT1 gene (146). These peripheral clock genes and pathways result in a rhythmic output that dominates over the SCN and influence gluconeogenesis, production of mitochondria, oxidative phosphorylation, lipogenesis, insulin sensitivity, and hormone production. These outputs become cues that signal other clock pathways throughout the body (31, 131).

The Effects of Sleep Habits on Circadian Rhythm

The sleep-wake cycle is controlled by a balance of input between the circadian system and the homeostatic process (26). Circadian and homeostatic systems work together to consolidate sleep. The homeostatic process of sleep states that as time spent awake increases, the need for sleep increases. After an adequate amount of sleep the circadian system awakes the body to transition from night to day. The circadian system is responsible for our time of sleep and wake tendencies (70, 74). The circadian system responds to darkness and prepares the body for sleep by decreasing core body temperature and blood pressure to allow for sleep to occur. In the morning, daylight triggers the body to increase metabolism in anticipation of increased activity (70). After a lesion of the SCN sleep still occurs, but in a less structured manner. Without circadian control (SCN-lesion), sleep is only under homeostatic control making sleep become highly fragmented and only short episodes of sleep are needed to recover from time spent awake (49). Disruption in the balance between homeostatic and circadian control, such as shift work or jetlag, causes a decline in sleep quality and

functioning during wakefulness.

Sleep deprivation is associated with alterations in glucose metabolism and leptin levels. In one study, subjects were allowed to only sleep for 4 hours for 6 consecutive nights and were then given a high carbohydrate meal. There was a 40% increase in the time it took to regulate blood-glucose levels and they displayed close to diabetic levels of insulin as compared to subjects with normal amounts of sleep (173). This is evidence indicating sleep deprivation can contribute to diabetes, obesity and hypertension. Sleep and wake are homeostatic conditions regulated by interactions between the SCN and peripheral clock genes. It has been shown that the sleep-wake cycle has the ability to cause changes in peripheral clock-gene expression. Just one day of sleep deprivation ranging from 1 up to 7 hours showed reduced amplitude in peripheral clock gene expression compared to sleep conditions (1).

Melatonin has been shown to be a significant factor in maintaining the circadian rhythm of sleep. The SCN uses inhibitory and excitatory factors to help control the daily secretion of melatonin by the pineal gland. Throughout the dark cycle, melatonin secretion is stimulated by glutamate and causes vasodilation leading to increased peripheral body temperature. During the light cycle gamma-Aminobutyric acid (GABA) inhibits the release of melatonin (45). At night, the high levels of melatonin induce gluconeogenesis and reduced glucose utilization ensuring adequate amounts of energy to the brain during fasting hours (86).

Melatonin produced by the pineal gland can be used to shift the circadian clock. In humans, taking melatonin exogenously promotes earlier onset of sleep and longer duration of sleep (148, 176). In a study involving blind humans, daily ingestion of melatonin entrains arrhythmic circadian rhythms indicating melatonin provides direct feedback to the melatonin receptors found on the SCN (122). Also, suppression of melatonin at night shows increased wake time (92). Peripheral tissues of melatonin-deficient mice display weak oscillations and expression of BMAL1, PER1 and CRY2 (183). In the SCN in rats, the rhythmicity of PER genes depends on the presence of melatonin (2). It appears melatonin secretion is required to maintain stable relationships between central and peripheral oscillators in order for complete functionality of the circadian system. Therefore, disruptions or deficiencies in melatonin secretion can lead to a disrupted circadian rhythm.

The Effects of Physical Activity on Circadian Rhythms

It has been known for quite some time that exercise has many physiological benefits for human health (87). Exercise as a zeitgeber has been shown in many studies involving mice to influence circadian rhythms (25, 165, 197) however fewer studies have demonstrated this in humans (14, 137). Schroeder and colleagues (165) found that scheduled exercise, even in the presence of the light/dark cycle, altered the phasing of molecular clocks in the SCN. It was also found that exercise with normal light cycles caused phase shifts in skeletal muscles and lung tissue (197). Furthermore, mice with access to a free wheel showed significantly higher amplitude in the SCN compared to mice with a locked wheel (142). In mice, there was a positive relationship between running activity and shift in circadian rhythm; the more they ran the more they shifted (25).

Exercise has also been shown to accelerate resynchronization after jet lag (170). Ogbagaber and colleagues (137) observed physical activity patterns in adolescent girls. Non-obese girls had higher activity levels than the obese girls. They also found a significant relationship between phase shift in activity and obesity. Although it could not be determined if the relationship was due to overweight girls having a tendency to begin later in the day or if the shift in circadian patterns result in ensuing weight gains (137).

The time of day physical activity occurs may play a role in the effect exercise has on circadian rhythms. The effect of exercise at different times of the day on circadian rhythms was assessed by comparing rhythms of a control group (no exercise), a morning exercise group and an evening exercise group. The morning group showed a more stable circadian rhythm than the control group, illustrating the positive effect exercise has on circadian rhythm. However, the evening exercise group showed a flattened and irregular rhythm compared to the control and morning groups. The decreased elevation of peripheral temperature at time of sleep in the evening exercise group may be explained by increased sympathetic input and thus decreased vasodilation and/or the accumulation of metabolites from exercise inhibit peripheral temperature from increasing (154). Another study observed similar effects of evening exercise on circadian rhythm. A 15-day clinical trial (accounting for the effects of light) observed the effect exercise in the evening has on the circadian phase of melatonin. The exercise group showed greater phase delays of melatonin (3.14 hours) compared to the no exercise control group (19).

It is difficult to determine the effect of physical activity on circadian rhythm because the intensity and duration may play a role in its ability to cause phase shifts in circadian rhythm. Some studies did see a phase shift caused by exercise while others did not, and it was difficult to determine if it was the exercise that caused the shift or a different factor (14). The mechanism behind physical activity as a zeitgeber on circadian rhythm is unknown. Although it is suggested that exercise may cause changes in the circadian rhythm by increasing the release of catecholamines during exercise resulting in pupil dilation and thereby causing an increased amount of light entering the eyes creating a shift through the photic pathway of the circadian system (198). It is also hypothesized that physical activity causes a stimulus to the hypothalamic-pituitary-adrenal system leading to increased levels of melatonin causing a shift in the cycle (63). Exercise has so many effects on the body it is difficult to determine the pathway that leads to circadian changes. Additionally, there is too much variability between intensity, duration and fitness levels of individuals to identify the primary contributors of circadian alterations (14). There needs to be more studies controlling for factors such as light, intensity and duration of exercise in order to determine the effect of exercise on the circadian system.

The Effects of Cardiorespiratory Fitness on Circadian Rhythm

Cardiorespiratory fitness (CRF) is defined as one's ability to perform large muscular movements at a moderate to high intensity for a prolonged period of time (5). Due to the duration and dynamic nature of movement, the cardiorespiratory fitness is dependent on a variety of systems within the body, such as the cardiovascular, respiratory, and skeletal muscle (189). Individuals, who are more fit and have higher maximum oxygen consumption, are known to have a higher cardiorespiratory fitness level. For most individuals to achieve an optimal or healthy level of CRF one needs to take part in some type of physical fitness or exercise routine several times a week. Several researchers have observed the impact of physical fitness on circadian rhythm. The research in rodents is quite conclusive in the fact that exercise does cause a phase shift in circadian rhythm, however these same results have not been consistently demonstrated in humans. The relationship is more difficult to observe in humans due to free living and the influence of other zeitgebers that cannot always be controlled for (14).

Although majority of the research observing the impact of physical fitness on circadian rhythm is inconsistent, it has been hypothesized that individuals with higher levels of CRF, who exercise or take part in some type of structured physical fitness, may have a more synchronized circadian rhythm than those who do not exercise regularly.

There are only a few studies that have reported similar findings. Atkinson et al. (13) found that individuals with higher fitness levels have higher amplitudes and lower night minimums in body temperature when compared to individuals with lower fitness levels. Van Someren et al. (186) found that after a three-month exercise program, elderly males saw a reduction in sleep-wake fragmentation compared to controls. Researchers theorize that exercising routinely may stabilize an individual's day-to-day daily habits, thus providing them with more consistent circadian rhythm. This has lead researchers to consider that a combination of exercise along with other zeitgebers may help to reset or influence one's clock (14).

Obesity and its effect on Circadian Rhythms

The prevalence of obesity in the United States is increasing at an alarming rate (182). A growing number of young adults are at risk of developing obesity due to poor diet (increase calorie consumption), lack of physical activity, and disrupted sleep patterns, especially in Western societies. Environmental changes over the last few decades have greatly influenced the prevalence and incidence of the obesity epidemic. The accessibility of fast food, improved technology, and a decrease in leisure time activities has led to increased weight gain. A number of causes such as nutritional, environmental, endocrine, and genetic factors have been identified to act independently and collectively in the etiology of obesity (20).

The development of obesity is a vicious cycle of circadian disruption. Increased weight gain or obesity can lead to a disrupted circadian rhythm but the reverse is also possible; a desynchronized circadian rhythm can lead to increased weight gain and/or obesity. The effect of obesity on circadian rhythm was assessed in mice. The obese mice showed reductions in peak circadian clock gene expression in adipose tissue compared to the healthy weight mice. Also, these obese mice exhibited lowered levels of adiponectin, which is known to improve insulin sensitivity, prevent atherosclerosis, and protect against the metabolic syndrome (7, 75). A study by Turek and colleagues (2005) examined the effects of feeding a high fat diet to both Clock mutant mice and wild-type mice. Over the course of ten weeks they observed body weight and found a 38% increase in body weight of wild-type mice and a 49% increase in Clock mutant mice. This indicates the composition of a high fat diet causes increased weight gain in both mice strains however; the lack of a synchronized circadian rhythm can cause an even greater increase in body weight than wild-type mice when fed the same meal composition (184). Circadian misalignment was shown to increase glucose, insulin, and mean arterial blood pressure as well as decrease leptin levels and sleep efficiency in humans. Chronic decreases in leptin stimulate appetite and decrease energy expenditure, which could lead to the development of obesity (161). Therefore, circadian disruption can be a cause and/or a consequence of obesity.

The Metabolic Syndrome and Circadian Rhythm

The metabolic syndrome (MetS) is a cluster of health-risk factors that is associated with increased risk of developing cardiovascular disease and diabetes mellitus (149). The five key factors of the metabolic syndrome include central obesity, high triglycerides, low levels of high-density lipoprotein cholesterol (HDL), high blood pressure, and elevated glucose levels (2) Over the last few years, different organizations have used different factors to set the standards for the diagnosis of the metabolic syndrome, but the presence of three of the five most common factors is used to consistently diagnose the metabolic syndrome (181). The prevalence of metabolic syndrome is hard to define because of its varying definitions and often differences in gender, race, and ethnicity can play a role in assessing an individual's risk. Although

clinicians use various definitions to diagnose the metabolic syndrome, the prevalence of MetS is still increasing. In the last few years the prevalence of the MetS has increased exponentially in both sexes. In 2009, the prevalence of the MetS was approximately 34% in adults; therefore, about 77 million adults in the United States have the metabolic syndrome (69).

The circadian system regulates metabolic activity in all tissues and organs. Thus, many studies have found that circadian rhythm and the metabolic syndrome influence one another and the disruption of circadian rhythms may lead to metabolic syndrome (175). Recently, some studies have shown the deletion of Clock and Bmal genes results in the metabolic syndrome (155, 184). The loss of Clock gene leads to the development of obesity, hyperglycemia, and dyslipidemia in mice (184). Various metabolic hormones and enzymes such as glucose, insulin, leptin and adiponectin exhibit circadian fluctuations over 24 hours. Many glucose and lipid receptors also display circadian expression (76). One study misaligned circadian rhythms in adults and found the subjects exhibited lowered leptin levels. They concluded that the decreases in leptin might be due to the misalignment between central and peripheral oscillators with meal times. It was thought that the misalignment caused decreased digestion and energy uptake resulting in a negative energy balance thus accounting for the suppressed leptin seen in the study. Leptin production is also controlled by insulin, indicating the circadian misalignment may cause insulin insensitivity. Furthermore, increased glucose levels despite increases in insulin were also observed indicating a decrease in insulin sensitivity to occur during circadian misalignment. Collectively, these metabolic changes due to a misaligned circadian rhythm can lead to the metabolic syndrome (161).

Type I diabetes patients exhibit lipolysis earlier in the evening and it remains elevated throughout the night compared to healthy individuals. This indicates there is an altered rhythm of lipolysis in Type I diabetes suggesting a relationship between circadian rhythm and the metabolic syndrome (84). Blood pressure has also been shown to be under circadian control (76). Recently, the loss of blood pressure rhythm was observed in obese children and furthermore, this disrupted pattern was correlated with insulin resistance (165). These studies show the metabolic syndrome is a clustering of factors that can all individually or jointly be affected by circadian rhythm disturbances and in turn can also cause disturbances in circadian rhythms.

The Effect of Alcohol on Circadian Function

Alcohol has a dramatic effect on circadian rhythm. Alcoholics exhibit low expression of Clock, Bmal, Per, and Cry genes in peripheral cells compared to non-alcoholics causing disruption of circadian rhythms in those cells (98). Similarly, a study by Ando et al. (7) found an inverse relationship between alcohol consumption and Bmal expression in peripheral cells. There are a couple of mechanisms by which alcohol consumption can affect circadian rhythm, including enzymatic activity and the breakdown of intestinal barriers. Many enzymes, including alcohol dehydrogenase (ADH) are used to metabolize alcohol mainly in the liver, however tissue in the stomach, intestines, and brain can also play a role in the metabolism of alcohol. Alcohol leads to the disruption of circadian rhythm by shifting the NAD+/NADH ratio as a consequence of the metabolism of alcohol by the enzyme ADH. The NAD+/NADH ratio influences the SIRT1 gene, which contributes to the regulation of circadian rhythms in peripheral cells.

Additionally, alcohol disrupts circadian rhythm by breaking down the intestinal barrier, thus allowing bacteria (such as lipopolysaccharides; (LPS)) to leak into the systemic circulation. The presence of LPS blocks the expression of PER genes in the liver, heart, and SCN, which causes inflammation and disruption of circadian rhythm (191). Alcohol consumption causes disruptions in circadian rhythms, but consequently,

disruptions in circadian rhythms can also lead to an increased consumption of alcohol. This cycle was demonstrated in a study that compared Period 2 mutant mice and wild-type mice in the presence of alcohol. They reported that the Period 2 mutant mice consumed more alcohol than the wild-type mice, demonstrating the cycle of circadian rhythm and alcohol disruption (172).

Circadian cycles of body temperature (53), glucose (147), sleep/wake (Brower 2001), and blood pressure (102) can all be affected by alcohol consumption as well. Researchers have observed the effects of alcohol on core body temperature in both mice and humans and they have reported that the effects are time dependent and hypothermic. Alcohol is known to shorten the circadian rhythm of core temperature. Alcohol consumption causes the core temperature set point to shift downward and a reduction in amplitude to take place, thus causing core body temperature to decrease (53). In a study with healthy, young, adult males the time dependent effects of alcohol consumption were observed. The study reported that when compared to evening drinking, both morning and daytime consumption of alcohol produced a greater decrease in core body temperature. The researchers also found that those consuming alcohol did not show as great of a decline in core body temperature during sleep compared to those who did not consume alcohol (59). Both of these studies demonstrate the negative effects alcohol has on the circadian rhythm of temperature and how alcohol consumption could lead to circadian disruption.

The Effect Smoking has on Circadian Rhythm

Many functions of the lung show daily rhythm and are under circadian control (83). Smoking influences the circadian rhythm through the SIRT1 pathway. Cigarette smoking causes a decrease in SIRT1 levels in the lungs causing alterations in clock gene expression in the lungs. This alteration was shown in a study that exposed mice to clean air or cigarette smoke during their active periods. The researchers found that the mice who were chronically (6m months) and acutely (10 days) exposed to cigarette smoke exhibited reduced amplitude of SIRT1, Bmal1, and Per2 expression and delayed phase expression of clock genes in the lung. They also observed decreased amplitude of clock gene expression and phase shifts in the SCN of those acutely exposed to cigarette smoke (100). This evidence suggests that cigarette smoke affects both central and peripheral (lung) clock function.

It is hypothesized that nicotine alters the circadian rhythm by acting on the SCN indirectly through a dopaminergic pathway. The presence of nicotine has been shown to cause a phase advance in the circadian rhythm, however these results have only been demonstrated in rodents. Furthermore, this phase advancement is dependent on the time of “high” and concentration of nicotine. The phase shifts are only present near the time of exposure to the stimulant (nicotine), therefore the effects may not be present, if only the mean rhythms are observed. Therefore, factors such as smoking behaviors (how often and how long an individual has been smoking) and how fast one is able to metabolize nicotine can influence the effect smoking has on circadian rhythm (138). Although smoking has been shown to affect circadian rhythm, it does not appear to have as large of an influence on the circadian system as timing of food or sleep does (100).

Chronotypes and Circadian Rhythm

There are three different chronotypes that people identify themselves with, morningness (larks), eveningness (owls), and intermediates. Larks are identified as early risers, who are more productive and alert in morning hours and go to bed early. Owls are described as late risers, who are more productive and alert in evening hours and go to bed late. Chronotype can be determined by a number of factors such as genetics,

age, social factors and environmental stimuli. Environmental factors such as early work/school schedules can interrupt an individual's natural chronotype and cause individuals to make adjustments, especially owls. These adjustments often cause owls to have a reduction in sleep duration and overall quality of sleep, which could contribute to weight gain. Therefore, evening types are more commonly associated with poor sleeping patterns and lifestyle habits (55).

A study by Olds et al. (139) found that adolescents with a late bedtime and late wake time were 1.5 times more likely to be obese. Evening types are also associated with greater alcohol intake and are more likely to experiment with smoking (79). Poor dietary habits such as an increased intake of fast food, increased caffeine intake, and decreased consumption of dairy products are all associated with evening types. However, there was no association between chronotype and vegetable, sweets, and meat consumption (68). Furthermore, a study with high school subjects reported that owls are associated with increased sedentary activity and decreased physical activity compared to morning types (139). Numerous studies have observed the relationship between chronotypes, lifestyle habits, and body compositions. For example, one study observing college freshmen did not find a significant association between chronotype and BMI, but did report that evening types developed an increase in BMI over time while morning and intermediate types BMI remained stable (55). A study completed in different chronotypes reported that evening types were more likely to skip breakfast compared to morning types (129).

Another factor that can determine one's chronotype is age; adolescents often undergo a shift from morningness to eveningness (104). Effects of the different chronotypes are present in both physiological and psychological aspects such as blood pressure, body temperature, sleep patterns, and arousal times (15). Evening types express a delayed phase of the circadian system of approximately 2 hours compared to morning types. This delay in evening types has been observed in both body temperature and melatonin levels compared to morning types (60).

Chapter 2

The Effect of Zeitgebers on Each Other

The sleep/wake cycle and food intake appear to be two of the most dominant zeitgebers that can reset peripheral circadian genes. However, factors such as physical activity, physical fitness, obesity, metabolic syndrome, alcohol, smoking and chronotype have all been shown to influence circadian rhythm. Many of these factors are associated with one another and may work together to alter circadian rhythms.

Obesity and Food Intake

The transition into adulthood is often associated with increased independence and more responsibility for food preparation and intake. This transition may cause an increased consumption of fast food and decreased consumption of breakfast. In a longitudinal study by Niemeier et al. (135) observed young adults transitioning into adulthood and found that skipping breakfast was correlated with weight gain. The incidence of skipping breakfast increased into young adulthood; during adolescence the subjects reported eating breakfast 4 to 5 times a week and during adulthood this decreased to only 3 times a week. It was also determined that those that ate breakfast regularly ate a lower percentage of fat throughout the day than those who skipped breakfast (134).

Fast food consumption was also correlated with weight gain in young adults. In a sample of 5000 students aged 11 to 18, approximately 75% reported eating at a fast food restaurant in the previous week (71). Additionally, in a longitudinal study from

adolescence to adulthood, it was reported that adolescents reported eating fast food an average of 2 times a week and into adulthood that increased to 2.5 times per week. Fast food meals have a higher density of fat and people often consume more total energy than when eating at home (135). This increased intake of high-fat fast food may lead to disrupted circadian rhythms in individuals.

In a study comparing mice fed a high fat diet versus controls it was observed that the high fat diet mice began to eat and increase activity more during the light hours whereas the controlled mice continued to eat and be active at normal times during the dark period. This indicates that the high fat diet led to a disruption in the normal circadian rhythm of the mice (105). Wu and Reddy (199) fed mice a diet to induce obesity and observed the changes that occurred in circadian rhythms due to this diet-induced obesity. They found that Clock and Bmal expression were blunted in adipose tissue but remained unaffected in aorta, liver and muscle tissue. They also found that the daily variations of metabolic homeostasis were impaired in the obese mice. Therefore, it appears obesity can cause a loss of rhythmicity in adipose tissue dissociating it from the regular circadian rhythm. They suggest that cardiovascular tissue may be more resilient to the effects of obesity and may require prolonged exposure to see a loss in rhythmicity caused by obesity (199).

While meal content may influence body weight, the time of meal consumption is another influencing factor. Ma (125) found that eating patterns are associated with obesity even after controlling for total energy intake and physical activity. Eating carbohydrate-rich meals late at night leads to increases in glycogen stored in muscle. If this glycogen is not burned as fuel it will ultimately be stored as fat. Thus, late night eating may be related to obesity through its effect on energy metabolism and hormone release (125). Also, the prevalence of night eating syndrome (majority of food is eaten late in the day into the evening and night) is higher in overweight and obese individuals compared to healthy-weight individuals (178). Those who ate a larger portion of food in the morning consumed less overall food for the day compared to those who consumed large meals for dinner. This indicates that large meals consumed in the morning (6am-10am) may suppress intake throughout the day and large meals later in the evening (10pm-2am) may supplement earlier intake leading to increases in overall consumption per day (58).

Obesity and Physical Activity

Physical inactivity has been associated with obesity in both mice and human subjects. A study found that college students who gained greater than 5% of their body weight in 16 weeks participated in less physical activity than those students who did not gain more than 5% of their body weight (195). Similarly, Butler at el. (32) found college freshmen had an increase in fat mass and a decrease in fat free mass after their first year due to decreases in physical activity. However, physical inactivity on its own may not directly cause obesity, instead it contributes to the development of obesity in combination with poor diet, disruption of sleep and/or hormonal disruptions. Therefore, one's risk of developing obesity is substantially increased when environmental factors along with a lack of physical activity occur.

Obesity and Sleep Habits

Researchers have recently observed the relationship between the sleep/wake cycle, leptin and ghrelin levels, and obesity. A higher Body Mass Index (BMI) has been associated with reduced sleep duration and decreased levels of circulating leptin (which is controlled by the SCN) and increased levels of ghrelin. Leptin, as previously discussed, is a hormone that suppresses appetite, whereas ghrelin is a peptide that

stimulates appetite (180). Vorona (192) reported overweight and obese subjects had a decreased total amount of sleep when compared to the healthy weight subjects over a 24-hour period. The reduction in sleep time, along with increased wake time and reduced leptin levels leads to an increased appetite and potentially overeating in the night time hours (24). Other studies have reported that leptin levels of obese individuals still expressed a 24-hour cycle, however the amplitude and concentration were lower than non-obese individuals. Therefore, these individuals are experiencing a decrease in appetite suppression, along with an increased wake time period (91). Not only are obese individuals acquiring less sleep, but their sleep is also disturbed, causing one to be more tired and less active during the daytime hours (72).

Sleep deprivation can also lead to the development of obesity. A study by Spiegel et al. (174) found sleep deprivation caused reduced ghrelin similar to those caused by obesity. Decreased time spent sleeping (<6 hours/night) was associated with a decrease in daytime ghrelin levels and increased hunger and appetite the following day. In addition, those subjects with decreased sleep time had an increased appetite for calorie-dense foods such as sweet, salty snacks and starchy foods with no reduction in appetite for fruits, vegetables and high protein foods. The exact causes for the decreased ghrelin levels associated with decreased sleep time are unknown; however, change in hormones and autonomic nervous system input may play a role (23). Therefore, obese individuals may experience a cycle of circadian disruption that is continuous unless intervention of lifestyle changes takes place.

Physical Activity and Sleep

Many studies have shown self reported exercise is associated with better sleep quality (103, 121, 169). It is widely accepted that a physically active day leads to enhanced sleep. However, direct evidence for the effect of physical activity on sleep has been inconclusive (136). One study found that the increases in body temperature associated with exercise caused increases in slow wave sleep but had no effect on REM sleep (97). Using survey data, Hasan and colleagues (88) found a lower prevalence of sleep problems and daytime sleepiness in the physically active compared to the sedentary people. Those who increased physical activity over 3 months reported improved sleep while 30% of those who displayed decreased levels of physical activity reported more sleep disturbances (88). In contrast, a study by Youngstedt et al. (201) found no significant difference in sleep between the highest active day and lowest active day.

There are many explanations for the positive association between exercise and sleep. First, it could be that people who sleep better are more likely and able to exercise (201). For example, a study by Suskin et al. (179) found that decreased sleep was associated with reduced physical activity. An explanation could be that people who exercise are also concerned with other healthy habits such as getting adequate sleep, or those who are highly stressed often spend less time exercising and it could be the stress that is causing disrupted sleep rather than the lack of exercise (201). More research needs to be performed in order to determine the effect physical activity has on sleep.

The Metabolic Syndrome and Obesity

Morrell et al. (132) found overweight and obese college-age adults are at risk for developing diabetes mellitus and cardiovascular disease, and many presented with multiple criteria of the metabolic syndrome. Overweight and obese males were 6 and 32 times, respectively, more likely to be diagnosed with metabolic syndrome when compared to healthy weight or underweight males (66). In a group of 163 college students, Huang et al. (99) reported that overweight students were 3 times as likely to

have at least 1 indicator of the MetS compared to healthy weight students. However, not all obese persons are at equal risk, and the regional distribution of fat on the body can play a role in the risk of developing the metabolic syndrome. Those with more centrally located body fat are at greater risk of developing Mets than those with fat distributed more around the hips (41). Furthermore, individuals with increased abdominal visceral fat have the greatest risk of developing the MetS (181).

The development of the MetS involves an important interaction of multiple environmental and genetic factors. The recent increase in the MetS incident rates has been associated with the trends in diet and decreased physical activity, along with genetic susceptibility. Various studies observing twins assessed the influence of genetic and environmental factors on the components of the metabolic syndrome. Poulsen et al. (145) observed the differences between monozygotic and dizygotic twins to determine the genetic influences of the MetS. They reported that glucose intolerance, elevated body mass index, and low HDL levels had a higher genetic influence. Whereas hyperinsulinemia, hypertension, triglyceride levels, and abdominal obesity did not show a genetic difference, indicating that these factors are more affected by environmental influences.

Environmental factors, such as diet and physical activity level, are major causal factors for the development of the MetS. Living a sedentary lifestyle or consuming a diet consisting of a high percentage of high caloric foods increases an individual's risk of developing the factors associated with the MetS (151). Both environmental and genetic factors influence diet and can cause one to be more susceptible to a high caloric intake, thus leading to increased adiposity and other health risks associated with the MetS.

The Metabolic Syndrome and Physical Activity

Current guidelines state that adults should accumulate at least 30 min of moderate-intensity activity 5 days a week or 20 min of vigorous-intensity activity 3 days a week to achieve significant health benefits (ASCM and AHA, 2007). Regular physical activity has a beneficial effect on many metabolic risk factors and reduces the risk of MetS, type II diabetes, and cardiovascular disease (43). A cross-sectional study found an inverse relationship between physical activity and the MetS (203). The amount and intensity of physical activity may play a role in the risk of developing the MetS. Many studies have found that moderate to vigorous activity has been associated with reduced risk of developing the MetS (64, 90). Scheers et al. (162) found that time spent in moderate to vigorous physical activity (MVPA) was inversely correlated to metabolic syndrome and its components. Similarly, time spent in MVPA as recorded by accelerometers was significantly associated with waist circumference, systolic blood pressure, HDL-C, triglycerides, plasma glucose, and insulin (12).

Previous studies have also observed the relationship between physical activity in adolescents and the development of the MetS and its factors in adulthood. It was reported that low physical activity in adolescence led to low physical activity in adulthood as well as predicted development of metabolic syndrome and its factors. Low physical activity was also associated with increased central obesity and high triglyceride levels in adulthood (196). Studies assessing physical activity and metabolic risk in college students, reported that students spent on average at least 4 hours a day in a sedentary position (either studying, playing video games, or watching television). Also the students' physical activity, measured via step count, was decreased as well. The combination of increased sedentary activity and decreased physical and leisure time activity (thus establishing a below average fitness level) increased the students' risk of developing abdominal obesity and/or the MetS **(**133).

The Metabolic Syndrome and Sleep

The hours an individual sleeps per day can influence one's risk of developing the MetS. It was reported that individuals who sleep 7-8 hours per day have a lower risk of developing the Mets, compared to individuals who sleep less than six hour per day (38). Although the exact mechanisms linking shortened sleep and metabolic syndrome are unknown many studies have shown that short sleep duration (less than six hours) was associated with increased sympathetic tone, increased blood pressure, increased insulin resistance, and a higher risk of obesity due to the effects of sleep deprivation on hormone levels, including leptin and ghrelin (120, 174). The lowered levels of leptin and higher levels of ghrelin due to sleep deprivation can affect metabolism and appetite causing an increase in food intake and blood glucose levels leading to weight gain (38 than nine hours of sleep a night was not significantly associated with the development of Mets (39). Therefore, various sleep durations may influence an individual's risk of developing metabolic syndrome through different pathways.

The Metabolic Syndrome and Cardiorespiratory Fitness

As the prevalence of the metabolic syndrome continues to increase, there is an increased effort to find ways to prevent and treat the syndrome. Recently, an inverse relationship between cardiorespiratory fitness and aspects of the MetS has been reported (115, 116, 118). One study found that men with a high level of CRF (measured with maximal graded exercise test) were approximately two-thirds (65-75%) less likely to develop MetS when compared to men with lower CRF. The study also stated that this inverse relationship was present even after they controlled for other factors including age, health habits, and body mass index (115). It was also reported that unfit middle-aged men (VO_2max less than 29.1 mL/kg/min) were roughly seven times more likely to have MetS than men with a VO_2max of 35.5 mL/kg/min or greater (116).

Following these studies, an intervention program found that twenty weeks of aerobic exercise, which caused increases in the subjects' CRF, resulted in a 31% decrease in the prevalence of the MetS in the subjects observed (118). Therefore, cardiorespiratory fitness may be used as either a treatment or a prevention tool for the development of the MetS. Additionally, using an objective marker, such as VO_2max from a graded exercise test, to assess one's fitness levels provides clinicians with both baseline information and a quantitative way to evaluate an individual's progress during an intervention. Increasing cardiorespiratory fitness can serve as both a treatment and protective mechanism by positively affecting factors associated with the MetS including blood pressure, insulin sensitivity, cholesterol levels (increases HDL), decreasing triglyceride levels, reducing visceral fat accumulation and body weight (116).

Researchers have stated that the protective mechanism of CRF is present in both sexes, as well as in overweight and obese individuals. However, high levels of CRF are needed to provide the most protection due to the inverse relationship between CRF and the MetS (118). Therefore, in order for protection to be present from the various factors associated with the MetS, individuals need to exercise for at least thirty minutes a day most days of the week in order to achieve the high levels needed (5).

Cardiorespiratory Fitness and Sleep

An individual's cardiorespiratory fitness level can affect a number of biological systems within the body and can even influence the quantity and quality of sleep one acquires. For many years the relationship between fitness levels and sleep has been observed, and although a lot of mixed results have been documented a few common

findings are present throughout the research. The most common finding is the association between CRF and slow wave sleep (SWS) or stages 3 and 4 of the sleep cycle (185).

Several studies have reported that individuals with a higher level of CRF or those who take part in chronic exercise, had a reduced sleep onset latency, woke up less during the sleep period, and slept for a longer duration (82, 119, 167). Griffin and Trinder (82) reported that fit subjects had greater amounts of SWS when compared to the unfit subjects. Another study conducted with young adults also reported a positive correlation between CRF (tested with a run/walk field test) and sleep quality (119). A study conducted on army recruits assessed the relationship between CRF levels and sleep before and after a nine-week training program. They reported that an increase in CRF (measured with a VO_2max test) was associated with an increase in sleep efficiency (both in duration and quality). The researchers stated that the increase in sleep efficiency was due to an increase in SWS, less awakening throughout the night, and a shorter latency to the onset of sleep. They also noted that there were no changes in REM sleep when comparing the results of before, during, and after the training program. The researchers projected that the increased CRF led to improved sleep quality due to the increases in energy expenditure. They believed that the increased energy expenditure required a longer recovery period, thus leading to more sleep (167).

Studies have documented the positive relationship between increased CRF and slow sleep waves in a variety of populations (82, 119, 167), however the exact mechanisms are still unknown. It has been hypothesized that hormones such as growth hormone (GH) and brain derived neurotrophic factors (BDNF) may influence the sleep efficacy. These hormones have been associated with sleep duration and sleep quality. However, the role of hormones, heart rate, temperature, and autonomic function during sleep require further research before a definite mechanism can be identified (185).

Furthermore, the time of day in which one takes part in exercise to improve their CRF levels may have the largest influence on sleep. For example, exercise in the afternoon has been shown to increase SWS during sleep, however exercise performed before going to bed does not increase and may actually reduce SWS during sleep. This reduction in SWS is thought to be a product of the increased stress that is associated with exercise (96). However, these results were reported during acute bouts, therefore individuals who habitually exercise and have higher CRF might express increased SWS. Overall increases in CRF level can increase sleep efficiency, thus improving quality of life and potentially decreasing risk of developing various health risks (185).

Smoking and Sleep

Smoking both acutely and chronically has an effect on both the quality and quantity of sleep. One study found that in non-smokers the exposure to nicotine caused a decrease in REM sleep and the total amount of time the subjects slept (57). Another study found that chronic smokers had difficultly both falling asleep and staying asleep (143). Nicotine activates the sympathetic nervous system thus increasing heart rate and blood pressure throughout the day and consequently elevating them at night as well, which can lead to a disruption in sleep. Therefore exposure to nicotine may influence one's sleep/wake cycle consequently causing alterations in one's natural circadian rhythm (138).

Obesity and Alcohol

Consumption of alcohol, a high calorie, energy dense substance that contains 7.1 kilocalories per gram, has been associated with increases in weight gain (160). Many studies have found a positive association between binge or heavy drinkers (2-3 drinks

per day) and body weight and measures of adiposity. Moderate drinkers had no association between consumption and body weight (28, 152). Researchers concluded that moderate drinkers may limit their food intake when consuming additional calories from alcohol, whereas heavy binge drinkers did not modify their food intake (152). Thus, the heavy drinkers were consuming additional calories from the combination of alcohol and food intake.

Alcohol inhibits lipid oxidation and causes the body to use acetate (produced by the liver) as an energy source instead of fats (166). Additionally, alcohol influences food intake and hormonal levels, such as leptin and serotonin, which can affect one's feeding behaviors (200). The type of alcohol consumed and gender can increase one's risks and studies have reported young men are at the highest risk of developing a pattern between heavy consumption and body weight (160).

Obesity and Smoking

Many studies have found that cigarette smokers weigh less and are leaner than those who do not smoke (3). However, there is a linear trend between number of cigarettes smoked per day and waist circumference. Heavy smokers (> 20 cigarettes/day) had an increased risk of developing obesity and researchers proposed that the increased risk was due to these individuals having more poor lifestyle habits, such as alcohol consumption, unhealthy diet, and lack of physical activity, than the moderate or light smokers (42).

The association between cigarette smoking and decreased weight is likely due to the effects of nicotine. Nicotine can increase gastrointestinal motility leading to a loss of food calories because of the decreased breakdown and absorption time. Nicotine is also associated with an increase in energy expenditure and a suppression of appetite (94). However, heavy smokers generally do not experience these effects. Even though smoking is a associated with decreased body mass index, the distribution of fat is more centrally located in smokers which places them at a higher risk of developing the MetS (21).

The Metabolic Syndrome and Smoking

The relationship between the MetS and smoking is dependent upon the dosage and duration of use. It has been found that the number of cigarettes smoked per day is positively associated with an increased risk of developing the MetS (44). Smokers have an increased risk of becoming insulin-resistant and develop Type 2 diabetes. Smokers also tend to exhibit higher levels of triglycerides, increased blood pressure, increased waist circumference, and lower levels of HDL cholesterol than nonsmokers (65). Cigarette smoking affects lipid metabolism and glucose by activation of the sympathetic nervous system, thus influencing fat accumulation and body mass index (62). Smoking habits are commonly associated with other lifestyle habits, such as drinking and lack of physical activity, placing one at a higher risk for developing the MetS.

The Metabolic Syndrome and Alcohol

There are inconsistent results for the association between alcohol and the MetS. One study found mild to moderate, and moderate to heavy alcohol consumption was associated with a decreased risk of the MetS (177). However, another study found that heavy drinking (>20g/day) is associated with increased prevalence of the MetS. This study observed higher triglyceride levels, blood pressure, glucose levels, and waist circumference measures in heavy drinkers compared to lighter drinkers or nondrinkers, thus placing the heavy drinkers at a higher risk (16). The inconsistent results may be due to other factors such as sex, race, ethnicity, and type of alcohol, which can all play a role

in the metabolism of alcohol (177).

Smoking and Physical Activity

A study exposed mice to cigarette smoke and observed the changes in physical activity. Researchers reported a decrease in locomotor activity at night (the active period of mice). Consequently, even after they stopped exposing the mice to cigarette smoke, after 2 weeks of breathing fresh air, physical activity of the mice increased, but only to 70% of previous activity level (100). Kurti and Dallery (114) found that after moderate exercise participant's delayed smoking longer than those who were inactive. Vans Rensburg and colleagues (150) found similar results in that exercise reduced the desire to smoke. Therefore, smoking can have negative effects on physical activity, yet exercise has a positive effect on cessation of smoking.

Obesity and Blood Pressure

Blood pressure can be affected by a number of factors such as sodium retention, sympathetic activity, inflammation, insulin, fat distribution, and hormone levels including leptin and aldosterone (107). An individual with increased adiposity is 3.5 times more likely to develop hypertension than a healthy weight individual (108). Zhang and Wang (202) found similar results among adolescents. Those with increased BMI and waist circumference are at an elevated risk of developing hypertension. They found that waist circumference was a better predictor of hypertension than BMI (202). A possible mechanism placing obese individuals at a higher risk of developing hypertension is homeostatic imbalances between sodium and water retention (85). Sixty to seventy percent of hypertension can be attributed to excess body weight and men had a slightly higher percentage than women (77).

Cardiorespiratory Fitness and Blood Pressure

An individual's fitness level can have an effect on systolic blood pressure. Increasing cardiorespiratory fitness can reduce an individual's blood pressure by increasing arterial compliance and decreasing sympathetic activity (40). Individuals, who significantly increased their VO_2 max during a 16-week exercise intervention program, had a reduction in both resting and daytime blood pressure measures of 3.0 and 2.4 mmHg, respectively (51). Another study by Gaya et al. (78) stated that poor fitness habits created in the early stages of life, could potentially lead to hypertension and low fitness levels later in life. Therefore, establishing a lifestyle with moderate to high levels of CRF earlier in life may help to prevent one from developing health risks later in adulthood.

Although higher levels of CRF are associated with lower systolic blood pressures, the association is strongest in normal weight individuals where the added stress of excessive body weight is not present. Thus, increasing one's CRF levels may help to reduce blood pressure or prevent hypertension, however in obese or overweight individuals, a reduction in body weight is the most effective method of reducing blood pressure (40).

Physical Activity and Blood Pressure

Carson et al. (36) observed the effects of different intensities of exercise on waist circumference, systolic and diastolic blood pressure, HDL and LDL cholesterol, triglycerides, insulin and glucose. They found that low light intensity physical activity (100–799 counts/min) and high light intensity physical activity (800 counts/min to <4 METs) was associated with low diastolic blood pressure. Each additional hour spent in low light and high light intensity physical activity decreased diastolic blood pressure by

0.59mmHg and 1.67 mmHg, respectively. Moderate to vigorous physical activity (> 4 METs) was associated with decreased systolic and diastolic blood pressure and lower waist circumference. Each hour of MVPA was associated with a 3.54 mmHg lower systolic blood pressure. Light intensity physical activity was not shown to be associated with changes in insulin, glucose, LDL or triglycerides. Yet, moderate to vigorous activity was associated with lower levels of insulin. These results indicate all intensities of physical activity can have beneficial health effects on blood pressure but moderate to vigorous activity is the most beneficial (36).

Chapter 3

Markers of Circadian Rhythm

As discussed earlier, disruption of a normal circadian rhythm can often lead to illness and disease. Thus, in order to determine circadian rhythm it is important to find a method that is relatively easy to measure and reflects the natural internal rhythms of the body. Some rhythms of the body fit these characteristics and are considered "marker rhythms." Previous methods of measuring circadian rhythm include the use of melatonin and/or cortisol concentrations, heart rate, blood pressure, and core body temperature (95). However, many of these methods are invasive and may alter the body's natural rhythms.

Melatonin concentration can be measured in saliva, plasma and urine samples (193). These methods are costly and quite disruptive because they require frequent sampling during both day and nighttime hours. This method often requires laboratory work and is inconvenient for both test subjects and investigators. Cortisol levels can be measured by taking serum or saliva samples but has similar disadvantages to melatonin sampling. Blood pressure monitoring can be automated but still can cause disturbances in normal daily living, especially during sleep. Using heart rate as a marker rhythm allows for easy sampling, however it has high variability and can be influenced by a variety of factors beyond just circadian rhythm. Core body temperature is most effectively measured using rectal probes. Yet, these probes are invasive, unpleasant for longer periods of time and often discourage subject participation (159).

Recently, some less invasive methods have been discovered to measure circadian rhythms in humans. One newer method is ingestion of a pill data-logger however the pill is expensive and can only record core body temperature during the time it takes for the pill to pass through the gastrointestinal tract leaving it ineffective for long term or large population studies (33). Another less invasive method to measure circadian rhythm is using an actigraph to record rest/activity rhythms. This method allows for high frequency. However, an actigraph is subject to external masking input; for example, car rides, removal of device, position changes, co-sleeping partners can affect the results. It is a good measurement tool of rest/activity cycles but is not recommended for direct observation of circadian rhythms because it does not account for feeding time or other zeitgebers (157). Using skin temperature measurements has allowed for noninvasive and high frequency sampling of distal body temperature to observe circadian rhythms. Distal skin temperature is indirectly related to core body temperature. As core body temperature decreases, heat dissipates via vasodilation out to the distal blood vessels and skin leading to an increase in distal skin temperature (112).

Circadian Rhythm of Body Temperature

Core body temperature is determined by the relationship between heat production and heat loss, with heat loss as the more influential factor (8). During resting conditions, heat production depends on the metabolic activity of organs in the body,

which contributes to 70 percent of the core body temperature (109). Blood transports heat from the core to the distal skin through vasodilation where heat can be lost to the environment (9).

Core body temperature is under homeostatic control by the SCN and oscillates throughout a 24-hour cycle. Under constant conditions, distal skin temperature has been shown to increase in the evening whereas heat production and core body temperature decrease. In the morning the opposite occurs, resulting in decreases in distal skin temperature and increases in core body temperature (112). The SCN regulates core body temperature by establishing a "set point" for the body temperature to oscillate around, however peripheral oscillators are also able to influence the "set point" thus affecting core body temperature rhythms. Zeitgebers such as food, sleep, and activity act through the HSF1 pathway to influence the peripheral oscillators to establish a temperature "set point" or rhythm as well. Therefore, peripheral oscillators respond to input from the SCN but are also sensitive to signals from zeitgebers (30).

If a normal cycle is present, the SCN synchronizes the temperature rhythm output of peripheral clocks to oscillate around the same "set point." However, desynchronization between the two systems can occur if the set points are different. If this desynchronization occurs, temperature would be regulated through signals the zeitgebers send to peripheral oscillators (30). For example, restricted feeding experiments are associated with lows in body temperature when food is absent (56). This association between feeding and temperature may be explained by glucocorticoids, which are able to reset peripheral clocks through the HSF1 pathway and change body temperature accordingly (17). Therefore, it appears peripheral circadian clocks set body temperature through the HSF1 pathway and can be influenced by either the SCN or zeitgebers such as food and activity.

In the evening hours, the secretion rate of melatonin increases, promoting vasodilation and a decrease in core body temperature. As core body temperature decreases and distal skin temperature increases, relaxation and sleepiness is induced. In contrast, an increase in core body temperature during the morning hours, prepares the body for awakening activities (111). The changes in distal skin temperature are a mirror image of core body temperature but changes are often delayed approximately one hour compared to core body temperature changes. Sarabia et al. (159) demonstrated this phenomenon by measuring wrist temperature. They found wrist temperature increased 30 minutes before onset of sleep; however, it did not decrease until after waking, indicating there is a delay between changes in core and distal body temperature. This relationship between changes in body temperature and sleep has been demonstrated in studies that applied cooling and heating effects to the body, inducing sleeping and waking activities (186).

The primary changing temperature (decrease in core temperature or increase in skin temperature) responsible for the onset of sleep has not been fully elucidated. Recently, stimulating increases in peripheral temperature caused suppressed wakefulness at night and initiated deeper sleep episodes (110). Sarabia et al. (159), reported that 90% of their subjects were sleeping when wrist temperature reached approximately 35 degrees Celsius. These studies indicate wrist temperature can be a valid marker of sleep activity.

iButton

Previous monitoring of wrist temperature required the subjects to wear both the temperature sensor and the receiving device. However, recently a wireless temperature system known as the Thermochron iButton placed in direct contact with the skin on the non-dominant wrist has been used to observe distal body temperature (188). Distal skin

temperature has been assessed on a variety of body sites yet placement on the wrist is ideal due to decreased adiposity and close proximity to the radial artery (188). The iButton is able to both measure and record temperature for up to 21 consecutive days at a sampling frequency of 10 minutes.

The device is a small (16 x 6 mm^2) stainless steel sensor that can be placed directly on the skin and measure temperatures between the range of 15 and 46 degrees Celsius with a resolution of 0.125 degrees. Other advantages of the iButton are that the sensor is wireless, durable, and inexpensive (89). In addition, the iButton can be worn constantly throughout the day and night causing little disruption to the wearer's normal cycle, thus allowing for continuous monitoring of distal body temperature. Additionally it allows the investigator to match specific zeitgebers and changes in body temperature when provided the necessary information.

Some disadvantages of the iButton are that the sampling rate allows for only one temperature value per minute and the sensor is inaccurate when exposed to extreme temperatures below 15 or above 46 degrees Celsius (188). Distal skin temperature fluctuates between 27.5 and 33.8 degrees Celsius and even with the changes in temperature due to activities of daily living, skin temperature remains within the iButton measurement range. Also, events such as eating, sleeping, and physical activity, have been shown to cause changes in wrist temperature and the iButton is sensitive enough observe these changes in temperature (159). Corbalán-Tutau et al. (50) found that the iButton measuring distal temperature on the non-dominant hand of women subjects was able to accurately assess the changes in body temperature experienced throughout everyday activities and was a valid method of assessing body temperature reflective of circadian rhythm.

Methods of Physical Activity

There are many different ways to measure physical activity; the best way for each study can depend on population, cost, time, and availability. Two types of methods, subjective and objective, are used to monitor physical activity. Subjective methods to measure physical activity involve using daily logs or completing various questionnaires regarding activity. Questionnaires are affordable and practical to use with large populations. There are a variety of approved physical activity questionnaires; yet, these may result in overestimation or underestimation of activity (168). A study found that the accuracy of questionnaires immediately after and up to a week after physical activity took place found subject bias to be common (80).

A type of objective measures is known as criterion methods, which are considered the "gold standard" when measuring physical activity. The most commonly used objective criterion methods are doubly-labeled water, indirect calorimetry, and direct observation. The doubly-labeled water method measures physical activity by having the subject drink a specified amount of a stable isotope and measuring urine excretion over 1-2 weeks in order to determine total energy expenditure (189). This method is considered to have an accuracy of within 3-10% of actual energy expenditure (164). However, this method is very expensive and does not discern between energy expenditure from light, moderate or vigorous physical activity (189).

Indirect calorimetry objectively measures physical activity using the volume of oxygen consumption and carbon dioxide production measures. It is considered accurate within 4%. Indirect calorimetry is relatively expensive, is most often measured within a laboratory, and it is impractical when measuring large populations (189).
Direct observation, another objective criterion method, uses a trainer to directly monitor a subject's physical activity. Although this can be an accurate method, it is very susceptible to the interpretation by the trainer. The presence of a trainer may also lead

to some reactivity by the subject, and this method is difficult to test a large population over a longer time period (189).

Additional objective methods to assess physical activity include the use of motion sensors such as accelerometers and pedometers. Both accelerometer and pedometers are lightweight, easy to use and are shown to be within 0.1% to 0.4% accurate for activity (counts/min) and within 1% to 3% accurate for counting steps per day (27, 54). However, the accuracy of these devices may depend on manufacturer and BMI status. Accelerometers use piezoelectric sensors that are capable of measuring acceleration and frequency in three different planes. Accelerometers can measure total physical activity counts over a period of time as well as estimate the intensity of physical activity based on activity counts per minute. Accelerometers are much more expensive than pedometers therefore, pedometers may be a more cost effective tool when observing large study populations (189).

There are two types of pedometers, spring-loaded and piezoelectric strain gauge. Spring-loaded pedometers must be placed in a vertical plane perpendicular to the ground, so positioning of this type of pedometer can affect its accuracy. This type only measures step counts and does not account for intensity of physical activity. The piezoelectric strain gauge pedometers do not depend as much on positioning for accuracy and can measure step counts as well as time spent in moderate to vigorous activity (163). Crouter et al. (54) showed that piezoelectric pedometers are more accurate at slower speeds, lower vertical displacement, and greater degree of vertical tilt than spring-loaded pedometers. Thus, piezoelectric pedometers are cost-effective, easy to use, and accurate, making them a good tool to use when measuring everyday physical activity of the general public. The Kenz Lifecorder (KZ), Yamaz Digiwalker SW-200 (YX200), New Lifestyles (NL), and Yamaz Digiwalker SW-701 (YX701) pedometers have been shown to the most accurate brands in assessing step counts during low and high speeds and are recommended for research use (54, 163).

Clemes et al. (47) found that participants who were asked to record their daily step counts into an activity log elicited the greatest degree of reactivity (46). This is most likely due to the participants being more aware of activity levels which causes the participant to set goals to increase their physical activity levels compared to normal. Sealed pedometers show the least amount of reactivity for similar reasons (48). It has recently been suggested that seven days of pedometer monitoring are sufficient to reliably estimate monthly habitual physical activity in most people (47).

Cardiorespiratory Fitness

Since CRF relies on three important systems (cardiovascular system, respiratory system and skeletal muscle) of the body to work together, it has been stated that cardiorespiratory fitness and mortality are related in that a small improvement in CRF may decrease one's risk of mortality (189). Therefore assessing an individual's CRF may be an important factor for potentially preventing or treating various health issues especially cardiovascular and metabolic diseases.

Cardiorespiratory fitness can be assessed using a variety of methods ranging from questionnaires, to field tests, to laboratory tests. Over the last few years the methods used to assess CRF have changed, especially the laboratory based tests due to advancements in technology. Maximal volume of oxygen consumed (VO_2) is an objective measure of cardiorespiratory fitness that can be obtained from either a maximal graded exercise test or estimated using a submaximal test. The values obtained from these measures are used to assess an individual's CRF level. CRF is measured or estimated using indirect calorimetry and requires measuring an individual's oxygen uptake and then comparing the measured or estimated values to a set standard

based on age and sex (189). For young men a maximum VO_2 above 42 mL/kg/min is considered fair or better (5).

As stated earlier, CRF can be either measured or estimated. Estimated measures generally consist of a field test, such as a cycle ergometer protocol, a shuttle run, a two-kilometer walk, or the Cooper 12 minute test. The technicians then use heart rate, duration, or distance traveled, to estimate the maximal amount of oxygen consumed. Direct measures of CRF take place in a laboratory setting and are conducted on a treadmill or cycle ergometer allowing the technician to acquire a direct measure of gases exchanged throughout the duration of the test. VO_2 uptake can be estimated or measured at both maximal and submaximal levels (189). The testing method and protocol used to assess an individual's CRF should take into consideration the subject being tested and the desired results due to the risks associated with different methods. Field tests (indirect) are less expensive, require less time, and are easier to administer (the technician requires less training). However, the values are estimated so these tests are not as accurate as direct tests. Laboratory assessment (direct) requires highly trained personnel, expensive equipment, and take longer to administer than a field test, however values obtained in a laboratory are the most valid and reliable (190).

The method of measuring CRF in the laboratory has changed over the last few decades. Originally in the mid-1900's the Douglas bag method was used to measure gas exchange and assess one's cardiorespiratory health. However, following the 1970's computerized systems using flow sensor devices and computer programs began being used in exercise testing environments, replacing the Douglas bag method. The Douglas bag method was the gold standard, which used large canvas bags to collect expired air in order to measure gas fractions (22). The Douglas bags method assessed oxygen consumption based on volumes. Now, the computerized metabolic systems assess oxygen consumption based on ventilation at a breath-by-breath rate and are considered the "gold standard" to assess CRF.

Even though the relationship between the gases (oxygen and carbon dioxide) has not changed, the method used to collect such data has. The ventilation rates are acquired from the expired side and are sensed by a phneumotachometer. This advancement in assessing CRF allows for a less invasive method to be utilized since only a few tubes and a mouthpiece connect the subject to the system (126). Even though the Douglas bag method was relatively accurate, a single analysis took a significant amount of time; therefore one advantage of the new computerized system is the nearly instantaneously available measures.

There are a number of computerized metabolic systems used to collect data concerning CRF. A few reliability and validation studies have been conducted over the years and researchers have identified a few potential sources of variability. Since CRF is assessed using the physiological measure of VO_2, variability is possible at both a biological and technological level. It has been reported that about ninety percent of the variability is biological and ten percent is technological (126).

It has also been stated that VO_2 measures vary between systems, therefore one needs to take caution when comparing results from various devices. For example, in one validation study, the SensorMedics absolute VO_2 results where higher than the Medikro system but lower than the Cosmed values (93). However, when comparing results from the same device, results are relatively precise with an expected error of 3 to 5%. One system that has been validated and compared to the gold standard of the Douglas method is the SensorMedics series. Validation studies have reported a less than 5% error rate with the SensorMedics, leading researchers to confirm that it is a valid and reliable (at both submaximal and maximal workloads) system to use when assessing CRF in terms of oxygen consumption (126).

Body Composition

There are a variety of ways to measure body composition. BMI is the most common way to assess adiposity due to its simplicity. BMI classifies individuals into three categories based on height and weight. A BMI between 18.5 and 24.9 kg/m^2 corresponds to healthy weight, a BMI between 25 and 29.9 kg/m^2 corresponds to overweight, and a BMI greater than 30 kg/m^2 is considered obese (5). However, BMI does not take into account fat free mass versus fat mass. Therefore, an individual with normal weight but excess body fat would not be classified as overweight or obese, conversely an individual with high amounts of lean mass and low fat mass may be classified as overweight or obese (52). Therefore, it is not a good measure to use when trying to determine an individual's risk of developing an obesity-linked disease.

Circumference measures can be a simple, inexpensive tool to assess adiposity. Although some limitations with circumference measurements are the many different locations the measurement is taken (52). In a review of literature by Ross et al. (153) they found there were eight different sites for measuring waist circumference. This variety in locations may lead to different measurements corresponding to different risks. Another low cost method for assessing body composition is skinfold thickness. Lohman (124) reported that skinfold thickness had an error of 2.6 kg for fat free mass and 3.5% for body fat, which are lower than for BMI. However, some limitations to skinfold thickness include variations in subcutaneous in relation to total fat, skinfold thickness in relation to subcutaneous fat and technical error of the skinfold measurement (123).

Bioelectrical impedance analysis (BIA) is yet another method that can be used to assess total fat. BIA works by sending an electrical current through the body and measuring the impedance to that current. The equipment used for BIA is portable, easy to use and relatively inexpensive. However, the BIA is influenced by sex, age, race and ethnicity. Thus, BIA measurements of adiposity may not be the best tool for diverse populations (52). Hydrostatic weighing analyzes body composition using a two-compartment model (fat and fat-free mass) based on density measures (194). Hydrostatic weighing had been the gold standard in body composition for many years. It exhibits strong levels of precision and has approximately a ±1.5% error for estimating percent body fat (124). Yet, it is not without disadvantages. Hydrostatic weighing requires active participation from the subject that if not done correctly can affect the results (52).

Air displacement plethysmography uses a BodPod to indirectly measure body volume based on the volume of air it displaces. The measurement is dependent on Poisson's and Boyle's Law. The BodPod has been shown to be as reliable as hydrostatic weighing (67). Another method used to assess body composition is Dual Energy X-ray Absorptiometry (DXA). DXA uses attenuation of radiation to determine 2 components of tissue, either bone and soft tissue or mineral-free lean soft tissue and fat. DXA is now considered the "gold standard" in body composition (52). Some studies have shown that DXA may underestimate body fat at low body fat percentages and overestimate body fat at high body fat percentages (187). A DXA machine is expensive but the measurement is quick and easy for all populations.

Chapter 4

MANUSCRIPT

INTRODUCTION

The circadian system of the human body produces oscillations of several physiological variables that undergo changes based on a 24-hour time clock (12, 33, 38). Regulation of these circadian oscillations is organized by a hierarchy system starting in the brain and extending to peripheral tissues and organs. Within the brain, these circadian rhythms are controlled by neurons found within the suprachiasmatic nucleus (SCN) located in the hypothalamus. The SCN, known as the central pacemaker, is synchronized to the light/dark cycles and coordinates many physiological processes through direct and indirect control of several peripheral clock genes. The peripheral clocks are located throughout the body in the heart, lung, kidney, pancreas, muscle, and adipose tissue (4, 12, 30).

In addition to the SCN input, the rhythms of the peripheral oscillators can also be influenced by behavioral signals. The light/dark cycle is the most dominant zeitgeber (synchronizer) but feeding signals and rest/activity signals have also been shown to have the ability to entrain peripheral clock genes (1, 3, 16, 30). Many studies have shown that altering metabolic, endocrine, and homeostatic events can change the expression of circadian gene clock expression in the peripheral tissue with no accompanied change in the SCN (1, 3, 20). This may result in an uncoupling of the central and peripheral clocks leading to a disrupted circadian rhythm. The disruption of these circadian clock genes is associated with significant adverse changes in metabolism (9, 23, 29, 37).

Some periodic cues, such as scheduled exercise, social interactions, sleep habits, and feeding time, have been shown to alter the circadian system (6, 24, 25). A disruption in circadian rhythms has been shown to have negative effects on health and may lead to some of the factors associated with the Metabolic Syndrome (40). The Metabolic Syndrome is a cluster of health-risk factors associated with obesity that is a strong predictor of the development of cardiovascular disease and metabolic derangements (27). Previously, measures of circadian rhythm were labor intensive and intrusive (18, 38). Recently, frequent consecutive measures of skin temperature monitoring have been successfully used to characterize several parameters of circadian rhythm in a variety of healthy and diseased populations (10, 38, 42) thus allowing for a valid, simple, non-invasive method to assess changes in body temperature reflective of circadian rhythm.

The transition from adolescence to young adulthood is an important time to evaluate cardiovascular health in young adult males. This transition period has been shown to be a time of increased risk of developing obesity due to changes in behavioral, nutritional and physical activity habits (17). Therefore, the aim of this study was to determine if there were significant differences in circadian rhythm (assessed by temperature amplitude, stability, and lag) measured by noninvasive wrist skin temperature rhythm monitoring among optimal, fair, and poor percentage fat (%Fat) categorized young men. The second aim of the study was to determine if the circadian rhythm parameters are associated with factors characterizing the Metabolic Syndrome including abdominal circumference, resting systolic and diastolic blood pressure, and lipid profile measures [total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride concentrations, and total cholesterol to HDL ratio],

cardiorespiratory fitness, physical activity levels, and/or nutritional intake (frequency and timing) in young men grouped according to %Fat.

METHODS

Subjects.

A total of fifty-nine young male participants aged 20 to 34 years old were recruited from the Lexington, KY area for this study. For recruitment purposes, the participants were categorized by BMI status (22 healthy weight: BMI < 25.0; 26 overweight: 25.0 ≤ BMI ≤ 29.9; 11 obese: BMI ≥ 30.0). All volunteers were apparently healthy and free from any known cardiovascular disease, diabetes mellitus, pulmonary disease, and/or orthopedic limitations. None of the volunteers were taking medications affecting insulin sensitivity. After receiving a written informed consent approved by University of Kentucky Medical Institutional Review Board, each participant filled out a Physical Activity Readiness-Questionnaire and Health History Form to identify any existing contraindication to the maximal graded exercise testing as specified in the American College of Sports Medicine Guidelines for Exercise Testing and Prescription (32). All resting heart rate and blood pressure, body composition, and maximal graded exercise testing were completed in a single testing session, followed by 7 consecutive das of circadian rhythm, daily questionnaires and objective physical activity recording. Subjects were then scheduled for a second study session in the early morning following an overnight fast (minimum 8 hours) to provide a resting venous blood sample.

Body Composition Measurements.

Standing height and body weight were determined for each participant using a wall-fixed stadiometer (Seca Statiometer Pat. No. 4694581) and a calibrated scale (Teraoka D1-10; Singapore), respectively. A total body DXA scan was performed on each participant using a Lunar iDXA (Lunar Inc., Madison, WI) bone densitometer. All scans were analyzed by a single trained investigator using Lunar software version 13.10. DXA fat-free mass (FFM; g), DXA fat mass (g), and DXA mineral-free lean mass (g), and DXA percent fat (%Fat) were assessed. For analyses purposes, DXA percent fat measures were used to recategorize the subjects into optimal (percent fat ≤ 17.9), fair (18.0 ≤ percent fat ≤ 24.9), and poor (percent fat ≥ 25.0) groups using cut points previous reported (32). Circumference measurements (waist, abdominal, and hip) were taken in triplicate and the mean measurement was used for analyses using a fiberglass anthropometric tape (Creative Health Products BMS-8) in accordance with the guidelines established by the Airlie Conference Proceedings for each participant (22).

Maximal Graded Exercise Test.

Each participant performed a maximal graded exercise test (GXT; 2 minute progressive speed and grade) on a treadmill using an indirect calorimetry testing system with integrated electrocardiogram (ECG) (SensorMedics Vmax Encore, CareFusion Corporation; San Diego, CA). During the tests, continuous measurements of oxygen consumption were taken and cardiovascular monitoring took place. At the final 30 sec of each stage, heart rate, blood pressure, and rating of perceived exertion (RPE) were taken and recorded. The test was terminated upon volitional fatigue. After completing the maximal GXT, five minutes of passive recovery data (heart rate and blood pressure) were taken. Each subject reached VO_2 peak ($ml \cdot kg^{-1} \cdot min^{-1}$) determined by the participant's ability to obtain a minimum of one of the following criteria: respiratory exchange ratio >1.10, maximum heart rate ± 1SD, Rating of Perceived Exertion (RPE) ≥ 17.

Circadian Rhythm Measures.
Circadian rhythm parameters (temperature amplitude, stability, and lag) were measured by noninvasive wrist temperature rhythm monitoring and recording devices (Thermochron iButton; Embedded Data Systems, Lawrenceburg, KY). Temperature amplitude, stability, and lag were determined for each participant. Temperature amplitude is defined as half the distance between the peak and the trough temperatures. Temperature stability is defined as the orderliness of the pulse wave. Temperature lag is defined as the number of hours after midnight at which the peak of the cycle hours (10). The iButton was programmed to record temperatures every ten minutes with a sensitivity of 0.0625 degrees Celsius. Each subject wore an iButton for 7 consecutive days over the inside of the wrist of the non-dominant hand. The subjects were given strips of latex-free dressing tape (Hypafix; Smith & Nephew Inc; Memphis, TN) and a double-sided cotton sports wrist band to maintain the iButton securely against the wrist, and allow for infrequent removal during times when the subject has direct contact with water (ie. bathing or swimming) followed by replacement. Following the 7 days of wearing the iButton, it was returned to the research team and the information was transferred through an adapter (SK-IB-R-iButton Connectivity Kit; Embedded Data Systems, Lawrenceburg, KY) and was analyzed using a new algorithm software program (JTK_CYCLE;19). While wearing the iButton, the participants were asked to record answers to daily questions concerning sleep, frequency and timing of nutritional intake, alcohol use, smoking, and removal times of the wrist skin temperature monitor.

Physical Activity Assessment.
All subjects were instructed to wear a New Lifestyles-1000 (NL; LeesTown, MO) medical grade activity monitor for 7 consecutive days coinciding with the days the wrist temperature-monitoring device was worn. The number of daily steps, miles and time spent in moderate to vigorous activity were recorded. To avoid reactivity, all activity monitors were sealed using stickers after stride length, time of day, and an intensity threshold were internally programmed.

Blood Sampling Procedure.
Participants were asked to give a fasted venous blood sample (minimum 8 hours fasted) to evaluate lipid profiles. Participants came in early in the morning to have blood drawn by trained nurses at the University of Kentucky Hospital. The blood sample was analyzed for total cholesterol, HDL, LDL, triglyceride concentrations, and total cholesterol to HDL ratio.

Statistical Analysis.
Data was analyzed using Statistical Package for Social Sciences (Version 22, Armonk, NY). Descriptive data are presented as means and standard deviations for all study variables. Group mean data among percent fat categories (optimal, fair, and poor) and circadian rhythm parameters (temperature amplitude, stability, and lag) measured by the noninvasive wrist temperature rhythm monitors were analyzed using a 3X3 analysis of variance. Group mean data of temperature amplitude, stability, and lag of those with or without factors of the Metabolic Syndrome was compared using a 2X3 analysis of variance. In addition, bivariate correlational and stepwise regression analyses were performed to determine the strength and significance of association among circadian rhythm temperature parameters with Metabolic Syndrome factors, physical activity, physical fitness, nutritional intake frequency and timing, and chronotype. The level of statistical significance was set at a P value < 0.05.

RESULTS

The subject characteristics are shown in Table 1. Fifty-nine healthy male participants (age: 24.79 ± 3.48 years, height: 177.85 ± 7.47 cm, body weight: 85.84 ±

18.14 kg, BMI: 27.00 ± 4.64, percent fat: 22.42 ± 7.97) participated in the study. For analysis purposes, the participants were organized into body composition groups according to %Fat defined by American College of Sports Medicine (32). The optimal category (percent fat ≤ 18.0) included 18 participants, the fair category (18.1 ≤ percent fat ≤ 23.9) included 20 participants, and the poor group (≥24.0 percent fat) included 21 participants. Of the 59 subjects that participated in this study, 17 Optimal %Fat; 17 fair %Fat; 18 poor %Fat were willing to participate in the fasting blood sampling procedure.

The ANOVA showed significant differences in temperature amplitude (Figure 1) and stability (Figure 2) among the %Fat groups. Those in the poor %Fat group had significantly lower temperature amplitudes than those in the optimal or fair group. Similarly, the poor %Fat group had significantly lower circadian temperature stability than the optimal or fair group. There were no significant differences in temperature lag among the three %Fat groups (Figure 3).

Mean differences in temperature amplitude, stability and lag were assessed between groups of participants with at least one factor of the Metabolic Syndrome as defined by Alberti et al. (2) (waist circumference > 94cm, triglycerides ≥ 150 mg/dL, systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85mmHg, HDL ≤ 40 mg/dL) compared to those with no factors of the Metabolic Syndrome. Figure 4 shows those with a minimum of one factor of the Metabolic Syndrome had significantly lower temperature amplitudes and stability but no difference in temperature lag compared to those without any factors of the Metabolic Syndrome.

Table 3 shows the correlations between study measures and temperature amplitude. For the total group of participants, temperature amplitude was significantly correlated with waist, abdomen, and hip circumferences, average steps, average miles, average time spent in MVPA, VO_2 peak, percent fat, fat mass, HDL, ratio of total cholesterol to HDL, triglycerides, and number of Metabolic Syndrome factors. Temperature amplitude in the optimal group was significantly correlated with number of late night snacks in a week (eating after 8pm), average time last eating in a day (minimum of four days of data) and number of the Metabolic Syndrome risk factors. In the fair group, temperature amplitude was significantly correlated with VO_2 peak and number of times skipped breakfast in a week. Temperature amplitude was significantly correlated with average steps, average miles, average time spent in MVPA, VO_2 peak, HDL, total cholesterol to HDL ratio, and LDL in the poor group.

Correlations between study measures and circadian rhythm temperature stability are shown in Table 4. The stability of temperature circadian rhythm for the total group was significantly correlated with waist, abdomen and hip circumferences, average steps, average miles, VO_2 peak, percent fat, fat mass, number of times skipped breakfast, HDL, total cholesterol to HDL ratio, and number of Metabolic Syndrome factors. The stability of temperature circadian rhythm in the optimal group was significantly correlated with average steps, average miles, number of times eating a late night snack in a week, and average time last eating In the fair group, temperature stability was significantly correlated with VO_2 peak and number of times skipped breakfast in a week. Stability of temperature circadian rhythm was significantly correlated with average steps, miles, and time spent in MVPA, HDL, total cholesterol to HDL ratio, and LDL in the poor group.

Table 5 displays the correlations of study variables with temperature lag. For the total group of participants, total cholesterol to HDL ratio was significantly correlated with temperature lag. Average miles and number of times skipped lunch in a week was significantly associated with temperature lag in the optimal group. In the fair group, LDL levels were significantly correlated with temperature lag. In the poor group, HDL and total cholesterol to HDL ratio were significantly correlated with temperature lag.

The stepwise multivariate regression analysis was statistically significant and accounted for approximately 50% of the variance of temperature amplitude. For temperature amplitude, the number of average steps alone gave an R^2 value of 0.30, adding in VO_2 peak into the equation increased the R^2 to 0.42. Furthermore, the addition of the variable number of times late night eating in a week gave an R^2 of 0.50. Collectively, average steps, VO_2 peak and the number of late night snacks in a week were significant predictors of temperature amplitude. Average steps shows the strongest weight in the model, followed by VO_2 peak and then number of late night meals. The stepwise analysis for temperature stability shows approximately 56% of the variance of temperature circadian rhythm stability was accounted for by four variables. Average steps gave an R^2 value of 0.411 for temperature stability. The addition of average time spent in MVPA increased the R^2 to 0.467. When adding the number of late night snacks to the model, R^2 increased to 0.515. The final model taking into account average steps, average time spent in MVPA, number of late snacks, and fat mass gave an R^2 of 0.562. Approximately 18% of the variance in temperature lag was explained by variance in day-to-day hours of sleep and total cholesterol to HDL ratio. For temperature lag, sleep variance gave an R^2 of 0.092 and the addition of the ratio total cholesterol to HDL to the model increased the R^2 to 0.182.

DISCUSSION

The first aim of the study was to determine if there were significant differences in circadian rhythm (assessed by temperature amplitude, stability, and lag) among optimal, fair, and poor %Fat grouped young men. Figure 1 shows that participants with in the poor %Fat group had significantly lower temperature amplitude and stability compared to the other %Fat groups (optimal and fair) indicating a disrupted circadian rhythm in the more obese participants. Corbalán-Tutau et al. (10) found similar results; reporting that obese women displayed flattened circadian rhythm temperature amplitude compared to the healthy weight women. Evidence for circadian disruption in humans has been found among a variety of populations including shift workers, mentally ill, sleep deprived, and diseased populations (1, 21, 36, 43). Previous studies showed similar effects of fat on circadian rhythms in mice. Ando and colleagues (3) found obese mice showed reductions in peak circadian clock gene expression in adipose tissue compared to the healthy weight mice. Collectively, the present study and previously reported results confirm that the development of obesity is a vicious cycle of circadian disruption. Increased weight gain or obesity can lead to a disrupted circadian rhythm but the reverse is also possible; a desynchronized circadian rhythm can lead to increased weight gain and/or obesity. Scheer and colleagues (39) found circadian misalignment decreased circulating leptin levels. Chronic decreases in leptin stimulate appetite and decrease energy expenditure, which could lead to the development of obesity. There were no significant differences in temperature lag among the groups indicating this parameter is not as significantly affected by increased adiposity.

The second aim of the study was to determine if the circadian parameters were associated with factors characterizing the Metabolic Syndrome (abdominal circumference, resting systolic and diastolic blood pressure, cholesterol and HDL concentrations), cardiorespiratory fitness, physical activity levels, and/or nutritional intake (frequency and timing) in young men grouped according to %Fat measures. Participants with a minimum of one factor of the Metabolic Syndrome had decreased temperature amplitude and stability compared to those without any risk factors of the Metabolic Syndrome. Evidence from Cobalán-Tutau et al. (10) supported these findings; reporting similar alterations in wrist skin temperature were associated with a higher risk of the Metabolic Syndrome. Scheer and colleagues (39) found many metabolic changes

in humans including increased circulating glucose levels and decreased insulin sensitivity when they disrupted their circadian rhythms. Many studies have found that circadian rhythm and the Metabolic Syndrome influence one another and the disruption of circadian rhythms may lead to the Metabolic syndrome (35, 40, 41). Studies show the Metabolic Syndrome is a clustering of factors that can individually or jointly be affected by circadian rhythm disturbances and in turn can also cause disturbances in circadian rhythms (10, 13, 39).

Temperature amplitude was significantly correlated with waist, abdomen, and hip circumferences. The higher circumferences were associated with lower temperature amplitudes and stability indicating larger participants had more disrupted circadian rhythms. Lower concentrations of HDL, and higher lipid levels were associated with lower temperatures amplitudes and stability in the whole group. Lipids display circadian expression (15) suggesting that unhealthy lipid concentrations can lead to circadian disruption. Participants with lower physical activity levels also showed reduced circadian amplitudes and stability. Similarly, mice with access to a free wheel showed significantly higher amplitude in the SCN compared to mice with a locked wheel (31). VO_2 peak was also significantly associated with temperature amplitude and stability indicating that a higher fitness level measured by VO_2 peak was associated with higher temperature amplitudes and better temperature stability. Atkinson et al. (5) found that individuals with higher fitness levels have higher amplitudes and lower night minimums in body temperature when compared to individuals with lower fitness levels. Researchers have surmised that exercising routinely may stabilize an individual's day-to-day daily habits, thus providing them with more consistent circadian rhythm (6). Physical activity and fitness level were also significantly associated with %Fat (data not shown). It is well documented that low levels of physical activity and fitness can lead to weight gain. Therefore, physical inactivity, low fitness levels, and increased weight may be compounding factors that lead to circadian disruption.

In the optimal %Fat group, a higher number of late night snacks and a later average time of last eating were associated with lower temperature amplitudes. Damiola et al. (11) found that eating at irregular times (late into the night) resulted in changes in circadian gene expression in liver, kidney, pancreas, and heart but not in the SCN. This can cause uncoupling of the peripheral clocks from input signals from the SCN leading to a disrupted circadian rhythm. Temperature stability in the optimal group was also negatively associated with late night eating as well as low physical activity levels. Furthermore, a higher number of the Metabolic Syndrome risk factors were associated with lower temperature amplitudes in the optimal %Fat group. These results indicate that those with optimal %Fat may experience circadian disruption and metabolic disorders if they have bad habits including late night eating and physical inactivity.

Higher numbers of skipped breakfast was significantly associated with lower temperature amplitude and stability in the fair %Fat group. Nicklas and colleagues (28) found that those that ate breakfast regularly consumed a lower percentage of fat throughout the day than those who skipped breakfast. Thus, skipping breakfast may lead to increased weight gain. In a study comparing mice fed a high fat diet versus controls reported that the high fat diet mice began to eat and increase activity more during the light hours whereas the controlled mice continued to eat and be active at normal times during the dark period. This suggests that the high fat diet led to a disruption in the normal circadian rhythm of the mice (20).

Temperature lag was negatively correlated with total cholesterol to HDL ratio for total group of participants. The explanation for this association is not clear. However, this ratio was also negatively associated with physical fitness and physical activity. The time of day physical activity occurs may play a role in the effect exercise has on

circadian rhythms. A 15-day clinical trial in humans (accounting for the effects of light) observed the effect exercise in the evening has on the circadian phase of melatonin (a marker of circadian rhythm). The evening exercise group showed greater phase delays of melatonin compared to the no exercise control group (8). Similarly, Rubio-Sastre et al. (34) found participants exercising in the evening had a flattened and irregular rhythm, compared to those exercising in the morning or those not exercising at all. Therefore, those more physically active and fit are associated with lower cholesterol to HDL ratios. However, if the physical activity is occurring later in the day this can cause a shift in an individual's circadian rhythm displaying a greater temperature lag. Unfortunately, this study did not record the time physical activity took place and thus the influence of the time of day physical activity occurred on circadian rhythm parameters could not be examined.

Average steps, VO_2 peak and number of times eating late night snacks in a week were primary predictors of temperature amplitude. Average steps, average time spent in MVPA, the number of late night snacks, and fat mass were predictors of temperature stability. These results suggest low levels of physical activity, late night eating and increased body fat can lead to a disrupted circadian rhythm. Variance in day-to-day sleep hours and cholesterol to HDL ratio were predictors of temperature lag. Changes in hours slept each day have been shown to affect circadian rhythm. Just one day of sleep deprivation ranging from 1 up to 7 hours showed reduced amplitude in peripheral clock gene expression compared to normal sleep conditions (1).

When observing characteristics between individuals with high temperature amplitudes and low temperature amplitudes, we found that those with high amplitudes all had a relatively high VO_2 peak (greater than 50 ml/kg/min) and did not have any risk factors of the Metabolic Syndrome. This suggests those who are more physically fit and healthier have a more robust circadian rhythm. Those with low temperature amplitudes all displayed low levels of physical activity and reduced hours of sleep at night (average of 7.2 hours per night) showing the importance of sleep and physical activity on circadian rhythm function. We also found that those with high temperature stability were all relatively physically active averaging approximately 10,000 steps per day. There was not one single variable that participant's with low temperature stability had in common indicating multiple variables may be responsible for low temperature stability. There were no common variables among those with high or low temperature lag.

A limitation in our study was that we were unable to tell what time physical activity occurred. According to recent studies, those who exercise more in the evening may cause a shift in their circadian rhythm that was not be accounted for in this study. Additionally, not enough variance in some variables could explain why we did not see some of the relationships to circadian rhythm that we expected.

Corbalán-Tutau et al. (10) found that wrist skin temperature measured on the non-dominant hand of women subjects was a valid method of assessing peripheral body temperature reflective of circadian rhythm. Numerous evidence has shown that circadian disruption predisposes an individual to increased risk of obesity, metabolic disorders, and cardiovascular diseases (7, 14). We suggest that increasing physical activity and fitness, reducing late night eating and getting constant and adequate sleep can improve an individual's circadian rhythm. For future studies, it would be advantageous to implement an exercise and nutrition program and observe the effect that would have on circadian rhythm.

Table 1: Descriptive characteristics of participants as a total group and percent fat group

	Optimal (n=18)	Fair (n=20)	Poor (n=21)	Total (n =59)
Age (yrs)	23.767 ± 3.1643	24.147 ± 2.7599	26.405 ± 3.9075*#	24.7949 ± 3.48170
Height (cm)	177.528 ± 7.6995	178.447 ± 7.4588	178.057 ± 7.4815	177.8475 ± 7.4732
Weight (kg)	77.611 ± 12.5038	83.074 ± 12.6781	95.900 ± 22.2905*#	85.8424 ± 18.14069
BMI (kg/m^2)	24.5278 ± 2.87111	25.9947 ± 2.78996	30.0476 ± 5.68081*#	27.0034 ± 4.64235
% Fat	13.917 ± 2.7908	21.379 ± 1.4831*	30.376 ± 6.1161*#	22.266 ± 7.8739

Data is displayed at mean ± standard deviation
* significance at $p < 0.05$ versus optimal %Fat
# significance at $p<0.05$ versus fair %Fat

Table 2: Characteristics and habits of participants as a total group and percent fat group

	Optimal % Fat (n=18)	Fair % Fat (n=20)	Poor % Fat (n=21)	Total Group (n =59)
Waist Circumference (cm)	81.08 ± 1.13	85.30 ± 1.15*	95.70 ± 2.89*#	87.70 ± 1.39
Abdomen Circumference (cm)	81.52 ± 1.30	88.13 ± 1.28*	99.84 ± 3.24*#	90.28 ± 1.62
Hip Circumference (cm)	97.52 ± 1.48	102.21 ± 1.04*	109.44 ± 2.17*#	103.35 ± 1.15
Sytolic Blood Pressure (mmHg)	120.44 ± 1.10	121.40 ± 1.21	125.48 ± 1.54*#	122.56 ± 0.80
Dystolic Blood Pressure (mmHg)	77.78 ± 0.664	78.40 ± 0.55	80.19 ± 0.81*	78.85 ± 0.41
Average Sleep (hours/night)	7.99 ± 0.17	7.92 ± 0.21	7.52± 0.16	7.81 ± 0.11
Variance in Sleep Hours	1.99 ± 0.58	1.51 ± 0.24	1.63 ± 0.26	1.70 ± 0.22
Chronotype	1.22 ± 0.236	1.10 ± 0.23	1.19 ± 0.21	1.17 ± 0.13
Average Steps (steps/day)	8911.54 ± 500.34	9055.94 ± 966.56	6823.49 ± 677.40*	8158.92 ± 442.28
Average Miles (miles/day)	4.19 ± 0.26	4.10 ± 0.40	3.34 ± 0.31	3.84 ± 0.19
Average MVPA (minutes/day)	32.28 ± 3.54	31.26 ± 4.19	24.78 ± 3.49	29.10 ± 2.17
VO_2 peak (ml/kg/min)	61.64 ± 1.82	55.95 ± 1.32*	45.76 ± 92.02*#	54.06 ± 1.32
Mineral Free Lean Mass (g)	63587.50 ± 2428.40	61611.15 ± 2083.99	62178.90 ± 2272.78	62416.19 ± 1286.45
Fat Mass (g)	10873.11 ± 677.25	17583.40 ± 668.60*	29821.76 ± 2871.20*#	19892.22 ± 1471.92
Fat Free Mass (g)	66936.33 ± 2526.72	65008.75 ± 2174.240	65545.86 ± 2357.22	65788.00 ± 1337.42
Cholesterol (mg/dL) $^{\Delta}$	147.71 ± 5.78	157.65 ± 4.43	161.22 ± 6.81	155.63 ± 3.38
HDL (mg/dL) $^{\Delta}$	62.00 ± 2.83	54.88 ± 3.11	46.28 ± 2.90*	54.23 ± 1.90
Tot Cholesterol/HDL $^{\Delta}$	2.44 ± 0.10	3.05 ± 0.21*	3.80 ± 0.40*	3.11 ± 0.17
LDL (mg/dL) $^{\Delta}$	73.00 ± 4.18	84.88 ± 4.90	92.50 ± 5.09*	83.63 ± 2.92
Triglycerides (mg/dL) $^{\Delta}$	63.76 ± 5.30	89.06 ± 11.48	112.17 ± 18.77*	88.79 ± 8.05
Metabolic Syndrome Factors $^{\Delta}$	0.18 ± 0.10	0.29 ± 0.11	1.33 ± 0.37*#	0.63 ± 0.15
Skipped Breakfast (number/week)	0.50 ± 0.28	2.00 ± 0.478*	1.43 ± 0.39	1.34 ± 0.24
Skipped Lunch (number/week)	0.78 ± 0.31	0.80 ± 0.24	0.67 ± 0.22	0.75 ± 0.14
Skipped Dinner (number/week)	0.50 ± 0.20	0.40 ± 0.13	0.48 ± 0.15	0.46 ± 0.09

Table 2: (continued)

Average last time eating (time/day)	8.24 ± 0.30	8.42 ± 0.32	8.27 ± 0.22	8.31 ± 0.16
Late Night Eating (number/week)	3.06 ± 0.48	3.40 ± 0.494	2.84 ± 0.40	3.11 ± 0.26
Temperature Lag (Hours)	7.55 ± 1.07	6.71 ±0.71	7.35 ± 0.98	7.20 ± 0.52
Temperature Amplitude (degrees Celsius)	1.46 ± 0.16	1.38 ± 0.13	0.96 ± 0.11*#	1.26 ± 0.08
Temperature Stability	166.52 ± 17.84	175.21 ± 23.96	109.10 ± 14.12*#	149.03 ± 11.49

Average steps, miles, MVPA (time spent in moderate to vigorous activity), and average last time eating all computed with a minimum of four days of data. Skipped breakfast, lunch and dinner and late night eating computed from seven days of data. Chronotype (0=morning type, 1=midday type, 2=evening type) $^{\Delta}$ indicates n= 52 (17 Optimal %Fat; 17 fair %Fat; 18 poor %Fat group). Data is displayed as Average ± SE.

* significance at p <0.05 versus optimal %Fat

significance at p<0.05 versus fair %Fat

Table 3: Correlation values for each study variable with temperature amplitude in optimal, fair, poor and total group of participants.

Temperature Amplitude				
	Optimal (n-18)	Fair (n=20)	Poor (n=21)	Total (n=59)
Waist Circumference (cm)	-0.304	-0.224	-0.402	-0.410*
Abdomen Circumference (cm)	-0.228	-0.262	-0.383	-0.406*
Hip Circumference (cm)	0.119	-0.228	-0.322	-0.297*
Systolic Blood Pressure (mmHg)	-0.322	0.243	-0.210	-0.218
Diastolic Blood Pressure (mmHg)	-0.089	-0.018	-0.189	-0.215
Average Sleep (hours/night)	0.162	-0.022	-0.212	0.146
Variance in Sleep Hours	-0.426	-0.063	0.039	-0.241
Chronotype	0.076	0.205	0.168	0.134
Average Steps (steps/day)	0.304	0.050	0.660*	0.409*
Average Miles (miles/day)	0.280	0.088	0.605*	0.394*
Average MVPA (minutes/day)	0.205	-0.108	0.478*	0.273*
VO_2 peak (ml/kg/min)	0.281	0.488*	0.455*	0.487*
Fat (%)	-0.075	-0.041	-0.305	-0.378*
Fat Mass (g)	-0.071	-0.261	-0.365	-0.390*
Mineral Free Lean Mass (g)	-0.007	-0.256	-0.260	-0.128
Fat Free Mass (g)	0.003	-0.262	-0.255	-0.126
Skipped Breakfast (number/week)	-0.34	-0.468*	0.149	-0.225
Skipped Lunch (number/week)	-0.134	-0.122	-0.069	-0.073
Skipped Dinner (number/week)	0.231	-0.166	-0.048	0.042
Late Night Eating (number/week)	-0.645*	-0.232	0.133	-0.257
Average last time eating (time/day)	-0.651*	0.048	0.200	-0.189
Cholesterol (mg/dL)$^{\Delta}$	0.128	0.205	-0.436	-0.135
HDL (mg/dL)$^{\Delta}$	0.064	0.208	0.606*	0.380*
Tot Cholesterol/HDL $^{\Delta}$	-0.005	-0.065	-0.595*	-0.388*
LDL (mg/dL)$^{\Delta}$	0.214	-0.015	-0.598*	-0.240
Triglycerides (mg/dL)$^{\Delta}$	-0.326	0.139	-0.449	-0.299*
Metabolic Syndrome Factors$^{\Delta}$	-0.485*	-0.170	-0.379	-0.414*

* significance at $p < 0.05$. Average steps, miles, MVPA (time spent in moderate to vigorous activity), and average last time eating all computed with a minimum of four days of data. Skipped breakfast, lunch and dinner and late night eating computed from seven days of data. $^{\Delta}$ indicates n= 52 (17 Optimal %Fat; 17 fair %Fat; 18 poor %Fat group).

Table 4: Correlation values for each study variable with temperature stability in optimal, fair, poor and total group of participants.

Temperature Stability				
	Optimal (n=18)	Fair (n=20)	Poor (n=21)	Overall (n=59)
Waist Circumference (cm)	0.053	-0.189	-0.362	-0.340*
Abdomen Circumference (cm)	-0.142	-0.234	-0.335	-0.342*
Hip Circumference (cm)	-0.140	-0.229	-0.286	-0.261*
Systolic Blood Pressure (mmHg)	-0.323	0.223	-0.143	-0.201
Diastolic Blood Pressure (mmHg)	-0.376	0.103	-0.118	-0.225
Average Sleep (hours/night)	0.220	-0.147	-0.374	0.164
Sleep Variance	-0.401	-0.148	0.112	-0.244
Chronotype	0.026	0.139	0.032	0.065
Average Steps (steps/day)	0.522*	0.259	0.647*	0.495*
Average Miles (miles/day)	0.517*	0.324	0.633*	0.505*
Average MVPA (minutes/day)	0.189	-0.034	0.435*	0.241
VO_2 peak (ml/kg/min)	-0.016	0.563*	0.387	0.403*
Fat (%)	0.010	0.009	-0.279	-0.305*
Fat Mass (g)	0.020	-0.237	-0.326	-0.333*
Mineral Free Lean Mass (g)	0.104	-0.238	-0.229	-0.109
Fat Free Mass (g)	0.111	-0.247	-0.221	-0.109
Skipped Breakfast (number/week)	-0.398	-0.481*	-0.117	-0.313*
Skipped Lunch (number/week)	-0.178	-0.226	-0.169	-0.148
Skipped Dinner (number/week)	-0.017	-0.229	0.160	-0.043
Late Night Eating (number/week)	-0.512*	-0.231	0.304	-0.152
Average last time eating (time/day)	-0.727*	-0.003	0.374	-0.134
Cholesterol (mg/dL) $^{\Delta}$	0.101	0.379	-0.405	-0.062
HDL (mg/dL) $^{\Delta}$	0.205	0.306	0.601*	0.336*
Tot Cholesterol/HDL $^{\Delta}$	-0.221	0.074	-0.620*	-0.327*
LDL (mg/dL) $^{\Delta}$	0.085	0.099	-0.545*	-0.173
Triglycerides (mg/dL) $^{\Delta}$	-0.323	0.124	-0.460	-0.213
Metabolic Syndrome Factors $^{\Delta}$	-0.468	-0.142	-0.379	-0.363*

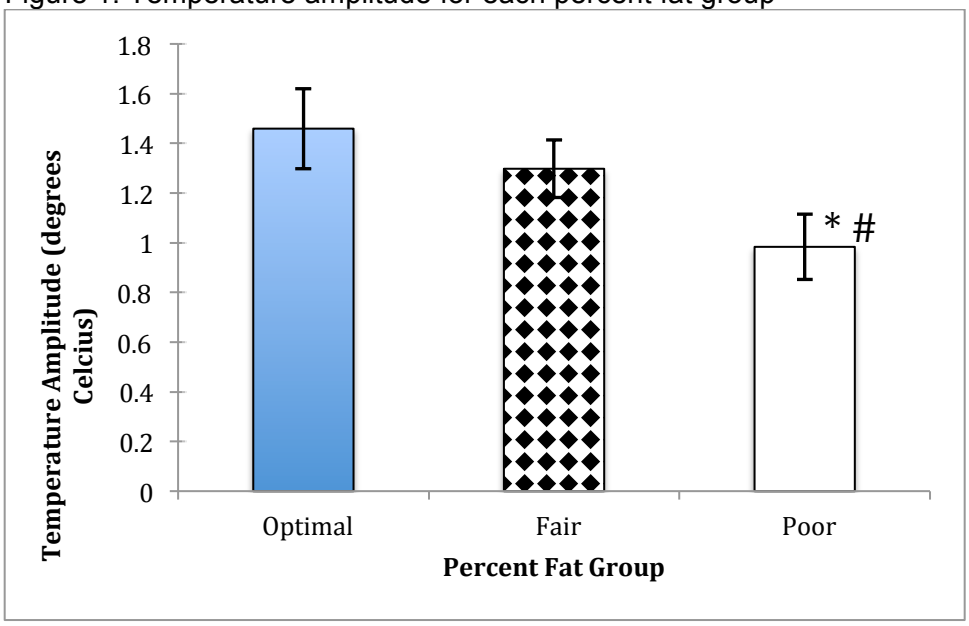
* significance at $p < 0.05$. Average steps, miles, MVPA (time spent in moderate to vigorous activity), and average last time eating all computed with a minimum of four days of data. Skipped breakfast, lunch and dinner and late night eating computed from seven days of data. $^{\Delta}$ indicates n= 52 (17 Optimal %Fat; 17 fair %Fat; 18 poor %Fat group).

Table 5: Correlation values for each study variable with temperature lag in optimal, fair, poor, and total group of participants.

Temperature Lag				
	Optimal (n=18)	Fair (n=20)	Poor (n=21)	Overall (n=59)
Waist Circumference (cm)	-0.254	0.182	0.281	-0.076
Abdomen Circumference (cm)	-0.264	0.174	0.259	-0.088
Hip Circumference (cm)	-0.275	0.264	0.335	-0.170
Systolic Blood Pressure (mmHg)	-0.323	0.137	0.028	0.038
Diastolic Blood Pressure (mmHg)	-0.188	-0.15	0.111	0.070
Average Sleep (hours/night)	0.00	0.159	-0.135	0.182
Sleep Variance	0.165	0.197	-0.200	0.123
Chronotype	-0.089	-0.098	0.199	0.024
Average Steps (steps/day)	-0.376	-0.151	-0.364	-0.151
Average Miles (miles/day)	-0.512*	-0.188	-0.321	-0.130
Average MVPA (minutes/day)	-0.051	0.062	-0.191	0.069
VO_2 peak (ml/kg/min)	0.457	-0.358	-0.295	0.150
Fat (%)	-0.206	-0.444	0.321	-0.069
Fat Mass (g)	-0.350	0.209	0.262	-0.099
Mineral Free Lean Mass (g)	-0.382	0.440	0.101	-0.122
Fat Free Mass (g)	-0.386	0.447	0.093	-0.125
Skipped Breakfast (number/week)	0.129	0.006	0.104	0.043
Skipped Lunch (number/week)	0.496*	-0.348	0.109	0.110
Skipped Dinner (number/week)	0.176	0.250	-0.300	0.083
Late Night Eating (number/week)	-0.052	-0.213	-0.119	-0.028
Average last time eating (time/day)	-0.146	-0.245	-0.409	-0.074
Cholesterol (mg/dL) $^{\Delta}$	0.101	-0.420	-0.270	-0.135
HDL (mg/dL) $^{\Delta}$	-0.075	0.312	0.562*	0.242
Tot Cholesterol/HDL $^{\Delta}$	0.182	-0.377	-0.521*	-0.298*
LDL (mg/dL) $^{\Delta}$	0.185	-0.595*	-0.406	-0.212
Triglycerides (mg/dL) $^{\Delta}$	-0.323	0.033	-0.374	-0.191
Metabolic Syndrome Factors $^{\Delta}$	-0.173	0.227	-0.209	-0.118

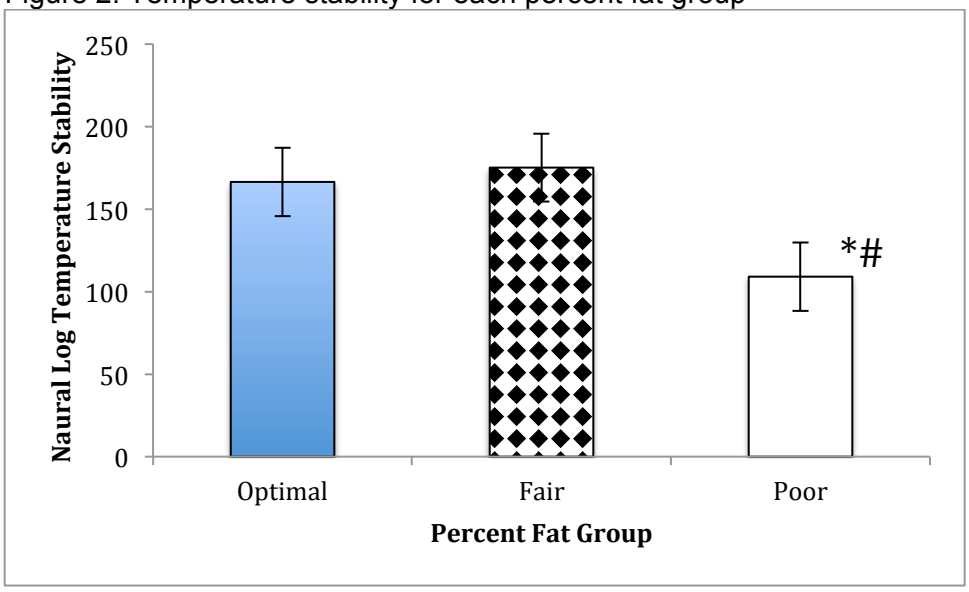
* significance at $p < 0.05$. Average steps, miles, MVPA (time spent in moderate to vigorous activity), and average last time eating all computed with a minimum of four days of data. Skipped breakfast, lunch and dinner and late night eating computed from seven days of data. $^{\Delta}$ indicates n= 52 (17 Optimal %Fat; 17 fair %Fat; 18 poor %Fat group).

Figure 1: Temperature amplitude for each percent fat group



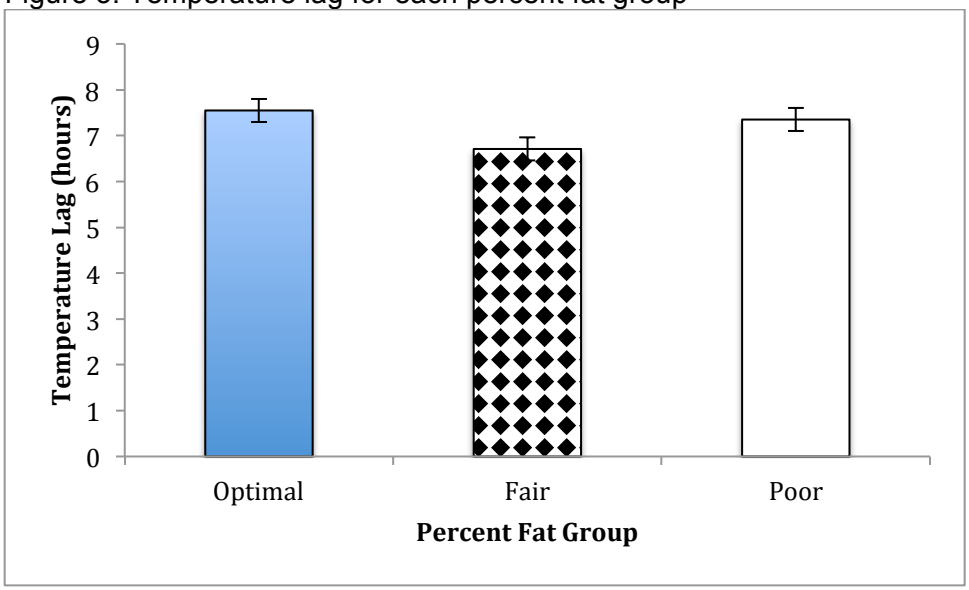
Mean ± SE for optimal group (percent fat ≤ 18.0; n=18), fair group (percent fat 18.1 to 23.9; n=20) poor group (percent fat ≥24.0; n=21).
* significance at p<0.05 versus optimal group
# significance at p<0.05 versus fair group

Figure 2: Temperature stability for each percent fat group



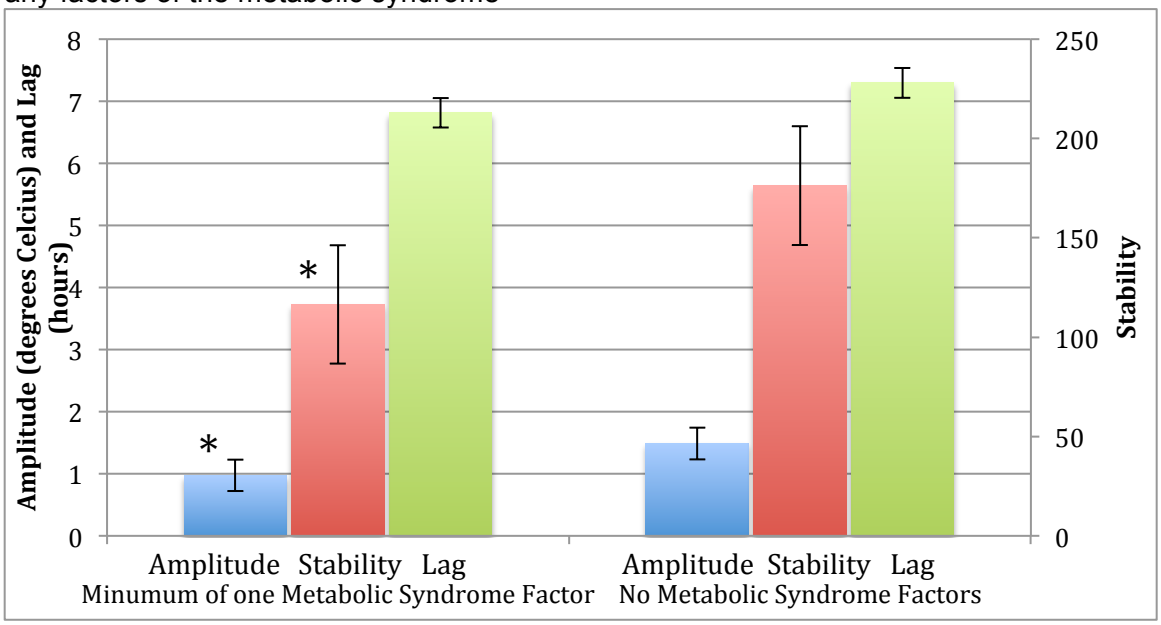
Mean ± SE for optimal group (percent fat ≤ 18.0; n=18), fair group (percent fat 18.1 to 23.9; n=20) poor group (percent fat ≥24.0; n=21).
* significance at p<0.05 versus optimal group
# significance at p<0.05 versus fair group

Figure 3: Temperature lag for each percent fat group



Mean ± SE for optimal group (percent fat ≤ 18.0; n=18), fair group (percent fat 18.1 to 23.9; n=20) poor group (percent fat ≥24.0; n=21).
* significance at $p<0.05$ versus optimal group
# significance at $p<0.05$ versus fair group

Figure 4: Temperature amplitude, lag, and stability for participants with versus without any factors of the metabolic syndrome



Participants with a minimum of one factor of metabolic syndrome (n=22) versus participants without any metabolic factors (n=30). The group with at least one metabolic syndrome factor had one of the following criteria: waist circumference > 94cm, triglycerides ≥ 150 mg/dL, systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85mmHg, HDL ≤ 40 mg/dL. Values are represented as means ± standard error.
* significant versus group with no metabolic syndrome factors at $p < 0.05$.

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